DIRECT-TO-CONSUMER ADVERTISING OF PRESCRIPTION DRUGS

EFFECTS ON PRESCRIBING AND POLICY IMPLICATIONS

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A THESIS SUBMITTED IN PARTIAL FULFILMENT OF
THE REQUIREMENT FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN

THE FACULTY OF GRADUATE STUDIES

Department of Health Care and Epidemiology, Faculty of Medicine

We accept this thesis as conforming
to the required standard

THE UNIVERSITY OF BRITISH COLUMBIA

June, 2003

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ABSTRACT

The United States and New Zealand are the only industrialized countries that allow direct-to-consumer advertising of prescription medicines (DTCA). Spending on this form of pharmaceutical promotion has grown rapidly within the last decade, and national governments – including the Canadian government – are under strong pressure from the industry to relax current restrictions on prescription drug advertising aimed at the public.

DTCA is highly controversial, with many claimed beneficial and harmful effects, and often little empirical evidence to back those claims. The aim of this thesis is to move the policy debate on DTCA beyond competing claims, to a better understanding of what is and is not known about the effects of this form of pharmaceutical marketing on health and health care services. It consists of four components: a critical review of the empirical literature; a patient-doctor survey examining the effects of DTCA on prescribing decisions in primary care; a historical overview and discussion of international policy developments; and an opinion survey of pharmaceutical policy experts in Canada in sectors likely to be affected by DTCA.

The original research component was a comparative cross-sectional survey in 78 primary care physicians' offices, involving 1431 patients, in Sacramento, California, and Vancouver, British Columbia. DTCA is expected to have the greatest impact in primary care, both because of the types of drugs that are advertised and because this is where most prescribing occurs. The unit of analysis was a matched set of patient and physician questionnaires covering a single consultation. The primary hypothesis was that patients in Sacramento, in an environment with full legal DTCA, would request and receive more advertised drugs than patients in Vancouver, where DTCA is illegal, but where there is exposure to cross-border advertising. Additionally, patients in each setting with higher individual self-reported advertising exposure were hypothesized to request more advertised medicines than patients with lower exposure.

Patients in the two samples had similar demographic and socio-economic characteristics. Exposure to DTCA was higher in Sacramento, but 90% of Vancouver patients had seen

DTCA. In general, Sacramento patients were more likely to request medicines: 15.8% of Sacramento patients requested new prescriptions vs. 9% in Vancouver (OR = 2.0; 95% CI 1.3-3.1). They were also more likely to request advertised drugs: 7.3% of Sacramento patients vs. 3.2% in Vancouver (OR=2.2; 95% CI 1.2-4.1). Patients with higher self-reported advertising exposure, conditions potentially treatable by advertised drugs, and/or greater reliance on advertising requested more advertised medicines.

Approximately three quarters of the patients who requested advertised drugs in both settings received prescriptions. The prescribing rate did not differ between the two samples. In both settings, physicians were often ambivalent about treatment choice, rating a drug they had prescribed as a 'possible' or 'unlikely' choice for other similar patients, versus a 'very likely' choice. They expressed some degree of ambivalence for 50.0% of new prescriptions for advertised drugs requested by patients vs. 12.4% of new prescriptions not requested by patients ($p<.01$). Ambivalence was nearly as high if patients had requested non-advertised drugs; most of these were in problematic drug classes, in terms of patient pressure: antibiotics, anxiolytics/hypnotics, and analgesics.

These results suggest a negative effect on prescribing appropriateness. They add to a body of empirical evidence indicating that costs to the public, to the patient-doctor relationship and to publicly financed health care services are likely to outweigh any potential benefits. From a public health perspective, there is little justification for the introduction of DTCA. However, this appears to be a highly successful marketing strategy, and thus pressure for legalization is likely to continue. National policy discussions are remarkably similar in different jurisdictions, with the pharmaceutical and advertising industries strongly supporting introduction, and health professional associations, private and public payers and consumer associations generally opposed. A similar division was observed in the survey of policy experts in Canada. Results were highly polarized, with most respondents from outside the pharmaceutical and advertising industries judging information quality to be poor and effects on health care quality to be negative.

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Abbreviations

ANZA	Association of New Zealand Advertisers
APMA	Australian Pharmaceutical Manufacturers' Association
CMA	Canadian Medical Association
CPMP	Committee on Proprietary Medicinal Products, European Union
DDMAC	Division of Drug Marketing, Advertising and Communications of
the U.S.	Food and Drug Administration
DTCA	Direct-to-consumer advertising of prescription drugs
FDA, U.S. FDA	United States Food and Drug Administration
FTC, U.S. FTC	United States Federal Trade Commission
GAO, U.S. GAO	United States General Accounting Office (research agency for the U.S. Congress)
G.P.	General Practitioner
IFPMA	International Federation of Pharmaceutical Manufacturers' Associations
MedSafe	New Zealand's national drug regulation agency (within the New Zealand Ministry of Health).
OECD	Organization for Economic Cooperation and Development
OTC	Over-the-counter; drugs for which no prescription is needed.
NZMA	New Zealand Medical Association
PAAB	Pharmaceutical Advertising Advisory Board, Canada
PBM	Pharmacy Benefit Manager
PHARMAC	Pharmaceutical Management Agency Ltd. of New Zealand
PhRMA	U.S. Pharmaceutical Manufacturers' Association
RMI	Researched Medicines Industry of New Zealand
Rx&D	Canada's Research-based Pharmaceutical Industry Association
TAAS	Therapeutic Advertising Advisory Service, New Zealand
TAPS	Therapeutic Advertising Pre-vetting Service, New Zealand

Acknowledgements

Many people contributed to this study. First, I would like to thank to my committee for all of their support. Morris Barer assisted with every step in the study conceptualisation, design, and review of drafts, as well as dealing efficiently – and imaginatively – with the inevitable and often seemingly insurmountable barriers that arose along the way. Joel Lexchin beat all records with the speed, efficiency and care with which he commented on drafts, as well as his depth of knowledge on pharmaceutical promotion. Ken Bassett raised the more fundamental questions about what I was trying to research and why, as well emphasizing the analysis of the strength and quality of evidence. Bob Nakagawa contributed expertise in pharmaceutical management and policy development.

I would like to thank Mary-Doug Wright for her help with development of database search strategies for the literature review, Diane Helmer for her work on the fugitive literature search, and Michelle Mozel for retrieval of many hundreds of articles.

Members of an Expert Advisory Panel Members provided assistance with design and questionnaire development for the patient-doctor survey: Wendy Armstrong, Consumers' Association of Canada; Alan Cassels, Canada Drug Guide Project; Jean-Pierre Grégoire, University of Laval; Matthew Hollon, University of Washington Physicians; Patricia Kaufert, University of Manitoba; Joel Lexchin, York University; Bob Nakagawa, Simon Fraser Health Region, B.C. Ministry of Health; Nancy Ostrove, U.S. FDA; Richard Pollay, Division of Commerce, U.B.C., and Ingrid Sketris, Dalhousie University.

Thanks also to Robert Woollard for his assistance with Vancouver physician recruitment and review of the physician questionnaire, and Steve Marion for his help with the data analysis. Richard Kravitz and Richard Pan managed the Sacramento arm of the survey; it was a very fruitful collaboration not only in terms of survey implementation, but also discussions on design and analysis. Thanks as well to Sara Lu Vorhes and Valerie Olsen who coordinated the Sacramento survey, and to the research assistants who administered

the survey in both cities: Amit Ahuja, Danielle Lapointe and Michael Tsang in Vancouver, and Christine Choi, Vanphen Chanthalangsy, Min H. Ku, Laura Shively, Erica Stranger, Nicollet Knopf, Bryan Faulstich, Karry Nagai and Meridith Cobari in Sacramento. Alicia Mintzes entered the data in Vancouver, Nhue L. Do in Sacramento.

Without the generous assistance of the physicians and patients who participated in this study in Vancouver and Sacramento, as well as physicians' office staff, this study would not have been possible.

A number of people also assisted with information on international DTCA policies: Rachel Wilson and Wayne McNee of PHARMAC, and Dee Richards and Les Toop of the University of Otago, New Zealand; Kit Aikin and Nancy Ostrove, U.S. FDA; Margaret Ewen, HAI-Europe; Charles Medawar, Social Audit U.K.; and Danielle Bardelay, *la Revue Prescrire*, France; Peter Mansfield, Healthy Skepticism, in Australia.

Jean-Pierre Grégoire, Olaf Koester, Ross Duncan, and Diane Helmer provided suggestions of individual and organizations to contact for the survey of pharmaceutical policy experts in Canada, and Anne-Marie Nicol helped with survey administration.

This study was funded by Health Canada, as part of a project to assess the potential impact of direct-to-consumer prescription drug advertising on the Canadian health system. I also received funding through fellowships from the University of British Columbia (Graduate Research Fellowship), the National Health, Research and Development Program (NHRD), and the Canadian Institutes of Health Research (CIHR).

Finally, I would like to thank my father, Joseph Mintzes, for his many suggestions that I pursue a post-graduate degree.

Chapter 1

Introduction

In October 2001, just over a month after the attack on the World Trade Centre, Glaxo SmithKline (GSK) ran an ad for the antidepressant Paxil (paroxetine) in the *New York Times* magazine. A woman is walking down a crowded street, her face strained, in a crowd otherwise blurred, with symptoms running across the photo: 'worry, muscle tension, sleep problems, anxiety, fatigue, etc.' For those living in New York who may have witnessed the attack on the twin towers or who feared another attack at any time, such symptoms were an understandable response. For GSK, they were clearly a market opportunity.

On the other side of the Atlantic, Novartis was urging the Dutch to visit their doctors if they had signs of toenail fungus, as a treatment was now available. According to the Dutch Health Inspectorate, visits for toenail fungus surged from an average of two patients per month to 20 per week.[1] In March 2002, a group of Dutch general practitioners called on their colleagues to boycott the company, angered by the call on patients to visit their doctors for such a trivial and benign condition.[2] The Dutch government had previously taken Novartis to court for this campaign, arguing that the company was illegally advertising its prescription drug terbinafine (Lamisil) to the Dutch public. The case was unsuccessful because the company had not stated the name of the product in the advertising campaign.

An uneasy alliance exists between medicine and the marketplace. Nowhere is this more evident than in the recent controversies surrounding direct-to-consumer advertising of prescription drugs (DTCA). Aggressive advertising campaigns such as those described above are accused of selling not only medicines but also the idea of a pill as a magic solution to everyday life problems, blurring distinctions between illness and health.[3] A commentary in the *British Medical Journal* referred to this process as "disease-mongering", or aiming to convince the healthy that they are ill. [4] Critics fear that they

will lead to unnecessary and inappropriate drug use, and create strains on the doctor-patient relationship.[5] On the other hand, proponents describe these ads as a means of ensuring that those who need care find out that there is a treatment available and obtain help at an earlier stage, avoiding more serious disease complications.[6] An added bonus is that these ads may help patients overcome social taboos. Pfizer's ads for sildenafil (Viagra), for example, are credited with making it possible for men to talk to their doctors about impotence. Ads for fluoxetine (Prozac) and paroxetine (Paxil) have been credited similarly with helping patients with anxiety and depression to feel less isolated and to discuss these problems more freely with physicians.

These hypothesized effects of DTCA reflect conflicting assumptions about the nature of pharmaceutical advertising and of consumer and physician responses to advertising messages. DTCA is a recent, rapidly growing, phenomenon and, as such, its effects have not been well studied. Many claimed outcomes of DTCA, both beneficial and harmful, are based on little or no research evidence.

The United States and New Zealand are the only industrialized countries in which prescription drug advertising aimed at the public is legal. Other countries, such as Canada, the countries of the European Union and Australia, forbid DTCA as a health protection measure. If a product has prescription-only status, manufacturers can neither sell nor advertise it directly to the public. Drug sales are forbidden unless accompanied by a physician's prescription; advertising may only be directed at health professionals. The rationale is that these products are prescription-only for a reason: they generally have greater toxicity and/or a less well-understood toxicity profile than over-the-counter drugs, and they usually treat health conditions that are not easily self-diagnosed or self-managed.

Canada and the European Union also forbid the advertising of treatments for specified lists of serious diseases. In Canada, this list encompasses a broad set of conditions, ranging in severity from anxiety disorders and sexual impotence to septicaemia, heart disease and cancer.[7] In this case, the rationale is linked to the condition rather than the

product, reflecting the greater vulnerability of those seeking treatment for troubling and serious illnesses, as compared to consumers who are seeking a new television set or pair of shoes, for example.

In the U.S. and New Zealand, national legislation covering prescription-only status is silent on the issue of the target audience for advertisements for prescription-only drugs. No legislative decision was made to introduce DTCA, but the industry traditionally only targeted health professionals in promotion of prescription-only products. In fact, prescription drug companies were referred to as "ethical" manufacturers during the late 19th century and much of the 20th century because they did not advertise their products to the public.[8] This marketing technique was introduced during the early 1980's in the U.S. and the 1990's in New Zealand. If the rate of increasing industry investments into DTCA is any measure of its success, it is a highly profitable form of marketing. Between 1996 and 2000, spending on DTCA in the U.S. more than tripled.[9] Heavily advertised drugs have also been found to contribute substantially to increases in prescription volumes and retail drug expenditures. [10]

It is within the context of recent growing industry pressure for the introduction of DTCA that Canada,[11] the European Union,[12] and Australia [13] have carried out legislative reviews and have considered whether DTCA should be allowed. New Zealand, on the other hand, carried out a review considering whether to restrict or ban the practice, linked in large part to concerns about the effects of DTCA as a cost driver. [14]

1.1 DTCA evaluation: the strength of evidence and burden of proof

In an announcement of the final version of a regulatory guidance that opened up U.S. television and radio to full DTCA, the U.S. Food and Drug Administration (FDA) stated that, "Despite years of print DTC advertising, no rigorous evidence has been presented to demonstrate that DTC advertising has had any of the hypothesized ill effects." [15] The agency failed to state that no rigorous evidence of effects of any sort, positive or negative, had been presented. Absence of evidence appears to have been taken as

evidence of absence of deleterious effects. In the U.S. context, where protection of free speech is paramount, this is not particularly surprising.

In Canada, and elsewhere where DTCA is currently forbidden, the interpretation of such gaps in evidence is likely to be quite different. Canada currently bans prescription drug advertising to the public as a health protection measure. The assumption behind this prohibition is that such advertising is not in the public interest because it is potentially unsafe and/or will have a deleterious effect on the provision of health care services. If legislative change to introduce DTCA is being considered, evidence is needed that this assumption is false. From a public health perspective, two key questions frame this discussion:

- Are there documented health benefits from DTCA?
- Is there sufficient evidence to exclude the possibility of harm?

Controversy over the evidence concerning the effects of DTCA has been in the forefront in the recent policy debate over its introduction. In order to move beyond a labyrinth of opposing assertions, the types and strengths of evidence available need to be examined, as well as their adequacy in measuring stated outcomes.

This is very similar to reviews of evidence on outcomes of medical interventions that are carried out for health technology assessments. David Hadorn discusses the need for policy-makers to make decisions about access to new types of care, often in the face of incomplete, flawed or conflicting evidence.[16] Hadorn argues that a strong parallel exists between such policy decisions and the treatment of evidence within the legal-judicial system. He supports the need for explicit, formal rules of evidence, guiding both the *admissibility* and *relevance* of evidence, as occurs within a courtroom.

In a courtroom, evidence is admissible only if it is relevant to the decision under consideration. For an evaluation of DTCA, research evidence is *relevant* only if the intervention being measured is clearly identified as prescription drug advertising aimed at the public. Thus for example the effects of consumer medicines information would fall

outside the scope of such an examination, given that the intervention in question is not advertising. Although this may seem obvious, discussions of DTCA sometimes blur such distinctions. For example, a review article states that: "They [physicians] also find that the ads promote a sense of empowerment among patients, which they insist is crucial for achieving faster, more successful outcomes." [17] Given the lack of research on whether or not advertising exposure empowers patients, the author may be attributing the effects of other types of interventions, such as patient education, to advertising.

In a courtroom, certain types of evidence may be *relevant* but not *admissible,* such as illegally obtained evidence or hearsay. A similar approach requires formal rules for the types of evidence considered admissible, stated explicitly before an evaluation is undertaken. Two key factors should guide admissibility of evidence:

- The type of outcomes that are measured;
- The validity of the scientific basis of the evidence.

Measured outcomes

Within the context of health technology assessment, Hadorn insists on the need for evidence concerning hard outcomes, such as mortality, morbidity, disability and pain or other symptoms, when evaluating a health intervention, as opposed to evidence only on intermediate physiological outcomes that a patient cannot directly feel, such as changes in haemoglobin, blood sugar level or bone mineral density.

Serious health outcomes are among the hypothesized effects of prescription drug advertising aimed at the public. The objective of health protection laws prohibiting DTCA is to prevent unnecessary harm from inappropriate prescription drug use, as well as to ensure that patients who are seriously ill receive needed care. Similarly, proponents of DTCA claim an effect on 'hard' clinical outcomes, such as fewer deaths or hospitalizations if DTCA leads to earlier treatment of otherwise untreated health problems.

However, advertising differs from a medical treatment, in that the intervention in question aims to influence care-seeking behaviour and medicine use, rather than being a direct medical therapy. Thus a link between exposure to DTCA and health outcomes requires an understanding of how DTCA affects care-seeking behaviour and medicine use. Additionally, the characteristics of DTCA, such as advertising content, types of advertised medicines and health conditions, determine potential outcomes.

Paralleling discussions of the need for active comparators versus only placebo-controlled drug trials when decisions are taken about which of a range of available treatments are to be financed, DTCA may not be the only 'drug information intervention' available to meet stated goals. The question then becomes how advertising compares to other options as a means for example of educating the public about available drug treatments.

Opinion surveys cannot provide the type of evidence needed to assess the impact of DTCA, as the link between opinions about an intervention and its potential effects on health or use of health care services is tenuous at best.

Validity of scientific evidence

The strength of evidence to support specific interventions reflects the body of available research, including study design and execution. Rating scales for study design place large randomized controlled (RCT's) trials or meta-analyses of RCT's highest, followed by smaller RCT's, cohort studies, case-control studies, uncontrolled case series or case reports, with expert opinion generally trailing last.[18] Key to the strength of evidence, however, is not only study design but methods and quality control measures used to avoid bias, such as testing the adequacy of randomization or blinding in an RCT.

Another way to examine the strength of scientific evidence for outcomes of DTCA is in terms of whether or not a causal association has been established. Epidemiological criteria for causation, such as those developed by Bradford Hill, [19] provide a useful framework to examine claimed outcomes of DTCA:

- Is the association **consistent**? (Has it been replicated in different settings?)

- What is the **strength** (or effect size) of the association?
- Is it **specific** to DTCA?
- Has a **dose-response relationship** been observed?
- Does exposure precede the outcome? (Is the **temporal relationship** correct?)
- Is the relationship biologically plausible? (For DTCA, associations would be judged in terms of **economic plausibility**.)
- Is the association **coherent**, compatible with existing theory and knowledge (Does it reflect known effects of other forms of pharmaceutical promotion, for example?)
- Is it supported by **experimental** evidence? (Can it be altered through experimentation?)

As is described in Chapter 2, much of the available evidence on DTCA is best described as cursory, incomplete and flawed, with the exception of studies of the content and quality of U.S. print advertising. In most cases a causal association between DTCA and hypothesized outcomes is yet to be established.

In courts of law, decisions must often be made without adequate evidence. Governments facing pressure to introduce pharmaceutical advertising are in a similar position. The question then becomes where the *burden of proof* should lie and what *standard of proof* is needed. [16] Thus a new health intervention would either be considered 'innocent until proven guilty' or 'guilty until proven innocent' depending on where the burden of proof was placed.

In its statement on lack of evidence of harm, the U.S. FDA clearly placed the burden of proof on opponents of DTCA to show that this intervention is sufficiently harmful to warrant restrictions.[15] Interestingly, this was in the context of introduction of a new form of DTCA – broadcast advertising containing limited risk information – a situation in which manufacturers might have been required to provide evidence of benefit. New Zealand's Ministry of Health, similarly, concluded a policy review in 2001 without

introducing new legislation, citing a lack of conclusive evidence of harm, in spite of an earlier statement by the Health Minister that a ban or restrictions were likely.[20]

The situation faced politically by countries that allow DTCA, as compared to those that do not, is similar to that faced by governments deciding whether to require market withdrawal of a medicine versus initial introduction. Manufacturers are required to provide evidence of sufficient safety to warrant introduction; for a market withdrawal, the burden of proof of harm rests with health authorities.

In terms of a *standard of proof* to be considered sufficient to warrant the introduction of DTCA, Hadorn suggests a general principle for new medical interventions that is also applicable to DTCA, that they be "reasonably well demonstrated to provide substantial net benefit to the patients who receive them." [16] For DTCA this also means a net benefit to the health care system: extra pharmaceutical costs should only be incurred if they have been shown to lead to greater savings elsewhere, or to better service quality.

A strong parallel exists between this framework and the application of the *precautionary principle* to policy decisions concerning health and environmental risks. This is one description of the precautionary principle: "When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically."[21] In a discussion of how this approach can be applied to preventive public health policy, Tickner identifies four central components:

- the idea that in the face of uncertainty, action should be taken to prevent harm
- a shift in the burden of proof onto those proposing activities that are potentially harmful to public health
- exploration of a broad range of alternative actions (in the case of DTCA, this might include alternative means to provide consumer drug information)
- a commitment to public participation in decision-making.[21]

Reliance on the precautionary principle is sometimes contrasted with a 'science-based' approach to risk assessment.[22] This falsely suggests that proponents of the precautionary principle ignore the available evidence. Instead, the key difference between approaches is in the way existing scientific evidence is interpreted, not only in terms of the degree of attention paid to scientific uncertainty, but also in the weighting of different outcomes. Within a precautionary approach, potential harm to public health trumps other outcomes, including economic development and private financial gain.

Influences on policy development

As suggested above, research evidence is only one of many influences on policy development, and barriers often exist to research uptake in policy decisions. Willison and McLeod discuss the theoretical foundations of the role of evidence in policy development, with specific reference to pharmaceutical policy.[23] They identify three models most often cited in the literature: the rational model, the incrementalist model and the mixed scanning and normative optimal model.

The *rational* model assumes a linear relationship from problem identification to policy formulation, implementation and evaluation. Policy-makers choose the option most consistent with their objectives from among a broad selection of researched options. This idealistic model omits the pressures facing policy-makers, the context of often ill-defined problems and conflicting goals, and the historical weight of past policy decisions.

The *incrementalist* model gives greater weight to the process by which decisions are made and the existence of constraints on this process. It suggests that usually a limited range of options are considered, differing only marginally from existing policies, and that negotiation between interest groups plays a key role. Research evidence is more likely to have a cumulative, indirect effect as the weight of a specific body of evidence grows, than a central direct effect.[24]

The *mixed scanning and normative optimal model* occupies a middle ground between these two poles. Policy makers are expected to superficially explore different policy options and focus on a few options seen to be viable. This allows for more than incremental policy options to be implemented when a window of opportunity exists.

Historically, the implementation of modern drug regulation following the thalidomide disaster could be seen as such a window of opportunity, in which the policy move towards an expanded role for regulation of pharmaceuticals had legitimacy, could be feasibly implemented, and enjoyed strong public support. In contrast, the lack of implementation of a systematic national post-market surveillance system in Canada by the beginning of the 21st century, in spite of greatly improved technical capacity for such surveillance, would be an example of an *incrementalist* approach to policy-development, in which the discussion of policy options is strongly limited by historical precedent.

This model is highly relevant to any comparison of DTCA policy development in different jurisdictions, as well as to differences in judgements about the same body of evidence on outcomes of DTCA. Although no laws have been passed as yet to introduce DTCA where it is not allowed, those countries whose laws did not explicitly prohibit this form of advertising (the United States and New Zealand), are now facing very different policy decisions than countries with explicit prohibitions in place. In other words, historical precedent appears to have a strong influence on policy development.

However, a fundamental question remains about why governments in several jurisdictions have put forward proposals to introduce DTCA. As is described in Chapter 2, the evidence to back claims of health benefits from DTCA is largely lacking in spite of nearly 20 years of experience with print DTCA in the U.S., and all of the evidence thus far on cost impacts suggests that DTCA leads to higher rather than lower health care costs. Why then would national governments in several jurisdictions be considering legislative change to introduce DTCA? Is this a reflection of conflicting roles of national governments to promote economic development as well as ensuring public safety and

access to health care? Are needed jobs being lost because of unnecessary prescription drug advertising restrictions?

In a commentary on the pharmaceutical industry as a 'political player', John Abraham [25] suggests that the key factor leading to a shift in pharmaceutical regulatory standards during the latter part of the 20th century and early 21rst century cannot be employment. He points out that the relative strength or weakness of regulation has little impact on employment within the pharmaceutical sector in comparison to the dramatic effects of company mergers. Instead, he suggests that the pharmaceutical industry has ceased being "merely a commercial entity", and is becoming instead, "a political player keen to shape the standards and processes defining regulation." Although Abraham was primarily examining the drug approval process, his analysis of industry influence over drug regulation is also highly relevant to policy discussions on DTCA. He describes a process of 'regulatory capture' leading to a shift in the purpose of regulation, with the interests of the regulated industry coming to dominate the perspective of regulatory agencies over and above those of patients and citizens.

In a commentary on the relationship between research and policy development, Jonathan Lomas points out that policy-decisions are strongly influenced by who has a voice at the table, and the values they bring to decisions, including ideologies, normative beliefs and interests (financial or otherwise).[26] In Canada controversies surrounding the potential introduction of DTCA reflect not only differences between private and public sector interests, but also differing priorities among various levels of government. The federal government is responsible for the regulation of pharmaceuticals, including the enforcement of regulations concerning pharmaceutical advertising and prescription-only status. Provincial governments are responsible for administration of health care services, including most public drug benefit plans. This division of responsibility has helped to shape policy discussions on DTCA in Canada.

Canadian DTCA policy: an identified need for research evidence

Health Canada hosted the first multi-stakeholder consultation on DTCA in June 1996, at which time provincial governments expressed concerns about the potential effects on provincial pharmaceutical budgets.[27] In May 1998, during a second round of discussion of potential legislative change, the Federal/Provincial/Territorial Advisory Committee on Health Services' Pharmaceutical Issues Committee requested that Health Canada fund research, "to investigate the issue of DTCA, and identify the impact on health and safety issues, as well as how it affects drug utilization." [28] This request was actioned by Health Canada, in the form of a Request for Proposals (RFP), issued in the summer of 1999.

The research carried out for this dissertation was funded by Health Canada in response to that RFP. It additionally develops the empirical and documentary analysis within a 'determinants of health care utilization' framework. This study examines not only how DTCA affects health and health care services, but also uses the case of DTCA to explore more broadly the type of evidence needed to inform health policy when a shift in health protection law is being considered. Of particular interest is where the burden of proof should lie in the face of uncertainty about potential benefits and harms and in the context of significant information gaps, as well as what standards of evidence might be considered sufficient to indicate that DTCA is "reasonably well demonstrated" to provide substantial net benefits.

1.3 Research focus and thesis roadmap: prescribing in primary care

This thesis contains of two main components. The primary analysis examines how DTCA affects prescribing decisions. This includes a review of empirical research on DTCA, and a patient-doctor survey in primary care settings, where DTCA is expected to have the greatest impact on prescribing decisions. The secondary analysis examines how DTCA is regulated, including a history of policy development and a comparison of experience in different jurisdictions. The aim is to place the primary empirical research on DTCA carried out for this thesis within a broader context of the historical growth of this form of pharmaceutical advertising, as well as broader societal concerns that help to frame

discussions of DTCA policy. This section includes a survey of pharmaceutical policy experts working within a variety of sectors of Canadian society affected by DTCA.

Primary analysis: how does DTCA affect prescribing?

DTCA targets people who cannot directly buy the advertised product. If this advertising is to stimulate sales, patients must request and obtain prescriptions from their doctors. Empirical research is needed to assess the effects of DTCA on prescribing decisions, the patient/doctor relationship, and ultimately on health outcomes and overall health care costs. The largest impact is expected within primary care because this is where most prescribing occurs, and most advertised products treat common conditions.[29]

The key component of this study was a comparative cross-sectional survey of patients and physicians, carried out in primary care physicians' offices in Vancouver, B.C., and Sacramento California. The aim of this survey was to examine the effects of DTCA on patient requests for medicines and prescribing in two primary care settings: a Canadian setting where DTCA is not allowed, but exposure to cross-border and partial advertising exists; and a U.S. setting where DTCA is allowed and public exposure is widespread. I hypothesized that in a setting with full, legal DTCA, patients would request and receive more advertised medicines from their doctors. I also hypothesized that in both settings individual self-reported advertising exposure and reliance on advertising would be associated with more requests for advertised medicines. The unit of analysis was a matched set of patient and physician questionnaires covering a single consultation. This design makes it possible to distinguish between prescriptions initiated following a patient request and those solely initiated by the physician.

Chapter 2 reviews the empirical evidence on the effects of DTCA on health and health care services, based on evidence from the U.S. and, to a lesser extent, from New Zealand (where there is little published systematic research). The main questions addressed in this literature review are whether there is evidence of benefits to health and the quality of health care services from DTCA, or sufficient evidence to exclude the possibility of

harm. In other words, has DTCA been reasonably well demonstrated to provide substantial net benefit to health and health care services?

The aim of the literature review is to provide an overview of current knowledge on the effects of DTCA, as well as key gaps in knowledge. This overview provides a context for the decision to carry out a comparative patient-doctor survey in primary care, given the lack of empirical studies on primary care prescribing decisions in response to patient-directed advertising.

Chapter 3 contains a review of the key methodologies for examining DTCA suggested by other researchers, and describes the background to the conceptual framework used in this study. Following from gaps in knowledge on the effects of DTCA identified in Chapter 2, how should DTCA research be carried out? In order to frame this question, I review the literature on social influences on prescribing, including studies that examine the influence of patients' desires for prescriptions (and physicians' perceptions of those desires) on prescribing decisions. Research on the effects of physician-directed pharmaceutical promotion on prescribing decisions also provides important background to any investigation of the effects of patient-directed pharmaceutical promotion. The chapter concludes with description of methodological approaches to DTCA research that have been recommended by other researchers, as well as a discussion of the strengths and weaknesses of these approaches.

The framework I have used for the comparative patient-doctor study builds on Andersen and Newman's behavioural model of health care service utilization, which provides a context for examining patients' decisions to request advertised drugs.[30] Advertising is expected to be one of a range of influences on patients' decisions to seek medical care. Andersen and Newman's model, originally developed to examine barriers to access to health care services, allows for modelling of the impact of DTCA within the context of individual and environmental influences on patterns of use of health care services. Chapter 4 describes the framework and explains its application in the doctor-patient study.

Chapter 5 describes the survey methods and results, and implications of the findings. The aim of this survey was both to compare two policy environments, one with and one without legal DTCA, and to examine the association between patient self-reported advertising exposure and reliance on commercial information sources, and behaviours influenced by advertising (requests for prescriptions for advertised drugs). An additional aim was to examine the influence of patient requests on prescribing patterns and on physicians' confidence in treatment choice.

Secondary analysis: DTCA policy development

Policy decisions on DTCA are highly politically charged, and any examination of the evidence on outcomes of DTCA inevitably returns to the political context in which this evidence will be judged. National governments with a commitment to meeting their populations' health needs are struggling with decisions about introducing changes to pharmaceutical advertising laws, often with conflicting pressures from private sector interests and public health care service providers and funders.[31 32] DTCA is highly contentious because of the likelihood that already rising pharmaceutical costs will become unsustainable, in other words will exceed available public financing through tax revenues, chiefly because of increased prescribing of new, expensive drugs. On the other hand, the pharmaceutical industry is highly profitable and national governments are conscious of the need to support industrial development. The U.S. experience with DTCA suggests that it is a very effective marketing strategy, creating strong pressures for liberalization from those private sector interests.

Chapter 6 examines policy development on DTCA in the U.S., New Zealand, Canada, Australia, the European Union, and South Africa. This includes both jurisdictions that currently have legal DTCA, and jurisdictions where legislative change to introduce DTCA has been considered. In Canada, shifts in the interpretation and enforcement of the law since 1999 have created a *de facto* partial introduction of DTCA, albeit without formal regulatory or legislative change. In addition to describing the historical background to the current policy debate on DTCA, Chapter 6 explores contentious areas

that fall outside of the field of health care service utilization, but help to shape the broader social context for DTCA policy, including legal concerns. The chapter concludes with a discussion of DTCA as a form of consumer drug information, as many commentators have suggested that advertising plays this role. I use a case study of a U.S. radio ad for esomeprazole (Nexium), a proton pump inhibitor used in the treatment of gastro-oesophageal reflux disease, to compare DTCA content to consumer drug information standards.

Chapter 7 reports the results of an opinion survey of pharmaceutical policy experts in Canada working in federal and provincial government, the pharmaceutical and advertising industries, health professional associations, and patient and consumer groups. The aim is to examine how opinions on the likely effects of pharmaceutical advertising on the quality and cost of health care services concur or differ by sector, as well as how pharmaceutical policy experts working in affected sectors believe that DTCA should be regulated in Canada. Canada's position is unique among countries where DTCA is illegal, both because of the degree of exposure to cross-border advertising and the liberal national approach to enforcement. This contradictory environment provides a backdrop to discussions about legal change to introduce DTCA.

How does this research contribute to knowledge about the effects of DTCA?

Chapter 8 concludes the thesis, with a summary of key research findings and their implications for DTCA regulatory policy in Canada and internationally. The main focus is on the results of the patient-doctor survey and their contribution to knowledge about the effects of patient-directed pharmaceutical advertising on prescribing decisions in primary care.

In 1988, before DTCA had become widespread in the US, Dr. Eric Cohen warned in a *New England Journal of Medicine* editorial that:

> "... if direct advertising should prevail, the use of prescription medication would be warped by misleading commercials and hucksterism. The choice of a patient's medication, even of his or her physician, could then come to depend more on the

attractiveness of a full-page spread or prime-time commercial than on medical merit..."[33]

Such advertising has since prevailed in the United States, New Zealand and – to a lesser extent – in Canada. Has the 'attractiveness of a full page spread or prime time commercial' begun to drive the choice of patients' medication? If so, what are the implications for the quality of health care services and patient health? By focussing on patient requests and prescribing decisions within primary care, this study aims to fill a key gap in research evidence on the effects of prescription drug advertising.

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Chapter 2: Literature Review

Direct-to-Consumer Advertising of Prescription Drugs: What do we know about its effects on health and health care services?

2. 1 Introduction

The United States and New Zealand are the only industrialized countries that allow direct-to-consumer advertising of prescription medicines (DTCA). Spending on DTCA in the U.S. has grown rapidly, from U.S. $55.3 million in 1991 to $340 million in 1995,[1] $1.8 billion in 1999,[2] and $2.5 billion in 2000.[3] Since late 1997, when the U.S. Food and Drug Administration (FDA) eased restrictions on broadcast advertising,[4] spending on television advertising has increased most rapidly. Although on the whole the pharmaceutical industry still spends far more promoting its products to physicians than to the public, the balance has shifted toward DTCA for specific products. For example, in 1998 the industry spent U.S. $706.9 million advertising ten products to the public, as compared to U.S. $494.2 million spent advertising the same products to physicians.[5]

Although DTCA is not currently allowed under Canada's Food and Drug Act, the federal government is considering legislative changes to introduce it as part of a broader process of legislative renewal.[6] The European Union has also begun policy discussions on whether to legalize DTCA.[7] Additionally, Canadians are exposed to cross-border prescription drug advertising via U.S. television, radio, magazines and the Internet, as well as to a range of 'patient education promotional activities' in Canada, such as disease-oriented advertisements, toll-free telephone numbers, information materials distributed by company-funded organizations, media reports generated by company-sponsored press conferences, and public meetings.[8]

The aim of prescription drug advertising is unequivocally to increase sales. Lisa Basara, senior market research analyst for Rhone Poulenc, states it succinctly: "Prescriptions for

the advertised product are the ultimate goal of the DTCA campaign."[9]

It is the 'side effects' of this advertising that are under discussion: what is its impact on individual and public health, on the appropriateness or inappropriateness of pharmaceutical use resulting from DTCA, on the patient/doctor relationship and on overall health care costs? The policy debate over whether advertising of prescription drugs to the public should be allowed in Canada hinges on much speculation about these side effects; to date, there have been many claims, often contradictory, but little evidence.

From a public health perspective, a reorientation in health policy would be expected to lead at best to better health outcomes, at worst to no deterioration in public health. Therefore, two key questions frame this discussion:

- Are there documented health benefits from DTCA?
- Is there sufficient evidence about potential harmful effects to exclude the likelihood of harm from a policy change to introduce DTCA?

This framework presumes that the burden of proof should lie with proponents of a policy change to remove current health protection measures prohibiting DTCA, to show that evidence exists of a net benefit from prescription drug advertising aimed at the public, over-riding potential harmful effects. As was discussed in Chapter 1, not only should the magnitude of observed benefit exceed observed harm, but the research evidence must be of adequate strength and quality to ensure replicability, to avoid biases in data collection, analysis or reporting that would compromise study validity, and to confirm that the appropriate interventions and outcomes are measured.

Rather than limiting this review to a small subset of studies with the strongest methodology, I have used broad inclusion criteria (see below) and discuss the strength and limitations of results for each category of studies. My rationale is that this approach provides a better understanding of conflicting claims about outcomes of DTCA than would be possible with stricter inclusion and exclusion criteria.

This literature review examines the existing evidence on the effects of DTCA, based in large part on the existing 'natural experiments' of legal DTCA in the U.S. and New Zealand. This experience cannot provide an exact picture of what DTCA might look like in Canada. However, it provides an overview of what is known about the effects of prescription drug advertising to the public on health and the health care system.

Objectives

The aim of this review is to synthesize the available literature on:

- The effects of DTCA in the U.S. and New Zealand on physician visits; prescribing decisions; prescription drug use; use of other health care services; and health outcomes;
- The types and classes of products advertised to the public thus far, types of health conditions and population groups affected, and the likely contribution to therapy;
- Assessments of the quality of DTCA and the information conveyed to the public on risks and benefits of pharmaceuticals in print and broadcast advertisements.

2.2 Methods

A search was carried out in electronic databases covering the period from January 1980 to January 2000. The following databases were searched: Medline, Embase, CINAHL, Healthstar (medicine and health sciences); Current Contents (general); Lexis-Nexis (law); CBCA (Canadian Business and Current Affairs), PAIS, Econlit, ABI-Inform (economics, business and marketing).

Appendix 2.1 lists core search strategies used for health, economic and business databases. Title and abstract lists were then hand sorted and all relevant references retrieved. Additionally, bibliographies of key review articles were checked for additional references.

Additionally, 1997, 1998 and 1999 issues of the pharmaceutical industry weekly trade bulletin *Scrip (*and monthly *Scrip Magazine*) were hand searched to cover the period leading up to and following the U.S. FDA relaxation of regulations governing broadcast advertising. Along with press releases from the pharmaceutical market research companies IMS Health and Scott-Levin, *Scrip* reports were used as an information source on spending, sales data, and regulatory issues related to DTCA. The U.S. FDA web site was consulted for additional regulatory information. A librarian skilled in fugitive literature searches carried out an Internet search for unpublished reports on U.S. and New Zealand DTCA, and relevant organizations were contacted for full reports as required. Additionally, reports of research on DTCA were retrieved if they were mentioned on an international pharmaceutical policy list serve (e-drug).*

The U.S. General Accounting Office (U.S. GAO) carried out a systematic review of research on DTCA covering the period from 1984 to 1990.[10] This included a thorough search for empirical research assessing outcomes of DTCA and critical appraisal of the methodology employed in this research. Given the rigour of the U.S. GAO review and the limited experience with DTCA prior to 1990, this review mainly focuses on empirical research carried out from 1991 to 2001. The U.S. GAO review is summarized in section 2.3.1.

An initial version of this review was completed in January 2000. A follow-up database search was carried out in health, medical and business databases in June 2001, using the same search strategy as previously, in order to obtain any published empirical studies that may have been missed. In the period from June 2001 to January 2003, further empirical studies of DTCA were retrieved if identified through two publication news services: weekly *Ingenta Search Alerts* (articles with 'consumer', 'advertising' or 'DTCA' in their titles), and *Medscape*, as well as bibliographies of recent review articles. Additional

* For a description of this list serve, see: http://www.essentialdrugs.org/index.php.

studies available only in the fugitive literature were obtained through follow up of news reports, postings on e-drug until January 2003, and contacts with experts in DTCA policy.

In the period to January 2000, all references on DTCA identified through computerized bibliographic and fugitive literature searches were retrieved in full (N=565). In the follow-up period to January 2003, all titles and abstracts were examined, but references were only retrieved in full if they were judged to potentially meet study inclusion criteria (see below), or were review articles (in order to check bibliographies), or news reports on DTCA campaigns or policies. (N=119) I was solely responsible for all judgments about whether or not inclusion criteria had been met, as well as data extraction, without blinding to study results.

Study inclusion criteria:

- Empirical studies measuring health, behavioural and/or knowledge outcomes, provision, use and/or quality of health care services, and/or effects of DTCA on health care costs;
- Analyses of advertising content and volume;
- Published and unpublished studies with methodology described in enough detail to allow evaluation of results (description of sampling methodology, population from which the sample was drawn; survey methods and outcome assessment).

Study exclusion criteria:

- Studies based on convenience samples that are unlikely to be representative of a larger population group; sample selection tied to assessed outcomes and therefore likely to lead to bias (example: physician survey left behind by a pharmaceutical sales representative);
- Studies that fail to include prescription drug advertising among assessed interventions;
- Surveys with unacceptably low response rates (<25%) that have failed to check for systematic differences between respondents and non-respondents;

- Editorial commentaries or opinion surveys only (no health, behavioural, knowledge, health care service use, cost or information quality outcomes assessed).

2.3 Background

2.3.1 U.S. General Accounting Office 1991 review

The U.S. General Accounting Office (U.S. GAO) carried out a systematic review of the empirical research on DTCA from 1984-1990.[9] The results of their review of outcomes research are briefly described below, followed by a review of the empirical research from 1991-2001.

The aim of the U.S. GAO review was to find out what was known about the effects of DTCA, both positive and negative, and U.S. consumer and physician attitudes about DTCA, and to identify gaps in research evidence. A computerized literature search was carried out, as well as hand searches of bibliographies and contacts with organizations to obtain unpublished reports.

Hypothesized outcomes of DTCA

108 non-empirical studies suggested 39 possible consequences of DTCA. Table 2.1 lists the main hypothesized benefits and risks of DTCA, most of which the U.S. GAO found to be untested.

Table 2.1 Hypothesized Consequences of DTCA: U.S. General Accounting Office, 1991

Benefits	Harm
Educational value	Misleading nature of promotional materials
Improvement in physician/patient relationship	Damage to physician/patient relationship
Support for consumers' right to information	Inability for consumers to understand technical information
Lower prices	Higher prices
Increase in regularity of physician visits	Waste of physicians' time
Increase in patient compliance	Pressure by patients on physicians to prescribe
Support for advertiser's first amendment rights	Overmedication and drug abuse

* Adapted from Table II.2 Benefits and Detriments of DTCA Cited in Non-empirical articles.

Although in total more than 120 articles and reports were collected, only four empirical studies were found assessing outcomes of DTCA and meeting minimum methodological standards to guard against selection and reporting biases. Two of these were part of a single study carried out by FDA researchers, and two assessed different aspects of communication of information in ads. Thus in total three studies had assessed two main outcomes:

- whether patients would pressure their doctors for drugs in response to advertising; and
- whether risk information could be communicated in advertisements.

Results of empirical studies

1. Will patients pressure doctors to prescribe? No conclusion

Perri and Dickson[11] studied a non-random sample of 200 patients in Georgia who were scheduled to see their doctors for periodic checkups or physical exams. They were mailed print ads for hypothetical drugs 10 and 3 days before the scheduled visit. Usable responses were available for 94 of the 200 (47%). Of these, 70% could remember seeing the ads, 11% could name the product, and 8.5 % asked their doctor about the drugs. Only four doctors participated in the study and they did not report pressure to prescribe. However, the small sample of doctors and of patient requests made it impossible to draw conclusions from this study.

2.a. Can risk information be communicated? Yes, but presentation matters.

2.b. Do consumers remember and understand information in ads? Yes, mostly

U.S. FDA researchers[12] carried out a study showing fictitious TV and magazine ads to 1509 of 6100 randomly selected members of the public in four cities: Cleveland, Buffalo, Seattle and Houston (25% response rate). Respondents did not differ significantly in age, race or marital status from 1980 U.S. census data. However, they tended on average to be older and better educated. The authors varied the amount of risk information provided (two or four items) and the emphasis and degree of integration of risk information, as well as the amount of detail provided. For example, in some ads a generic warning was provided, in others drug-specific information.

The amount of risk information remembered increased with the amount presented and was higher for the fictitious print than TV ads.[13] The exception to this was 'full disclosure' (i.e. FDA required labelling information in fine print, which accompanies all prescription drug advertisements). Respondents' knowledge did not differ significantly whether they saw full disclosure ads or ads with no risk information, indicating that this fine print labelling is a poor means to communicate drug risks to the public. Viewers of TV ads, women, older people and those living in the three cities other than Seattle were more likely than others to say that they would ask their doctor for a drug in response to advertising. Seattle subjects also tended to be more sceptical of advertising, of physicians, and of their own ability to evaluate the truthfulness of ads than other respondents. The authors suggest that there may be underlying cultural differences in the Northwestern U.S. fostering general scepticism, but caution that this is speculative.

The FDA study also included questions testing retention of specific information contained in the fictitious ads. Understanding was generally considered acceptable: most advertising points could be recalled and only 5-20% were misunderstood.

A second study by Tucker and Smith[14] in a shopping mall tested four formats for risk information. Respondents reported feeling more reassured by the ads containing no risk information or only general risk statements. However, their attitude was more positive towards ads containing any amount of risk information than ads with no risk information.

Conclusions: many claimed effects; little research evidence

The U.S. GAO concluded that the available research did not provide an adequate basis to determine the effects of DTCA. Most of the hypothesized outcomes of DTCA were untested; the one test of patient pressure on physicians was inconclusive and not broadly generalizable. The U.S. GAO also reviewed opinion surveys and found that no credible studies permitted conclusions to be drawn about the extent to which consumers and physicians supported or opposed DTCA or the effects of exposure on attitudes.

The two studies of consumer responses to differing risk information presentation did provide results of potential importance to regulators. For example, the FDA found that the fine print 'brief summary' information, which includes the risk portion of product labelling, did not add to public knowledge.[†] This makes intuitive sense, given that this labelling information is written in medical language for physicians. The font size may also be too small for many elderly people to read with comfort. Additionally, different media and presentation of risk information were found to affect public attitudes towards the product and awareness of risks.

2.3.2 Hypothesized outcomes of DTCA: 1991 to 2001

The U.S. GAO uncovered many claims about the effects of DTCA, both positive and negative, but little research evidence to back those claims. How did things change in the intervening decade? Table 2.2, below, lists hypothesized positive and negative consequences collected from the non-empirical publications included in this review, including hypotheses specific to policy discussions in Canada. Many are similar to those identified in 1991. They are effects on:

- Drug utilization
- The doctor/patient relationship
- Consumer knowledge and education
- Health outcomes
- Health care service utilization, costs and public/private mix of health services
- Broader social outcomes, and legal issues.

When the U.S. GAO reviewed the research evidence on outcomes of DTCA to 1990, little empirical evidence existed on the effects of DTCA. Since 1990, spending on DTCA and public exposure to this form of advertising in the US, and increasingly in Canada, has grown enormously. However, most hypothesized outcomes remain untested.

[†] These findings did not lead to regulatory changes in requirements for format or content of risk information.

Table 2.2: Hypothesized Benefits and Risks of DTCA: 1991 – 2001

BENEFITS	RISKS
DRUG UTILIZATION	
More appropriate use of medicines, saving lives and improving the quality of life	Inappropriate demand for medicines and/or a demand for inappropriate medicines.
Better compliance	More 'off-label' drug use
Risk information in ads will lead to better recognition and reporting of adverse reactions	Risk information in ads will lead some patients not to take needed medicines.
THE DOCTOR/PATIENT RELATIONSHIP	
Empowers patients to take care of their own health, encourages active partnership with doctors and debate.	Actively disrupts the therapeutic alliance between patients and doctors; encourages 'doctor shopping' to obtain a prescription, pressures doctors to prescribe
Helps patients to initiate discussions, improves communication	Doctors' time is wasted disabusing patients of misinformation.
	Creates consumer demand for specific products.
CONSUMER KNOWLEDGE AND EDUCATION	
Educates and informs patients about medicines	Ads may confuse patients into believing that inconsequential differences represent major therapeutic advances.
'Made in Canada' ads would reflect Canadian product labelling, lead to less confusion.	
HEALTH OUTCOMES	
Leads to earlier symptom recognition, improving treatment outcomes	Exaggerates disease risks and promotes anxiety: "To what extent does ill-health result from fear of ill-health, loss of confidence and personal autonomy." [15]
Higher treatment rate among patients with undertreated conditions, improving outcomes.	Greater harm may result from widespread use of new drugs before their risk profile is well known.
Leads to better drug treatment outcomes through an enhanced placebo effect.	Distortions in care provision because of a focus on specific conditions linked to marketing; targets people with mild symptoms who may not need care.
Brings patients in to doctors who can then be screened for serious diseases; such as erectile dysfunction and prostate cancer screening.	
HEALTH CARE SERVICE UTILIZATION, COSTS AND PUBLIC/PRIVATE MIX	
By promoting drug use, reduces costs for surgery and hospitalization	Higher overall health care costs through use of new, expensive drugs instead of lower cost alternatives.
Lower public drug costs because patients pay for heavily advertised drugs out-of-pocket	Higher drug prices to pay for expensive ad campaigns.
TV ads are an egalitarian form of health information provision as they reach the poor.	Promotes unsustainable demand, promoting inequality in access to health care services.
BROADER SOCIAL OUTCOMES	
Helps remove the social stigma of certain diseases.	Creates unrealistic expectations of drugs, e.g. Prozac "certainly does not make the sun shine on an otherwise miserable life."[16]
Helps patient groups; raises disease awareness	Takes advantage of extra vulnerability of the ill
	Targets vulnerable population groups: negative impact on children & adolescents; on women.
	Increased medicalization of healthy life stages
LEGAL ISSUES	
Freedom of commercial communication	Increases legal liability for manufacturers, weakening the learned intermediary defense.[‡]
Freedom of information	Infringement of personal privacy because individual health records become valuable to marketers.

[‡] The learned intermediary defense protects companies from liability for drug-induced injuries if they provide adequate warning of potential harmful effects to physicians (the 'learned intermediaries'), who must in turn inform their patients.

2.4 Results of computerized database and fugitive literature searches

The aim of this literature review was to obtain an overview of known outcomes of DTCA on patient health, knowledge, use of health care services and health care costs. The following types of empirical studies were included:

- analyses of the content and accuracy of advertisements;
- consumer surveys of advertising exposure, opinions and behaviours (both actual and hypothetical);
- health professional surveys of opinion, experiences and behaviours;
- retrospective data analyses on advertising spending, prescribing, sales and related use of physician services.

New Zealand has a shorter and less extensive experience with DTCA than the US.[17] Thus most of the retrieved articles describe and evaluate experiences with U.S. advertising. In the initial database and fugitive literature search carried out in late 1999 and early 2000, 565 references relevant to DTCA were retrieved. In the follow-up period to January 2003 an additional 119 articles were retrieved (N=684).

Of these 684 articles, 49 empirical studies, described below, met study inclusion criteria. These studies assessed patient health, knowledge and/or behavioural outcomes, advertising content and quality, and effects on prescribing volume and/or shifts in drug utilization and cost, as well as meeting minimum methodological requirements. The 49 studies include 10 studies of advertising information content and quality, three regulatory reviews also examining information quality, 25 consumer surveys, two health professional surveys, and nine retrospective data analyses examining spending on DTCA, prescribing patterns and drug sales.

Studies were excluded if they did not adequately describe methodology. Description was judged to be adequate if it included the population from which a sample was drawn, sample selection techniques, and a description of any interventions, data gathering procedures and analysis. Additionally, studies were excluded if a sample selection

method associated with the anticipated outcome was used, increasing the likelihood that the estimate would be biased.[§]

Six of the 25 consumer surveys used sample selection methods unlikely to be broadly generalizable to a regional or national population. They were included because they relied on sampling strategies that attempted to minimize bias and were independent of measured outcomes.

There were few health professional surveys with adequate methodology. Only one published study of physicians adequately described methodology, sampled randomly, and obtained a reasonable response rate, 48%.[18] However, this study was carried out before the 1997 FDA regulatory change leading to higher broadcast DTCA exposure. A second survey, with a 46% response rate, has only had key findings published through a power point presentation posted on the Internet.[19] Two other health professional surveys were excluded because they had less than 25% response rates [20 21]

[§] In one example, only a subset of patients continuing on therapy for at least six months were surveyed, with no follow-up of people who discontinued earlier and no information provided on the proportion continuing, rendering measures of compliance and satisfaction with treatment meaningless.

2.4.1 Advertising Information Content and Quality

Table 2.3 below provides an overview of studies of DTC advertising content and quality.

Table 2.3: Studies of DTCA Content and Quality (N=10)

Study	Main outcomes assessed	Methodology	No. of ads
Television ads			
Lipton, 2002	▪ frequency of English & Spanish TV ads ▪ targeted drugs ▪ types of ads ▪ measures of educational value	▪ 360 hours of TV videotaped (prime time & daytime) ▪ 2 coders (kappa=0.90) ▪ educational value (presence or absence of information on condition and drug)	322 (58 brands)
Waxman, 2002	▪ accuracy and balance of risks and benefits in U.S. broadcast ads ▪ types of advertised products and conditions	▪ FDA information and videotape of broadcast ads, August 2001-2002 ▪ Four independent expert assessors	74 ads (28 brands)
Lill and Peterson, 2001	▪ Age group of patients portrayed in TV DTCA and OTC drug ads ▪ Favourable or unfavourable portrayals of young and elderly adults	▪ In 1998, 10 random days/ month, 16 hours/day, 3 networks, 1 local, 6 cable ▪ No duplicate ads included ▪ 2 coders (kappa=0.93)	639
Print ads			
Woloshin et al, 2001	▪ advertising frequency and product type ▪ content, types of advertising claims ▪ incentives for drug use	▪ all ads in 10 magazines, 7 issues each, July 1998-9 ▪ no duplicates;	67
Bell et al, 2000	▪ characteristics of drugs and associated diseases ▪ advertising frequency ▪ advertising claims ▪ incentives for drug use	▪ all drug ads in 18 consumer magazines, 1989-1998 ▪ magazines market leader in category; ▪ two judges independently coded ads , reliability high	320
Bell et al, 2000a	▪ educational value of print advertising, ▪ defined as whether 5 key pieces of information on the treated condition and 6 on the product were present or absent.	▪ same 10 year sample of ads as above	320
Pinto 2000	▪ frequency of ads ▪ types of conditions treated ▪ content analysis of emotional appeals ▪ key messages	▪ 1996-1998; 12 types of magazines; 2/class; 2 issues / magazine (n=48) ▪ two independent judges; reliability high	58
Parker and Delene 1998	▪ characteristics of drugs and associated diseases ▪ advertising frequency ▪ type of ads	▪ 384 issues of 8 most popular monthly magazines were reviewed, 1992-1995 ▪ tabulation of types of ads, products and diseases	110
Roth 1996	▪ characteristics of drugs and associated diseases ▪ fair balance of risk & benefit (as per FDA criteria) ▪ presence or absence of specific types of information	▪ content analysis of ads ▪ pharmacist judges; 2 reviewers/ad ▪ inter-rater reliability 0.95 ▪ standardized coding ▪ >90% of print ads, 1993-95	39
Consumer Reports 1996	▪ accuracy, fair balance; ▪ usefulness of ad to the consumer	▪ content analysis of ads ▪ panel of 32 medical specialist ;2-3 per ad; ▪ ads from recent leading U.S. magazines	28

Television advertising

Lipton, 2002

This is an unpublished conference presentation of an analysis of U.S. television advertising.[22] The aim was to compare frequency and educational content of English and Spanish language ads. A total of 360 hours of prime time and daytime TV programming was videotaped on ABC, CBS, Telemundo and Univision during two separate months.

Nearly all ads were in English (99%); therefore the analysis was confined to English ads: 318 ads, representing 58 brands and 28 conditions, were found within the 180 hours of English programming. This is an average of 1.8 ads per hour. Repeat broadcasts of the same ads were included in the analysis according to the number of times they were shown. The most frequent indications were allergy, high cholesterol, asthma, menopause/osteoporosis, arthritis, depression, obesity and ulcer.

Among the 318 ads, 80% made no mention of non-pharmacological approaches to treatment; 84% provided no risk information related to having the condition, and 92% did not include information on prevalence or incidence of the condition. No single ad mentioned all three factors. The accuracy of the information provided was not assessed.

Waxman 2002

A U.S. Congressional office (Henry Waxman, Democrat from California) undertook a review of U.S. broadcast DTCA in September 2002. The context was a precipitous drop in FDA enforcement actions following the introduction of a new administrative policy in November 2001 requiring the FDA's Division of Drug Marketing, Advertising and Communication (DDMAC) to send regulatory letters to the legal department of Health and Human Services before sending them to the company. [23] DDMAC provided background information on televised DTCA for this investigation, including a videotape containing 74 of the 225 ads submitted between August of 2001 and August of 2002. The sample was selected by DDMAC staff to include a range of advertised products (n=28) and campaigns initiated from December 2001 onwards.

Table 2.4: Broadcast ad campaigns: Aug 2001 to Aug 2002 (Submissions to FDA)

Product	Indication	Total no. of ads	Full Product Claim	Reminder	Help Seeking
Celebrex (celecoxib)	Arthritis	22	12	10	
Flonase (fluticasone)	Allergy	17	11	6	
Zyrtec (cetirizine)	Allergy	14	12	2	
Vioxx (rofecoxib)	Arthritis	13	4	6	3
Singulair (montelukast)	Asthma	13	11	2	
Viagra (sildenafil)	Impotence	13		13	
Clarinex (desloratadine)	Allergy	10	8	2	
Zocor (simvastatin)	Lipid lowering	10	6	4	
Fosamax (alendronate)	Osteoporosis	10	10		
Advair Diskus (fluticasone/salmeterol)	Asthma	9	9		
Differin (Adapalene)	Acne	8	8		
Imitrex (sumatripan)	Migraine	8	6	2	
Detrol LA (tolterodine)	Overactive bladder	8	8		
Zoloft (sertraline)	Antidepressant	6	6		
Lipitor (atorvastatin)	Lipid lowering	6	4	2	
Allegra (fexofenadine)	Allergy	5	5		
Paxil (paroxetine)	Antidepressant	5	4	1	
Valtrex (valacyclovir)	Antiviral/herpes	5	5		
Ditropan XL (oxybutin)	Overactive bladder	5	5		
Actonel (risedronate)	Osteoporosis	4	4		
Nexium (esomeprazole)	Ulcer/reflux	4	1	3	
Prevacid (lansoprazole)	Ulcer/reflux	4	3	1	
Altace (ramipril)	Hypertension	3	3		
Epipen (epinephrine)	Allergy/anaphylaxis	2			2
Prozac weekly (fluoxetine)	Antidepressant	2		2	
Lamisil (terbinafine)	Antifungal	2	2		
Diflucan (fluconazole)	Antifungal	2	2		
Denavir (penciclovir)	Antiviral	2	2		
Serevent (salmeterol)	Asthma	2	2		
Ortho Evra (norelgestromin/EE)	Contraceptive	2	2		
Wellbutrin (bupropion)	Antidepressant	1	1		
Sarafem (fluoxetine)	Antidepressant/PMDD	1			1
Aldara (Imiquimod)	Antiviral	1	1		
Ortho Tri-Cyclen (norgestimate/EE)	Contraceptive/ acne	1	1		
Avandia (rosiglitazone)	Diabetes	1		1	
Protopic (tacrolimus)	Eczema	1	1		
Prempro (CEE/medroxyprogesterone.)	HRT	1		1	
Ambien (zolpidem)	Hypnotic	1	1		
Sum (N=38 products)		**224**	**160 (71%)**	**58 (26%)**	**6 (3%)**

Source: DDMAC, September 2002 [unpublished; response to question from Waxman's office]

As shown on Table 2.4, 38 products were advertised in broadcast media for 19 broad indications during the one-year time period from August 2001 to August 2002. This is a list of newly initiated advertising campaigns, as companies must submit ads to the FDA when they are first broadcast. Over half of the ads were for 10 products Most TV ads were full product claim ads, including both a product's brand name and health claims. About one-fourth were reminder ads, which mention a product's brand name but not the indication, and are not required by U.S. law to include any risk information. These tended to be concentrated among the most heavily advertised products. Only 3% were help-seeking ads, which mention only a disease and not a brand. There are also not required by law to include risk information.

Waxman's office asked four researchers to review a videotape of 74 ads, a subset of the 224 ads listed in Table 2.4. They were not informed of each other's identities and thus the reviews were carried out independently. The aim was to judge the quality of advertisements, in terms of accuracy and balance of benefit and risk information. Two of the reviewers, Michael Wilkes and myself, summarized the findings in letters, which were posted on the web:

Reviewer 1 (Wilkes):

"The advertisements I reviewed contained numerous problems (errors, omission or misleading statements/images) and . . . as a group they are often intended to mislead a consumer about the drug's effectiveness or the seriousness of their medical condition (creating fear and concern over conditions that are ordinary and have no impact on quality or quantity of life") . . . I am also bothered by drugs that insinuate or actually claim they are better than other drugs or classes of drugs where there is no data to support such a claim."[24]

Reviewer 2 (Mintzes):

"[T]he advertisements consistently treat benefit and risk information differently, in ways that tend to minimize even the relatively brief statements of major risks required by the FDA guidance on broadcast advertising. They also fail to provide key information allowing viewers to obtain a realistic sense of how effective a product is or how it compares to other treatment options . . . I would question whether they are consistent with the aim of regulatory requirements for a fair balance of benefit and risk information in pharmaceutical advertisements and accurate representation of product characteristics."[25]

Of the 74 ads, 69 were full product ads and 5 reminder ads. Thirty-one of the full product ads (45%) used techniques such as a faster voice, louder background music and distracting images during risk information provision; 14 (20%) only mentioned limits to efficacy in a printed statement, not the voice-over; and 9 (12% of total) offered financial incentives such as free trials.

All four reviewers independently judged an ad for zolpidem (Ambien), a hypnotic, to be inaccurate. The ad stated that, "Patients who abuse prescription drugs may become dependent," whereas approved labelling states that anyone can become dependent, regardless of abuse history. Three of the four reviewers found that an ad for penciclovir (Denavir) misleadingly implied superior efficacy, and three of the four reviewers judged that the efficacy of tolteridone (Detrol) had been misrepresented.

This was a subjective preliminary analysis of advertising accuracy, rather than a formal study. Therefore findings are provisional. It is included mainly because of the paucity of other data on television advertising. Additionally, sample selection by FDA staff was independent of the aims of the analysis, and reviewers assessed the ads independently.

Lill and Peterson 2001

This analysis of 1998 TV pharmaceutical ads examined the frequency with which older (65+) versus mid-age (45-64) and younger (<45) adults were depicted in advertisements, and the proportion of times these were favourable versus unfavourable depictions. The authors collected ads by randomly selecting 10 days/month for all of 1998, and recording 16 hours per day (8:00am to 12:00pm).[26] Three TV networks, one local and six cable channels were recorded. In total, this was 19,200 hours of television. A total of 1849 ads were found (~1 per 10 hours) but the text does not specify whether this is before or after duplicates were eliminated; 639 (35%) met study inclusion criteria.

The authors do not report the number or identity of advertised products or product classes. They included all commercials sponsored by pharmaceutical manufacturers. Thus

this study included both DTCA and OTC drug ads, without differentiating between these different types of ads.

Content analysis was used as a framework, and models were classified as being depicted in a positive or negative fashion according to pre-set categories. 'Positive' was defined as displaying mental and physical competence in carrying out roles portrayed in the ad; 'negative' as displaying mental or physical incompetence, including seeming uninformed, lazy, rejected, helpless, weak, or defeated. Coders assessed ads independently and inter-rater reliability was high, over 90% for most measures, including whether depictions were favourable or unfavourable.

Table 2.5: Age of model in ad versus favorable or unfavorable depiction

Age group of models in ads	# of ads	Depiction	
Ads in total*	639	Favourable	Unfavourable
Less than 45	343 (54%)	304 (89%)	39 (11%)
45-64	209 (33%)	167 (80%)	42 (20%)
65 +	87 (14%)	58 (67%)	29 (33%)
Products not age targeted*	259		
Less than 45	131 (51%)	117 (89%)	14 (11%)
45-64	96 (37%)	76 (79%)	20 (21%)
65 +	32 (12%)	19 (59%)	13 (41%)

* significantly less favourable with increased age; 2 x 3 table, p<.001 (chi square, 2 degrees of freedom)

Although the elderly use more pharmaceuticals than younger adults, they were less likely to be depicted in advertising, and if they were depicted, the image portrayed was more likely to be negative. This was the case for all of the ads, analyzed together, and for products not identified by the coders as being specifically age-targeted. The direction of effect was similar for products targeted to those 45 and under and those over 45. This study does not differentiate between OTC and prescription-only drugs. However, it does raise questions about one claimed benefit of DTCA, patient empowerment, as negative stereotyping of older people in advertising is unlikely to contribute to empowerment within this population group. The authors note that in spite of their focus on products frequently used by older adults, pharmaceutical ads appeared to maintain a trend described for other types of consumer advertising, of fewer depictions of elderly people, and a more negative presentation when they are depicted, as compared to younger adults.

This study is also consistent with earlier assessments of problematic depiction of the elderly in medical journals ads. Lexchin found that only 7% of ads in two major Canadian medical journals portrayed people who appeared to be over 65, and that the images and text in these ads could contribute to inappropriate prescribing in the elderly. [27] A review of ads for antidepressant and anti-anxiety drugs in a U.S. family practice and psychiatric journal found that both women and the elderly were strongly over-represented in these ads, even after accounting for higher disease prevalence rates in these population groups, potentially reinforcing existing social stereotypes. [28]

Print advertising

Woloshin et al., 2001

Woloshin et al. analyzed DTCA in 10 U.S. consumer magazines during a one-year period, July 1998-1999 (7 issues, or every other month, per magazine).[29] These magazines were selected by type of readership and distribution: four have >70% women readers; three > 70% men, and three target the general population. All were among the top five magazines in its category by circulation. Two independent coders analyzed advertising content. Inter-rater reliability was generally high (average kappa 0.81), and items with unacceptably low inter-rater reliability ratings (≤ 0.4) were excluded. There were three such items: overall focus of the ad, suggestions related to self-worth, and presentation of products as life enhancing.

Woloshin et al. found 67 unique ads (211 appearances in total, or around a mean of 3.1 times per ad). Two-thirds of the ads were for symptomatic treatments; around one fourth curative, and the rest (11%) for disease prevention. Thirty-eight products were advertised, of which two (5%) have since been removed from the U.S. market for safety reasons, troglitazone (Rezulin) and cisapride (Propulsid).

DTC ads appeared more often in women's magazines than men's or general readership magazines: median=4.5 versus two for men's magazines and one for general readerships,

p=.0001. Table 2.6 describes the most frequently advertised conditions and products.

Table 2.6:
Most frequently advertised products and conditions by target audience, 1998-1999

	Target audience for the magazine		
	Women	Men	General
Median no. ads/issue	4.5	2	1
Most frequently advertised products	Claritin: allergy Detrol: overactive bladder Renova: wrinkles Aricept: Alzheimer's	Propecia: Hair loss Crixivan: HIV Claritin: allergy Allegra: allergy	Claritin: allergy Viagra: impotence Detrol: overactive bladder Lymerix: lyme disease

Most ads (58, or 87%) described benefits only in vague, qualitative terms. Three main techniques were used:

- phrases such as 'clinically proven' or 'proven relief', without provision of evidence to back these claims, in 24%
- appeals to widespread use in 18% ("more than 1,000,000 people have begun using Rezulin to help manage diabetes")
- testimonials from patients (12%).

Only nine ads (13%) provided any evidence to support claims. Ads for two products included absolute rates of clinical outcomes for two products, finasteride (Propecia), a hair-loss drug, and tolteridone (Detrol), for overactive bladder. Risk information is required by FDA regulations, and thus 66 (98%) explicitly listed side effects; 34 (51%) also included quantitative information on frequency of occurrence.

Table 2.7 describes the key findings in terms of advertising content. The results raise questions about the educational and informative content of print advertising, particularly concerning efficacy and cost. Few ads included any explicit description of expected benefit, and vague, emotional claims were common. References to frequency of product use and testimonials cannot adequately inform treatment decisions. Many ads encouraged readers to suspect a medical cause for symptoms; and nearly one fourth included financial incentives. The results also suggest that regulatory standards strongly determine content. Explicit statements about major risks are required in advertising copy; no such

requirements exist for information on effectiveness.

Table 2.7: Advertising content, 1998-1999 magazine ads

Advertising content	No of ads (N=67)
Explicit description of any beneficial effects	9 (13%)
Explicit description of any harmful effects	66 (98%)
Emotional appeals	45 (67%)
Helps a person to get back to normal	*40 (60%)*
Focus on a feared outcome	*5 (7%)*
Encouragement of medical self-diagnosis (symptom lists, etc)	26 (39%)
Financial incentives (free trial offers or rebates)	16 (24%)
Product price stated	0

Bell et al, 2000

Bell et al. analyzed print DTCA in 18 U.S. consumer magazines over a 10-year period, 1989-1998 inclusive.[30] The magazines were chosen to represent a broad range of target audiences and to be market leaders in their category. The aim was to describe targeted conditions, advertising appeals, and any inducements offered. Two judges independently coded each advertisement. Inter-rater reliability was high (mean kappa =0.93).

They found 320 ads, for 101 brands treating 14 conditions, as outlined in Table 2.8. A dramatic linear increase in advertising frequency was observed over the decade, with only three new ads in 1989 versus 76 in 1998. The most frequent appeals were effectiveness (57%); controls symptoms (41%); innovative (41%); convenience (38%); disease prevention (16%); non-medicated effect (14%); psychological enhancement (11%); and 'safe' (11%). Most ads were gender neutral but women were 2.6 times as likely as men to be targeted in gender-specific advertising

Slightly less than one in five (17%) offered a monetary incentive such as a free trial offer to the reader for using the promoted drug. For some conditions, a large proportion of ads included such monetary inducements: 46% of allergy products, 41% of dermatologic products, and 67% of products for respiratory disease. The authors raised concerns about this trend: "We believe that such incentives may be inappropriate when issued to people who have not had a diagnosis of the indicated condition."

Table 2.8: Ads in 18 leading U.S. consumer magazines, 1989-1998

Condition	Number of ads	Number of products
Allergies	46 (14%)	8
Obstetric/gynaecologic	45 (14%)	10
Dermatologic	37 (12%)	12
Cardiovascular	36 (11%)	10
HIV/AIDS	33 (10%)	11
Tobacco addiction	23 (7%)	6
Urological	19 (6%)	8
Psychiatric/neurologic	17 (5%)	7
Muscoskeletal	17 (5%)	7
Gastrointestinal/nutritional	17 (5%)	7
Infectious (non-HIV)	16 (5%)	6
Diabetes	9 (3%)	4
Respiratory	3 (1%)	3
Cancer	2 (1%)	2
Total	**320 (100%)**	**101**

Bell et al, 2000a

A separate analysis was published of the educational content of the 320 ads described above.[31] The authors identified six key types of information patients need to know about a drug treatment in order to participate in informed decision-making, and five key types of information about the health condition it treats. These were identified a priori as factors that should be addressed in order to help patients to seek appropriate care for conditions that might otherwise be left undiagnosed and untreated. Two coders measured the presence or absence of this information in advertisements. Inter-rater reliability was very good (0.91, range 0.88-1.0).

The authors used a very low bar for educational content: whether not specific types of information were present or absent, not their accuracy, completeness, relevance to the target audience, or readability. As indicated by Table 2.9, however, most ads did not contain basic elements of information a person might need to judge the usefulness of a treatment, such as how a drug works, the likelihood of treatment success and what alternatives are available. Very few provided educational content on the treated health condition beyond its name and, in 60% of ads, one or more symptoms. The authors conclude that: "A time may come when DTC advertising is recommended for its educational value, but that day is not yet at hand."

Table 2.9: Educational content in 10 years of U.S.print DTCA

Does the ad mention?	Ads in 18 magazines 1989-1998 N=320
Drug treatment:	
The likelihood of treatment success	No, in 91% of ads
On average, how long a person needs to take the drug	No, in 89% of ads
How long it takes the drug to start to work	No, in 80% of ads
Other helpful activities, like exercise or diet	No, in 76% of ads
Any other possible treatments	No, in 71% of ads
How the drug works	No, in 64% of ads
Treated condition:	
The name of the condition	Yes, in 96% of ads
Any symptoms	Yes, in 60% of ads
Any myth or misconceptions debunked	No, in 91% of ads
Prevalence of the disease or condition	No, in 88% of ads
Any causes or risk factors	No, in 73% of ads

Adapted from: Figure 1, p 1095, Bell et al, 2000

Pinto 2000

Pinto carried out a content analysis of DTCA in a stratified random sample of 24 popular magazines (two issues per magazine), which appeared between 1996 and 1998. [32] After classifying magazines into 12 categories by target audience, the two magazines per category with the largest circulation were selected. All ads were included if they were over half a page in size.

Independent judges trained in content analysis assessed the types of emotional and informational appeals used. Products were classified according to the type of condition treated: chronic or acute, life-threatening or not, mental health, acute bacterial infection, life stage, or lifestyle choice. Inter-rater reliability was high (0.92 for drug class, 0.98 for type of appeal, 0.90 for message).

Ads for all drugs for high blood pressure, cholesterol and diabetes used fear appeals, as did all mental health drugs, 71% of ads for 'life change' drugs, and half of the life-style choice drugs. Guilt and fear appeals were generally made through text or both text and images. All sex appeals were visual. The authors did not find any statistically significant associations between the type of condition treated and type of emotional appeals used. However, their sample size was small in comparison to the number of categories.

Table 2.10: Magazine advertising frequency and content, 1996-1998

Number of ads in total in 48 magazines	N= 3028 (all products)
DTC ads (includes repeats)	84 (2.8%)
Unique DTC ads	58
Mean number of DTC ads per issue	1.75
Emotional appeals used	**N=58**
Fear	25 (43%)
Humour	18 (31%)
Guilt	5 (8.6%)
Sex	5 (8.6%)

Parker and Delene 1998

This is a study of eight monthly consumer magazines. All issues appearing between January 1992 and December 1995 were reviewed (384 issues).[33] The magazines were chosen for their high circulations and to capture a range of demographic groups likely to be targeted by DTCA. They were: *McCall's, Good Housekeeping, Mademoiselle, Better Homes and Gardens, Esquire, Popular Science, Reader's Digest* and *National Geographic.*

The frequency of ads per magazine issue increased by 44% between 1992 and 1995. The proportion of full ads, with product names and claims, increased from 63% in 1992 to 96% in 1995. A total of 473 advertisements appeared in the 384 magazine issues. These were based on 110 unique ads (average of 4.3 repeats per ads), mentioning 21 medical conditions. Nearly half of the ads (45.8%) were for drugs for three conditions: hair loss, menopause and allergy. Two of these are healthy aspects of ageing; the third is a relatively mild health problem. The content and accuracy of ads were not assessed.

Roth, 1996

Martin Roth asked a panel of pharmacists to analyze the content of over 90% of print direct-to-consumer ads published between 1993 and mid-1995.[34] Only full ads were assessed, i.e. those that contained both the product name and health claims. After eliminating duplicates, 39 ads were identified. The aim of this analysis was to assess both the types of drugs and diseases advertised and advertising content, judged in terms of the

U.S. FDA's criteria for fair balance of risk and benefit information. A trained panel of pharmacists evaluated the ads. Two pharmacists reviewed each ad; inter-rater reliability was nearly 0.95 (range 0.89-0.97).

Thirty-five percent of the ads (14) were judged not to contain a fair balance of benefit and risk information and 15% made no mention of risks in the advertising copy. This is in spite of U.S. FDA regulations requiring a fair balance of risk and benefit information in the advertising text. Most of the advertisements also omitted information on the potential for drug misuse (88%) and directions for proper use (58%).

TABLE 2.11: 1993-1995 Magazine ads: more than 75% treat 8 conditions

Condition	Number of ads	Number of brands
Allergy/ Antihistamine	7	4
Antihypertensive	4	3
Menopausal symptoms	4	3
Smoking cessation	4	3
Benign prostate enlargement	4	2
Acid/ulcer	4	1
Baldness	3	1
High cholesterol	2	1

In addition to the conditions listed in Table 2.11, the remaining ads included treatments for arthritis, acne, Alzheimer's disease, birth control, osteoporosis, and epilepsy. Most of the advertised products were indicated for chronic use; a few were for repeated intermittent use; and only one, used for smoking cessation, was for occasional use. Most also had large target markets and were for relatively new products, early in their life cycle, as defined by the number of remaining years of patent protection. Roth states that most of the drugs have relatively mild side effects, but does not explain the criteria used to judge severity. For example, one of the products judged to have mild side effects is the acne treatment tretinoin (Retin-A), a drug associated with a serious risk of birth defects. Roth also mentions that one product, an anti-epileptic, has since been withdrawn from the market for safety reasons.

Roth used a systematic approach to evaluating information quality, based on U.S. FDA regulatory standards. This study provides an independent assessment of how well the

FDA was able to regulate print DTCA, similar to a study of ads in U.S. medical journals by Wilkes et al.[35] In both studies serious concerns were raised about information quality, and particularly about the adequacy of warnings about risks in advertising copy.

It is appropriate to use pharmacists as judges of information quality, given their professional expertise, access to independent information sources, and knowledge of drug risks and benefits. Additionally there was a high degree of inter-rater reliability. However, pharmacist reviewers cannot assess how members of the public understand and interpret the information in the ads. Additionally, this study did not assess the images and emotive content of the ads.

Consumer Reports 1996

Consumer Reports evaluated 28 new prescription drug ads appearing in top U.S.magazines in 1996, asking a panel of 32 medical specialists to assess accuracy, information content and the potential usefulness of the information in the ads to consumers.[36] Two to three doctors specializing in the relevant field reviewed each ad. In tallying the results, Consumer Reports only recorded instances in which at least two judges agreed, with the exception of overall assessment of whether an ad was likely to be more harmful or helpful. They found that:

- one third of the ads contained factual inaccuracies
- one half did not convey important risk information in the main promotional text
- only 40% were honest about efficacy, and described risks and benefits fairly
- at least one reviewer considered 11 ads (39%) to be 'more harmful than helpful'.

The reviewers found the 'brief summaries' accompanying the ads to be especially problematic. The 'brief summary' contains the risk sections of the drug's approved labelling information, as required by the FDA, and is usually anything but brief. Only one company had reworked the information into everyday language. Consumer Reports asked a psychologist who is an expert on reading comprehension to assess the language level of the un-reworked brief summaries. He rated them as ranging from extremely difficult to

ultra-difficult.

Consumer Reports also found some product sales pitches objectionable:

- ads for antihistamines inaccurately implying the products are 100% effective
- an ad for a drug for bed wetting suggesting that mothers who fail to use it are neglectful, although there are other possible solutions, including waiting for the child to outgrow the problem
- an ad for a hair growth product that fails to say it does not work well in men over 40
- ads for smoking cessation aids that fail to mention that most people stop smoking on their own, without a nicotine product
- the use of sex to sell menopausal hormone therapies and psoriasis drugs.

This report provides only sketchy information about how the ads were selected and the criteria used for review. Expert assessments do not always reflect the latest scientific evidence. However, the researchers did not consider a result to be valid unless two or more reviewers agreed, lending additional weight to the results. Most of the findings also concerned major inaccuracies and failure to provide needed information.

Conclusion: Advertising Information Quality

Little research exists on the information quality of broadcast advertising, with two unpublished analyses of television DTCA, only one of which used pre-set criteria and systematic assessment methods, and one published report on depictions of elderly people in televised prescription drug and OTC ads combined. Additionally, there are no published systematic analyses of New Zealand advertising content, either print or broadcast.

Research on print DTCA (in U.S. magazines from 1989-1999), on the other hand, is extensive and is generally of high quality in terms of use of predetermined criteria, independent assessors, reliability checks showing high inter-rater reliability scores, and

representative sampling techniques. Earlier research mainly focused on the balance of information presentation and presence of necessary risk information, in other words whether advertisements met regulatory criteria, as well as the types of products and conditions advertised. Over a third of ads were judged not to contain adequate risk information.

More recent research has gone beyond regulatory information requirements to examine types of product claims, educational content, and use of sales techniques such as celebrity endorsements or financial incentives. The starting point is not whether advertisers have met regulatory requirements but whether or not they have provided the type of information consumers need in order to make informed health care choices. The results again are unpromising, with over 90% of ads failing to provide basic information such as how likely a medicine is to work, and much more frequent reliance on vague, emotional claims than precise information on expected treatment outcomes.

2.4.2 Regulatory Reviews of DTCA Information Quality

Information from regulatory reviews complements that of systematic analyses of samples of ads. In the U.S., companies must submit all advertisements to the FDA when they are released. Thus overviews of the FDA's regulatory experiences provide comprehensive information on all advertising that has appeared in U.S. media. New Zealand relies on industry self-regulation, but MedSafe, the national drug regulatory agency, has carried out spot checks to assess compliance with New Zealand's Medicines Act. In both cases the unit of analysis is an individual ad, regardless of the number of times it is broadcast or published, and the main criteria examined are compliance with the law, in terms of the accuracy and completeness of information provided, and whether it is consistent with approved product labelling, including necessary warnings of risks and promotion only of approved indications.

U.S. Regulatory experience with DTCA since August 1997

U.S. DTCA is covered by the same regulatory requirements as pharmaceutical ads aimed

at health professionals, with the exception of a guidance introduced in late 1997, and finalized in 1999, allowing less detailed risk information in broadcast advertising.[37] Table 2.12 presents an overview of current U.S. regulations for content of print and broadcast ads.

Table 2.12: U.S. regulatory requirements for DTCA information content

Type of DTCA	Regulatory requirements	Explanation
Print and broadcast	Cannot be false or misleading Must present fair balance Must present 'facts material'	Excludes information that is inconsistent with approved labelling. Must include drug risks and benefits The information must be relevant to the representations made, and describe consequences that may result from recommended use
Print only	Must describe risks	Must disclose all risks in a product's labelling (the 'brief summary')
Broadcast only	Must describe risks Must make adequate provision for directing consumers to full labelling information on product risks	Must present major side effects and contraindications in audio or audio and visual form Additional information sources must be listed, such as toll-free phone numbers, a web site, and a print ad in a magazine, and a suggestion to contact their physician; otherwise must include the 'brief summary'

Adapted from: Table 1. Heinrich J. Prescription Drugs. FDA oversight of direct-to-consumer advertising has limitations. U.S.General Accounting Office, Report to Congressional Requesters. GAO-03-177 October 2002

From late 1997, when the FDA relaxed its broadcast advertising regulations, until early 1999, 33 products were fully advertised on U.S. radio or TV, i.e. with product name and one or more health claims.[38] Seventeen of the 33 (52%) were found to violate the Federal Food, Drug and Cosmetic Act. In most cases the FDA sent 'untitled letters', the first stage of regulatory response, asking the company to stop running the ad immediately. In two cases, the agency issued a 'warning letter', the next step in regulatory response, indicating a lack of compliance to an untitled letter or a more serious offence requiring immediate corrective action.

The most common violations were inadequate communication of risks, overstatement of benefits, and a lack of fair balance between presentation of benefit and risk information.[39] Was this simply a result of the industry's lack of experience with new regulations for broadcast advertising? This appears unlikely: in June 2000, an FDA official described an

increase in submissions of questionable quality occurring both across the board and specifically in broadcast ads, and asked whether outrageous overstatements of efficacy had become the norm.[40]

In some cases the audio and visual portion of the ad would compete for the viewer's attention when risk information was presented, or the voice would speed up as risks were mentioned, but the information on benefits would be clear and easy to understand. Some drugs were promoted for uses not approved by the FDA. In the case of a menopausal hormone therapy, conjugated estrogens (Premarin), an all-encompassing health claim was made, for benefits that have "yet to be substantiated or even identified."[41]

One of the two warning letters was sent to Novartis, requiring the company to produce a corrective advertisement for its cholesterol reducing agent fluvastatin (Lescol). The company had run the ad for three months without complying with post-marketing reporting regulations and submitting copies of the ad to the FDA. This resulted in much wider dissemination of misleading messages than might have occurred otherwise. The ad included claims of effectiveness in reducing risks of stroke and transient ischaemic attacks in spite of a lack of evidence to back these claims. Risk information was also inadequate. Viewers were told they needed liver function tests if they took the drug, but not that the drug could cause liver damage. Claims that the product was much less expensive than competitors were also found to be misleading.[42] Table 2.13 presents an overview of the indications of advertised drugs versus numbers of violations. In one highly competitive drug class, cholesterol-lowering drugs, ads for all four advertised drugs were found to violate the law.

Table 2.13: early FDA regulatory experience with broadcast DTCA

Indication	Number of drugs advertised on TV & radio, late 1997 - early 1999	Number found to violate FDA regulations
Allergies	7	3
Skin or hair conditions	5	1
Cholesterol reduction	4	4
Smoking cessation	2	2
Asthma	2	1
Contraception	2	1
STDs	2	1
Migraine	2	0
Hypertension	1	1
Impotence	1	1
Menopause & osteoporosis	1	1
Weight loss	1	1
Acid Reflux/ulcer	1	0
Benign prostatic enlargement	1	0
Overactive bladder	1	0
Total	***33***	***17 (52%)***

A report in *Pharmaceutical Executive* stated that in 1998, the FDA sent over 100 notices of violation and warning letters to 50 pharmaceutical companies concerning both print and broadcast DTCA. This is a larger number than that reported by the FDA (see below). The reason for the discrepancy between this industry information source and the regulatory agency is unknown. The main stated reasons for violations were that the ads lacked fair balance between risk and benefit information, and that risk information was insufficient, omitted, or not readable or prominent enough, for example presented in small type against a dark background. Additionally, safety and efficacy claims were not always backed by methodologically sound studies, and confusing language or technical terms were used that were unlikely to be understood by the general public.[43]

Violations continue to be relatively common, with over 90 DTC ad campaigns found to violate FDA regulations from 1997 to May 2001.[44] The FDA sent out 92 regulatory letters informing manufacturers of a violation and requiring them to pull an ad between August 1997 and the end of 2001 (88 'untitled letters' and four 'warning letters'). Forty-four of the untitled letters covered broadcast ads, 35 print ads, and nine both print and broadcast ads.[45] The four 'warning letters' indicate a more serious violation or lack of response to an earlier regulatory action.

Repeat violations for a specific product were common; Schering-Plough's advertising of loratadine (Claritin) was found to violate FDA regulations 11 times from 1997 to January 2001. The FDA also cited Glaxo Wellcome 14 times for illegal advertising of two forms of fluticasone (Flovent and Flonase),[46] and Pfizer four times for broadcast and print ads for atorvastatin (Lipitor).[38] The U.S. General Accounting Office also notes that, "FDA warning letters often cite multiple, serious offenses or violations that raise public health issues."

In 2001 the FDA sent out 14 regulatory letters, half of which cited inaccurate information on product efficacy. Table 2.14 provides an overview of these violations. The FDA does not have the statutory authority to levy fines in response to violations; it generally only requires the company to withdraw an offending ad. The agency can request corrective action, but rarely does so, even in cases of repeat violations for the same product.

Table 2.14: U.S. FDA Regulatory Letters on DTCA, 2001

Product	Condition	Violation
Prilosec (omeprazole)	Acid reflux	Inadequate information on approved indication and use, lack of fair balance
Protopic (tacrolimus)	Eczema	Fails to provide necessary information for product claims
Protopic (tacrolimus)	Eczema	Overstates efficacy, broadens approved product indication, minimizes risk
Xenical (orlistat)	Obesity	Inadequate information on full indication, lacks fair balance, fails to fulfill 'adequate provision' requirement (for full risk information)
Plavix (clopidogrel)	Heart disease	Minimizes physician's role, fails to fulfill 'adequate provision'
Avandia (rosiglitazone)	Diabetes	Minimizes risks
Ditropan XL (oxybutin)	Overactive bladder	Overstates efficacy, minimizes risks, fails to convey indication
Cerezyme (imiglucerase)	Gaucher disease	Minimizes risks, fails to disclose prescription status, fails to fulfill adequate disclosure provisions
Niaspan (niacin)	Lipid lowering	Fails to present significant risks; misleading efficacy claims; implied use inconsistent with label
Luxiq (betamethasone)	Psoriasis, eczema	Overstates efficacy, misleading reference, compliance, and superiority claims
Differin (adapalene)	Acne	Inadequate risk information
Actonel (risedronate)	Osteoporosis	Inadequate risk information; minimizes role of health provider, fails to fulfill adequate provision requirements
Nolvadex (tamoxifen)	Breast cancer	Misleading efficacy claims, minimizes risks, failed to submit ad to FDA (postmarket reporting requirement)

Source: Table 4, Heinrich J, GAO-03-177. 2002, p 20

Regulatory reviews of information quality in New Zealand

New Zealand's Medicines Act states that advertisements must neither claim nor imply that a product is infallible, and that they cannot include testimonials from patients or physicians. The accompanying regulations state what information must be provided, including authorized use, precautions, contra-indications, and poisonous effects or adverse reactions. These requirements do not differ for ads for health professionals or the public, and in both cases, enforcement of regulations has been delegated to the advertising industry (Advertising Standards Authority). Neither the legislation nor industry self-regulatory codes define the level of detail required. Television ads generally do not include risk information in the audio portion. Hoek and Gendall state that, "most technical details appear in an end-screen that features for approximately five seconds," and market research indicates that consumer retain little of this information.[47]

MedSafe, New Zealand's national drug regulatory agency, carried out a review of DTCA in February 2000, asking companies to submit all current ads.[48] A total of 52 ads were submitted, 46 print and 6 broadcast. Eleven of the print ads (24%) were found to violate the Medicines Act and 5 of the broadcast ads (83%). In 87.5% of non-compliant ads, needed risk information was absent, incomplete or illegible. This was a voluntary review as New Zealand relies on industry self-regulation of advertising. The results indicated an improvement over an earlier review; in 1998, MedSafe had judged only 33% of submitted DTC ads to be in compliance with the law.[49] However, no details of this earlier review have been published.

The February 2000 issue of a newsletter for physicians funded by New Zealand's national drug benefit plan, PHARMAC, [50] focuses on a full-page newspaper ad for sildenafil (Viagra) that appeared in *The Dominion*, a national paper, in February 1999. The aim was both to evaluate the ad and to provide tools doctors can use when looking at other pharmaceutical advertising. The ad was criticized for exaggerating the prevalence of the problem to expand the market ("disease mongering"), exaggerating product efficacy by

presenting the best results obtained in clinical trials, not the range of observed results, and not adequately warning readers of potential risks, including a description of potentially fatal reactions ("a severe drop in your blood pressure, that may be difficult to treat") without explicit mention that such reactions may result in death.

Conclusion: Regulatory Reviews

These reviews suggest that the content of advertising messages is strongly affected by regulatory standards and enforcement procedures. The same companies are advertising the same products in New Zealand in many cases as in the U.S., but without similar details on product risks. On the other hand, New Zealand forbids personal testimonials; U.S. ads frequently use this technique, including celebrity endorsements. The many repeat violations in the U.S. also suggest that deterrence is inadequate. The public almost never receives corrections of misinformation and may be unaware that ads have been judged to be inaccurate or otherwise in violation of the law. The regulatory experience does not allow for an assessment of whether or not the public is educated, empowered or informed by advertising. However, it does indicate that, not infrequently, the public is misinformed about product risks, benefits, and conditions for appropriate use.

2.4.3 Consumer Surveys

Table 2.15 on the following page presents an overview of surveys of the public in the U.S., Canada and New Zealand.

Table 2.15: Consumer Surveys 1991-2002 (N=25)

STUDY	MAIN OUTCOMES ASSESSED	METHODOLOGY
1. Surveys of U.S.nationally representative samples		
National Consumers' League, 1998, 2000	▪ Awareness, attitudes to DTCA ▪ Drug requests ▪ Prescriptions of requested drugs	▪ National random digit dialled survey ▪ Self-report based on recall ▪ Time period unspecified
Prevention magazine. 1997, 1998, 1999, 2000	▪ Awareness, attitudes to DTCA ▪ Drug requests, prescriptions ▪ Risk communication	▪ National random-digit dialled survey ▪ Self-report based on recall ▪ Time period unspecified
Time magazine 1998, 1999	▪ Awareness, attitudes to DTCA ▪ Drug requests, prescriptions ▪ Risk communication	▪ National random-digit dialled survey ▪ Self-report, based on recall over the last 3 months.
U.S.FDA survey, 2000, 2002	▪ Awareness, Attitudes to DTCA ▪ Drug requests, prescriptions ▪ Effects on doctor/patient interaction ▪ Risk communication	▪ National random-digit dialled survey ▪ Follow-up mail survey ▪ Self-report based on recall ▪ 90% had seen a doctor in the last 3 months
AARP, 2000	▪ Awareness, attitudes to print DTCA ▪ Risk communication • Reading of fine print labelling	▪ National random-digit dialled survey, with oversampling of respondents over 50 to reflect U.S.adult population distribution
Thompson and Freedman, 2000	▪ Moderation of patient demand for an advertised medicine	▪ Telephone survey ▪ Random sample, insurance plan members ▪ Self-reported hypothetical response
Bell et al, 1999	▪ Hypothetical responses to a refused drug request; ▪ Misplaced faith in regulation ▪ Doctor/patient communication	▪ Random digit dialled survey, Sacramento ▪ Self-reported hypothetical response.
Doucette and Schommer, 1998	▪ Information seeking following exposure; effect of age & knowledge	▪ Mail survey, random sample of 360 households
Peyrot et al, 1998	▪ Awareness of DTCA ▪ Drug requests	▪ Random digit dialled survey, Maryland ▪ Self-report based on recall
3. Randomized experimental intervention – response to ads or scenarios (real or fictitious)		
Kaiser Family Foundation, 2001,	▪ Effects of a viewed TV ad on knowledge and attitudes ▪ Previous drug requests	▪ Two nationally representative samples compared: 1872 viewers (randomized to 3 subgroups, different ads); 639 non-viewers
Davis, 2000	▪ Completeness of risk information & consumer perceptions of drug safety	▪ U.S.university students, randomized to 2 groups ▪ Written questionnaire
Christensen et al, 1997	▪ Effects of content & presentation on attitudes & risk perception	▪ Elderly subjects ▪ Random assignment of fictitious ads;
Maddox and Katsanis, 1997	▪ Effect on doctor-patient relationship ▪ Information seeking after exposure	▪ Random digit dialled survey, Canadian city ▪ Hypothetical response

Table 2.15 Consumer Surveys 1991-2002 (N=25) - continued

4. Other sampling techniques: malls, street surveys and convenience samples		
San Francisco Health Dept, 2001	▪ Survey of men attending city clinics ▪ Exposure to ads for HIV/AIDS drugs	▪ Questionnaire survey ▪ Interim results of a larger survey
Colmar Brunton, 2000	▪ Response to a print DTC ad found to violate NZ Medicines Act	▪ Women aged 16-30 ▪ Street surveys in Wellington and Auckland
Chandra and Sarpong, 1998	▪ Awareness, attitudes to DTCA ▪ Comprehension	▪ Convenience sample, U.S.university students ▪ Written questionnaire
National Consumers League, 1998a	▪ Awareness, attitudes to DTCA ▪ Drug requests, prescriptions ▪ Comprehension, trust in information	▪ Survey in 10 malls, different regions ▪ 20% of sample were > 65 ▪ Self-report based on recall
Schommer et al, 1998	▪ Information retention following exposure to a televised DTC ad	▪ Patients waiting to see doctors at a clinic
Williams and Hensel, 1995	▪ Attitudes to DTCA; recall of information in an ad ▪ Information-seeking behaviour	▪ Retired elderly people ▪ Written questionnaire

U.S. National Random Digit Dialled Surveys

Surveys by Prevention, Time and the National Consumers League

Prevention magazine has carried out four population-based random digit dialled surveys on DTCA. The first was a joint study carried out with the American Pharmaceutical Association in 1997[1]; the second, third and fourth surveys were carried out in 1998 [51], 1999[52] and 2000.[53] Time magazine has also carried out national surveys in 1998[20] and 1999, and the National Consumers' League in 1998. [54]

In 2000 Prevention Magazine surveyed samples from Finland, France, Germany, Poland and the U.K. as well as carrying out a U.S. survey. Only one set of questions concerned DTCA: whether respondents would be willing to talk to their doctors about an advertised medicine and whether they thought their doctors would prescribe it. Questions were general and hypothetical "if DTC advertising were allowed". Around 70% of French, German and U.K. respondents said they would be 'very willing or somewhat willing' to discuss an advertised medicine, fewer (43%) in Poland. Only 6-11% believed their doctors would be very willing to prescribe an advertised drug.

Each of the U.S. surveys included 1000 to 1200 respondents. Full reports were available

for all three 1998 surveys and the 1999 and 2000 Prevention surveys, and only reports in secondary sources for other surveys. None have been published in peer-reviewed journals. The key outcomes assessed in these surveys are the proportion of consumers discussing advertised drugs with their doctors, directly requesting drugs, and receiving prescriptions for requested drugs.

Around 28% of the respondents to the *Time* survey had discussed a drug with a physician after seeing an ad and 7% had received a prescription for the drug. In 1998, around 23% of respondents to *Prevention*'s survey had spoken with their doctor about an advertised drug; 6% had requested a prescription; and 5% (or 80% of those who asked for a drug) had their request honoured. The National Consumers' League survey also indicated that 5% of the sample had received a prescription for a requested advertised drug. In 1999, 31% of Prevention respondents had spoken with their doctor about an advertised drug; 7% had requested a drug; and 6% (or 84% of those who asked) received a prescription.

Extrapolating the survey results to the U.S.population, *Prevention* estimated in 1998 that 15.1 million Americans and in 1999 that 15.3 million Americans had directly requested a prescription drug in response to DTCA and 12.1 million (1998 estimate) to 12.9 million (1999) had received them. The survey did not specify a time limit for past requests. Therefore, 1999 figures are a revised estimate, rather than being added to the 1998 figures. Table 2.16, below, summarizes the survey results on DTCA awareness, respondents' opinion of the quality of information, and actions they reported in response to advertising.

Attitudes to DTCA

Most of the 1998 *Prevention* respondents judged the communication of risk information in DTCA to be poor, both in television and magazine advertising. Most respondents were more positive about the communication of benefits, but a sizable minority also judged this information to be poor. The 1999 results indicate a trend towards a more positive view of information quality. Whether this reflects quality improvements or a shift in

public opinion is unknown. Responses on the role of DTCA were contradictory, with many people considering it both a source of education and confusion about the risks and benefits of medicines.

In both the 1998 *Prevention* and National Consumers' League surveys most respondents said they read some or all of the fine print information accompanying print ads, the 'brief summary' of risk information required by law. The question did not specify the proportion of ads or of fine print text. In 1999, *Prevention* used more specific wording and fewer people said they read this text.

These answers could also reflect a bias towards socially desirable responses. In the *Time* survey, 94% of respondents agreed with a statement that, "I only take medication when absolutely necessary." The sample was representative of the U.S. population, and at a population level many prescriptions are arguably not 'absolutely necessary' such as the use of antibiotics for viral upper respiratory infections, and many minor symptomatic treatments. Patients may have provided a socially desirable answer, or they may inaccurately believe that each prescription is absolutely needed. If so, this highlights a gap in education on appropriate use of medicines.

Table 2.16: Prevention, Time and National Consumer League surveys: awareness, actions and opinions

	PREVENTION			TIME	NCL
	1998 N=1200	1999 N=1183	2000 N=1222	1998 N=1157	1998 N=1013
Proportion who remember seeing or hearing a prescription drug ad	70%	81%	80%		80%
TV ad	**77%**	**83%**			**88%**
Of these people, the proportion who thought:					
- information on minor side effects is fair to poor	65%	51%			
- information on serious side effects is fair to poor	62%	50%			
- information on drug benefits is fair to poor	40%	39%			
Magazine ad	**63%**	**57%**			**50%**
Of these people, proportion who thought:					
- information on minor side effects is fair to poor	56%	47%			
- information on serious side effects is fair to poor	52%	44%			
- information on benefits was fair to poor	36%	28%			
- said they read some or all of fine print risk information	67%	39%*		39%*	56%
Proportion who have taken this action:					
Spoke to doctor about a disease because of an ad	13%				23%
Spoke to doctor about the advertised drug	23%	25%	29%	28%**	-
- Proportion of women	25%		35%		
- Proportion of men	20%		23%		
Directly asked for a prescription	**6%**	**7%**	**7%**		
Received a prescription for advertised drug	**5%**	**6%**	**5-6%*** **	**7%**	**5%**
Made a doctor's appointment as a result of an ad		2%		7%	
Proportion who believed they would take an action because of advertising:					
Were reminded to have their prescription refilled	5%	8%			
Were more likely to take their medicine	5%	7%	5%		
Agree somewhat or completely that they can choose medication without their doctor's advice				32%	
Agree somewhat or completely that they would switch doctors to get a desired medicine				28%	
Beliefs about DTCA:					
Allows people to be more involved in their health care	74%	76%			
Helps people make their own decisions about drugs	59%	63%			
Educates people about drug risks and benefits	67%	72%			
Confuses people about drug risks and benefits	61%	60%			
Makes prescription drugs seem harmless	55%	49%			
Causes tension between patients and doctors	38%	39%			

*For Prevention 1999, includes people who read it thoroughly (12%); read key information (12%) or skimmed (15%); Prevention;NCL 1998 had scaled responses; Time asked a yes/no question.
** includes people who spoke to their doctor about either the drug or the condition it treats.
***5% received a prescription for the advertised drug; 6% either the drug or a competitor.

Requests for advertised drugs

As indicated in Table 2.16, about one fourth of respondents initiated a conversation with their doctor about a drug in response to advertising. The proportion of patients who reported having requested prescription drugs from their doctors and received them was remarkably consistent: between 5 and 7% of respondents in all five surveys. The *Prevention* surveys asked whether patients had received a drug after directly asking for it, and found that a large proportion of those who asked, 80% in the 1998 survey and 84% in 1999, received a prescription for the drug. In 2000, a question was added to differentiate between patients receiving the drug or a competitor; 71% received the advertised drug and an additional 10% a competing product in the same class.

TABLE 2.17. Drugs Requested by more than 1% of respondents, Prevention 1998

Drug	Indication	Percent who asked doctor about drug (N=1200)
Claritin (loratadine)	Allergy	5% (60)
Prozac (fluoxetine)	Depression	2% (24)
Allegra (fenoxifenadine)	Allergy	2% (24)
Prilosec (omeprazole)	Ulcer/reflux	1.5% (18)

Source: Prevention 1998 Survey

Table 2.17 indicates the four drugs most commonly requested by patients, representing 46% of patient requests. They are all among the top 10 drugs by DTC advertising spending in 1998.[55]

A high proportion of the *Prevention* sample reported having, or being at risk for, one or more conditions treated by heavily advertised drugs, as shown in Table 2.18. This may be due to a liberal interpretation of 'at risk for'. For example, patients might consider themselves to be at risk for high cholesterol if their physician has ordered a cholesterol test, whether or not the results indicated elevated levels. The *Time* respondents also indicate a high prevalence of these conditions, but these were combined reports about their own and family members' health. Table 2.18 compares reported prevalence of conditions within these samples to U.S. population prevalence.

Table 2.18:
Prevalence of self-reported health conditions, 1998 Prevention & Time surveys

Condition or illness	Prevention (has or is 'at risk' for condition)	Time (person or family member has condition)	Adult U.S. Prevalence
Allergies	45%	64%	9% (hay fever) *
Hypertension	44%	34%	23%*
Arthritis	44%	37%	20%*
High cholesterol	36%	24%	19% *
Migraine	23%	21%	4%‡
Depression	22%	18%	10%†
Asthma	19%	23%	9%*
Menopause or osteoporosis**	15%	10%	-

Source: Prevention and Time 1998 surveys
*National Center for Health Statistics, CDC. U.S. population rates, ages 18 and over. Available at: http://www.cdc.gov/nchs/fastats/pdf/sr10_205t3.pdf ; 1997 rates except high cholesterol (1994)
‡ MMWR Weekly http://www.cdc.gov/mmwr/preview/mmwrhtml/00001982.htm †National Institute of Mental Health. http://www.nimh.nih.gov/publicat/depression.cfm#sup5
**whether this was a measure of the proportion of post-menopausal respondents or those diagnosed with osteoporosis is unclear.

Compliance

One of the hypothesized benefits of DTCA is that a person taking an advertised drug will feel more positive about a product they are taking and comply with a recommended treatment and/or remember to have a prescription refilled. *Prevention* asked people who were taking advertised drugs several questions related to these outcomes.

In 1998, one fifth of the respondents had seen ads for drugs they were currently taking; in 1999, nearly one quarter. Most said that seeing ads affected neither their feelings about the safety of the medicine (61% in 1998; 52% in 1999) nor their likelihood of taking it (69% in 1998; 66% in 1999); nor were they reminded to have prescriptions refilled (73% in 1998; 66% in 1999).

About one in four of those taking advertised drugs said that the ads made them more likely to take their medicines in 1998, or 5% of total sample; in 1999 this had grown to one third, or 8% of the sample; in 2000 it was similar again to 1998: 5% of the sample or 22% of those taking drugs they had seen advertised.

These results leave a number of questions unanswered. For example, when consumers feel better about a medicine's safety after seeing an ad, is it because they were unnecessarily worried, for example because risks are minor, because the ad tends to downplay the product's risks, or because they now know what serious side effects to watch out for? Reviews of advertising information quality, as described above, indicate that ads do commonly downplay risks. Secondly, if respondents report that they are more likely to take a medicine or refill a prescription after seeing an ad, is this reflected in any behavioural change? If they do take a medicine they might have otherwise forgotten, is this medicine likely to improve their health?

Some categories of heavily advertised drugs are used for symptomatic treatment, for example NSAIDs, allergy and migraine medications, and greater compliance or earlier refills would play a different role in health than that of disease-modifying treatments. Better compliance with a symptomatic treatment can improve quality of life if symptoms are troublesome and treatment is effective. However, it sometimes provides little advantage and may lead to harm. NSAID users who continue to take their medicine in spite of gastric pain are more likely to be hospitalized for gastric bleeding than users who stop when they experience symptoms.[56] The *Prevention* survey did not distinguish between users of different types of treatments or conditions of use.

Another unanswered question is the effect of ads on patients taking non-advertised treatments. Are they more or less likely to take their medicines if they see ads for competing products for the same condition?

In summary, a link may exist between changes in rates of compliance and exposure to advertising, but the *Prevention* survey results do not provide adequate information to ascertain either the nature of this link nor its likely influence on health.

Additional information in 1999 Time and Prevention Surveys

In 1999, *Time* carried out a second random digit dialled survey of 1000 adults. In the

1999 survey:

- 29% of respondents had discussed an ad with a health care professional;
- 7% received a prescription for an advertised drug they requested; [57]

Additionally, half of the respondents said that they would switch doctors if they could not get a desired prescription for heartburn, allergies or migraines. However, far fewer reported that they would switch if their physician failed to provide a desired medicine for depression (20%) or impotence (7%). The reasons for this difference were not examined. Three quarters of respondents said that what they wanted most from DTCA was 'ads that clearly state all associated risks'.

The 1999 *Prevention* survey also tested knowledge of drug's indications for use. The results show an increase in awareness of drug-specific advertising, but much more limited awareness of what conditions these products treat. Most people who were aware of ads for a drug and had the condition it treats remained unaware of the drug's indication.[58] This suggests that DTCA may be more successful in stimulating brand recognition than in conveying information on product use.

Table 2.19: Awareness of drug Indication: 1998-9 Prevention surveys

Product	Percent aware of ads for the drug		Indication	Percent aware of the indication		Percent w/ health condition aware of indication
	1998 N=1200	1999 N=1183		1998 N=1200	1999 N=1183	1999 (N= has condition & is ad aware)
Claritin (loratadine)	60%	75%	Allergy	30%	45%	68% (429)
Propecia (finasteride)	-	54%	Baldness	-	26%	46% (169)
Allegra (fenoxafedine)	45%	65%	Allergy	21%	25%	44% (387)
Zyban (bupropion)	-	67%	Smoking cessation	-	17%	40% (125)
Premarin (conjugated estrogen)	36%	36%	Hormone replacement	15%	16%	69% (126)
Meridia (sibutramine)	-	44%	Weight loss	-	11%	30% (242)
Prilosec (omeprazole)	23%	32%	Acid reflux	6%	9%	39% (171)
Zyrtec (cetirizine)	-	43%	Allergy	-	6%	21% (269)
Glucophage (metformin)	11%	14%	Diabetes	5%	7%	52% (47)
Zocor (simvastatin)	39%	39%	Lipid lowering	8%	6%	29% (138)
Imitrex (sumatripan)	17%	19%	Migraine	5%	4%	27% (98)
Accolate (zafirlukast)	-	20%	Asthma	-	1%	6% (78)
Detrol (tolterodine)	-	21%	Overactive bladder	-	1%	9% (77)

Adapted from: Charlish P. 1999; figure 2, p10; Prevention,1999.

National Consumer League Survey 2002

The National Consumer League commissioned a second national consumer survey, which was carried out in October 2002.[59] In addition to surveying a nationally representative sample of adults 18 or over, they over-sampled adults aged over 65 in order to examine the effects of DTCA on the elderly. The request rates and the rate of prescribing following requests were similar to other consumer surveys. The survey included a number of attitudinal statements, and asked respondents if they agreed or disagreed. Only two statements of 10 statements had majority agreement: that ads are largely responsible for the increased costs of prescription drugs (63% of seniors), and that ads just help pharmaceutical companies to sell their drugs (60% of total and of seniors). Most of the tested statements were positive towards advertising.

Table 2.20: Key results of 2002 National Consumer League survey

	Total (N=1012)	Age 65 + (N=308)
Aware of prescription drug ads	77%	69%
Ads seen for a condition of interest to them	28%	33%
Spoke to their doctor about the ad	5%	6%
Doctor prescribed the drug	4% (83% of requesters)	5% (89% of requesters)

*The report contains contradictory prescribing rates.
Question C14 reports these figures, with additional detail on how patients responded to the drug. Question C12 reports a lower prescribing rate (2% of total), but the question was worded confusingly: respondents chose the best description of their physician's response among a range of options, some attitudinal, some on prescribing. This was likely to lead to undercounting of prescriptions.

U.S. FDA Surveys

The U.S. FDA carried out a survey on DTCA in 1999, based on random digit dialing, as part of an evaluation of the impact of the 1997 draft guidance on broadcast advertising.[60] The aim was to assess the impact of DTCA on doctor/patient interactions as well as consumer attitudes and general knowledge about risks and benefits of prescription medicines. The survey results were posted on the web in January 2000.[61] A second survey was carried out in 2002. However, thus far only preliminary results have been made public.[62] The response rate for the 1999 survey was 65% and for the 2002 survey was 53%. [63]

In order to improve the accuracy of reports and to limit them to a single doctor's visit, 90% of the 1999 sample included only people who had seen their doctor within the last three months (N=960). The remaining 10% (N=121) had seen their doctor more than three months previously. In 2002 the survey was limited to people who had seen their doctor within the last 3 months.

Respondents reported more exposure and more influence from broadcast advertising than other forms of advertising. They also reported influence from articles in magazines and newspapers and TV and radio programmes. They were less aware of ads on the Internet (6-13% in the two surveys). However, it is sometimes difficult to distinguish advertising from other information on the Internet.[64] Between 1999 and 2002 the proportion of respondents aware of ads on television, magazines and the Internet had increased.

In the 1999 survey, some of the questions posed about drug requests could be interpreted to refer both to advertising-induced requests and other types of requests unrelated to advertising. It is therefore difficult to know what proportion of the patients requesting advertised drugs received prescriptions. The proportion who mentioned a specific ad (8%) or who asked their doctor about a specific brand name drug (8.6%) may provide a better estimate of requests in response to advertising than more general questions that may have been interpreted differently by different respondents.

The 2002 survey included a more direct question about whether respondents had asked their doctor for a specific brand: 7% reported that they had, 69% of whom were prescribed the drug. This is roughly consistent with the results of the Prevention surveys listed in Table 2.16.

In the 1999 survey, the FDA found a significant difference in response to advertising between people who had seen their doctor recently and those who had last seen a doctor more than three months previously. Twenty-seven percent of those who'd seen their doctor recently reported having discussed a health condition for the first time because of advertising, versus 8% of those who had seen their doctor less recently ($p<.001$). No difference was observed in health insurance coverage for the two groups, but those who had seen their doctor recently reported greater awareness of TV and magazines advertising and significantly poorer health status (21% vs. 8% with fair to poor health). People in poorer health consult physicians more often than those in better health, so the latter is expected. However, the relationship to advertising influence is unknown. Few patients reported that they had visited the doctor because of advertising, but ads could have had a secondary role in prompting physician visits. Alternately, those in poorer health may be more aware of advertisements for medical treatments than others.

This survey confirms the results of other U.S. surveys indicating that the public reports a generally positive attitude to DTCA, particularly in comparison to doctors. Similar as well was the finding that more detailed questions elicited less positive responses: most

respondents wanted more information on risks and side effects and felt that ads made drugs look better than they are. The survey included an open-ended question about what information should be included in ads that is currently not included; the most frequent response was side effect information. Respondents also said they would prefer not to see ads that over-glamorize products or are unrealistic.

More than half the respondents were unable to explain what prescription-only status meant and more than one fourth mistakenly thought that only the safest drugs could be advertised to the public. This is similar to the results of a survey by Bell et al. in Sacramento, described below, in which 43% of respondents thought only the safest drugs could be advertised on televison.[65] This suggests a serious gap in knowledge about the regulatory context surrounding DTCA.

The 1999 survey also included a follow-up mail questionnaire with a 34% response rate. (N=375) Respondents were given copies of advertisements and asked whether they had seen the ad before and what condition the drug treats. The question on indications was frequently left blank (up to 56% of respondents per ad). It is therefore not possible to know how many people knew what condition an advertised drug treats. Within the subset who answered the question, few responses were incorrect or 'don't know' (2-12%). This survey included an ad for one product eventually withdrawn from the market for safety reasons, troglitazone (Rezulin). Fifteen percent of the respondents remembered having seen the ad, about half in magazines and half on TV. No questions on safety were included so it is not possible to know whether respondents were aware of the growing safety concerns that preceded its withdrawal.

TABLE 2.21: Key Results of 1999 and 2002 FDA Surveys

	1999 Survey		2002 Survey
	Have seen doctor in last 3 months (N=960)	*Saw doctor more than 3 months ago (N=121)*	*Have seen doctor in last 3 months (N=944)**
Can explain prescription-only status	**47%**	**47%**	
Have seen or heard DTCA in last 3 months	72%	69%	81%
▪ On TV	67%	66%	78%
▪ In magazines	48%	40%	61%
▪ On the Internet	6%	8%	13%
Of those aware of having seen /heard DTCA			
▪ mean (s.d.) # of drugs they've seen advertised	5 (3)	5 (3)	
▪ proportion who usually read some fine print info	66%	51%	59%
▪ proportion who find this information hard to read**			55%
Like seeing DTCA	52%	44%	
Dislike seeing DTCA	27%	31%	
Percent agreeing somewhat or strongly:			
▪ Ads don't give enough information on benefits	49%	33%	
▪ Ads don't give enough information on risks	59%	57%	
▪ Ads make drugs seem better than they are	58%	57%	
▪ Ads make it seem a doctor is not needed	24%	19%	
▪ Ads help them make better health decisions	47%	41%	
▪ Only the safest drugs may be advertised to the public	29%	25%	
Actions in response to DTCA			
Spoke with their doctor about a condition for the first time because of an ad	27%	8%	18%
Asked about a specific brand name drug	9%	N/A	7%
Received requested drug			5% (69% of requesters)
Doctor gave them desired prescription (link to advertising unspecified)	11% (50% of queries)	N/A	
Satisfied with doctor's response	19% (85% of queries)	N/A	
Before their appointment, they thought their doctor would prescribe a new drug or switch to a different drug:			
▪ for any reason	32%		
▪ because of a TV or radio ad	3%	N/A	
▪ because of a magazine ad	1%	N/A	

*only preliminary results available in a power point presentation
**judged to be somewhat or very hard to read

AARP survey

The American Association of Retired Persons (AARP) carried out a telephone survey of a random sample of adult Americans, with over-sampling of respondents aged 50 and over to obtain an age distribution reflecting the current U.S. adult population distribution.[66] The results were analyzed by age, to look at the educational messages younger and older people obtain from print advertising, and to explore safety issues and the role of physicians as gatekeepers. A total of 1310 adults were contacted, 898 of whom had seen print DTCA in the last six months.

Findings among those who had seen print DTCA in the last six months:

- One third failed to notice the fine print labelling information;
- Among respondents 60 and over, more than half, 52%, failed to notice fine print labelling information;
- Only 1/3 of the respondents who had noticed fine print labelling usually read it;
- 50% of those 60 and over thought the ads usually made it clear that a prescription was needed;
- 49% of the total sample, and 44% of those 60 and over said that ads provide enough information to let them know what the drug is for;
- 50% said the ads contain enough information on risks and side effects; 43% of those aged 60 and over (significantly different from 18-39 year old group, 60% of whom thought it was enough information).

Only 54% reported that their doctor usually talks to them about risks or side effects when prescribing. Those 60 and over were less likely than younger respondents to have these conversations: 17% of those 60 and over versus 10% of those under 60 reported that their doctor rarely told them of drug risks. Most respondents thought that comprehensive risk information should be included in print DTCA, including both common side effects and infrequent risks. A large majority (86%) believed that ads should also state contraindications ("who should not take a drug").

The researchers raised concerns about a 'medication information gap' because of the many respondents who reported not receiving adequate information from their doctors and pharmacists. They were particularly concerned that older respondents, who take more medicines, were less aware of risk information, less likely to read fine print labelling, and less likely to be informed by health professionals.

Kaiser Family Foundation

The Kaiser Family Foundation (KFF) carried out a survey among an existing randomly selected nationally representative panel assembled by Knowledge Networks for a range of survey research.[67] Participants in this panel obtain free web TV, e-mail and Internet access. KFF randomly selected 1872 respondents to view one of three television ads, as well as a comparison group of 639 non-viewers. Each of the viewers saw three ads in their own homes: a public service announcement, a prescription drug ad and a car ad. They were not informed of the purpose of the survey at the time. The aim was to simulate normal viewing of television advertising. The three advertised products were atorvastatin (Lipitor), a lipid-lowering drug, montelukast (Singulair), an asthma drug, and esomeprazole (Nexium), a drug for heartburn/reflux.

General impressions of the educational value of the ads were not positive: 70% of the viewers of any of the ads said they had learned little to no new information about the treated condition, and 59% believed they had learned little to no new information about the medicine. However, as shown on Table 2.22, respondents were much more positive about the information content of the ads they had viewed, as compared to non-viewers who were asked a general question about the information content of DTCA. Those who had just seen ads were also much more likely to say that they trusted the information in an ad than those asked a general question about DTCA they had seen. Viewers' responses did not differ significantly depending on which ad they had just seen. This suggests a connection between increased trust and the act of having recently viewed an ad, rather than the specific content of individual ads.

Within the sample as a whole, including both viewers and non-viewers, 30% reported having spoken to their doctor about a medicine in the past in response to advertising, and 44% of these respondents (13% of the sample) reported having received a prescription as a result. Although a 44% prescribing rate is lower than that reported in the FDA or Prevention surveys, this is likely to reflect a difference in the question. Respondents were asked if they had spoken to their doctor about a medicine in response to advertising, not if they had requested a medicine.

Table 2.22: Kaiser Family Foundation Survey respondents' opinions of ad content

	Viewers of specific ads (N=1872)	Non-Viewers – DTCA in general (N=639)
Percent who thought DTC ads did a good or excellent job of telling about:		
The condition the medicine treats	84%	58%
Benefits of the medicine	72%	60%
Who should take the medicine	66%	47%
Who should not take the medicine	55%	41%
Questions to ask the doctor about the medicine	55%	34%
Potential side effects	52%	30%
Directions for use	47%	18%
Percent who trusted the information ("some" or "a lot") in the ads:		
On the health condition	64%	33%
On the medicine	62%	46%

The researchers also tested knowledge. In this case there were individual variations related to the content of the ads. For example, 74% of those seeing the atorvastatin (Lipitor) ad identified liver problems as a serious side effect, whereas only 42% remembered muscle pain and weakness (signs of rhabdomyolosis, a serious adverse effect of this class of drugs). Only around 30-50% of respondents remembered specific adverse effects of the other two drugs. In contrast 86% of respondents could name the health problem each drug treated.

Montelukast (Singulair) is one of two products in a new class of oral anti-asthma drugs, leukotriene antagonists. Its average clinical effects are so small as to be unlikely to be detectable by individual patients, and it is less effective than the standard therapy used to prevent asthma attacks, inhaled corticosteroids.[68]

More viewers of the montelukast (Singulair) ad knew that there were pills people could take to prevent or limit asthma attacks than non-viewers (71% vs. 36%). However, more montelukast (Singulair) ad viewers came away misinformed about what these pills do: 25% thought they could take a pill rather than use an inhaler during an asthma attack versus 13% of non-viewers. This is a dangerous misinterpretation, as it could delay effective treatment during a potentially life-threatening situation. The ad says that montelukast (Singulair) doesn't work during an acute attack. However, this voice-over is accompanied by different text on screen and viewers may be distracted. The main emotive message is one of effective relief. Nowhere does the ad even hint that effectiveness is mild or inferior to inhaled steroids, which are also used for prevention of asthma attacks. The KFF survey did not examine viewers' knowledge of montelukast's efficacy in comparison to alternatives.

Similarly, the researchers did not examine whether viewers of the esomeprazole (Nexium) ad knew that this drug is an isomer of omeprazole (Prilosec), which is converted into precisely the same active metabolite in the body as its parent drug. Therefore the only potential difference, in terms of the drug's pharmacological activity, is dose-related.[69] They did measure whether viewers of the atorvastatin (Lipitor) ad knew that this product had not been demonstrated to prevent heart attacks: 34% of viewers knew that it did not versus 5% of non-viewers. However, 15% of viewers incorrectly thought that it did prevent heart attacks versus 8% of non-viewers. The ad provided this information, as required by regulation. However, it was provided only in text, not in audio. KFF did not test whether viewers knew that better evidence existed for heart disease prevention for some of atorvastatin's competitors.

This survey provides an interesting glimpse both into viewers' greater trust in the information in advertisements just after they have seen an ad than when reflecting more generally, and also in the capacity of ads to convey both accurate and inaccurate information to viewers.

Local Population-based Surveys

These studies are based on representative samples of local or regional populations and provide useful additional information about the factors determining a patient's response to DTCA, effects of demographic variables, and information processing.

Thompson and Freedman, 2000

A random sample of members of Kaiser Permanente, a large health insurance plan, in North California were phoned to asked to respond to three vignettes, two of which were related to use of heavily advertised medicines.[70] Young adults (aged 18-39) were asked if they would switch from a brand-name non-sedating antihistamine, loratadine (Claritin), to a similar lower cost product; men over 40 were asked to imagine they had come in to request a sildenafil (Viagra) prescription and asked how they would react if their doctor suggested a non-pharmacological intervention instead.

Most participants said they would try a less expensive allergy medication (77%) or might try it (10%), in response to a doctor's explanation that this would save the health plan money. Two-thirds of the men over 40 (n=76) were willing to go talk to a 'behavioural medicine specialist' about sexual problems; one third said they would prefer just to get a prescription for sildenafil (Viagra).

These scenarios are hypothetical and would not necessarily reflect actual behaviours among patients with these conditions. They are also a measure of response to the offer of an alternative to advertised products, rather than directly to advertising. However, in open-ended discussions participants said they would be receptive if recommendations for more cost-effective therapy came from a trusted physician and if they were provided a choice of alternatives. Refusers were on average less satisfied with their health plan, less trusting of Kaiser physicians, and in poorer health.

Bell et al, 1999

Bell et al. carried out a random digit dialled telephone survey of residents of Sacramento County.[58] The authors asked members of the public how they would respond if they requested an advertised drug and their request was refused. Would they:

- feel disappointed
- attempt to persuade their doctor
- go to another doctor for the prescription
- and/or switch doctors?

The survey included questions on attitudes to DTC advertising, current quality of communication with their doctor and satisfaction with care. Additionally, the researchers used a four-point test of 'misplaced faith in regulation'. Respondents were asked whether four false statements were true or false; those who said that at least 3 were true were classified as having misplaced faith in regulation.

TABLE 2.23: Misplaced Faith in Regulation

False statement on U.S. regulation of prescription drug advertising	Percent who believed statement was true (N=329)
DTC ads must be submitted to the government for pre-approval	50%
Only prescription drugs found to be completely safe can be advertised to the public	43%
The advertising of prescription drugs with serious side effects has been banned	22%
Only extremely effective drugs can be advertised to the public	21%

Thirty percent of respondents said that they would both be disappointed by a refusal and take some kind of action, most often attempts to persuade their doctor (21%). The authors found that the most consistent predictors of resistance to a doctor's denial of a request for an advertised drug were the quality of the pre-existing doctor/patient relationship and the patient's attitudes towards DTCA.

Additionally, those with misplaced faith in regulation were four times as likely as others to say they would use persuasion, three times as likely to say they would shop for a prescription, and more than seven times as likely to say they would switch doctors. They were also more likely to hold positive opinions towards DTCA. Middle-income

respondents were more likely to say that they would try persuasion and prescription shopping than lower or higher income respondents, and minority respondents were significantly more misinformed about regulations than white respondents.[71]

Bell et al. also asked about past behaviours in response to DTCA: 19% of respondents reported that they had requested a medicine from their doctor in response to advertising. Those who had asked for a medicine in the past in response to advertising were more likely to be female, to be aware of current ad campaigns, to have positive attitudes towards DTCA, and to overestimate the extent of FDA regulatory control of DTCA (positive responses to at least 3 of 4 questions above).

This study raises questions about the interaction between public misunderstanding of regulatory safeguards and patients' decisions to override doctors' refusals to prescribe requested drugs. It also highlights the importance of the quality of doctor/patient communication if misleading advertising messages are to be countered effectively. An industry commentator, Pines, has suggested that one of the factors driving the growth of DTCA in the U.S. is the shift to less personalized provision of medical care, "Today, we have limited flexibility in choosing our physicians and are less likely to establish a close, traditional relationship with them."[72]

Peyrot et al, 1998

Peyrot et al. carried out a random digit dialled survey of 440 greater Baltimore area residents in 1990, looking at the effects of demographic factors, media exposure, and attitudes and awareness on requests for advertised drugs.[73] On average, respondents knew two of eight listed drugs, and 5% reported having asked their doctor for a specific drug. Interestingly, this request rate is similar to rates in the 1998 surveys described above, although it was carried out in 1990 when exposure to DTCA was lower. Peyrot et al. found that women were more likely to request drugs than men; whites than non-whites; professionals and better-educated people than those with less education. Non-whites had a more negative attitude towards advertising and less exposure. When attitudes and

exposure were controlled for in the analysis, no difference was found by race. No association was found between age and requests for advertised drugs.

People who reported better knowledge of medicines were more negative towards advertising and were less likely to request advertised drugs. Those who supported use of generic drugs were less likely to make requests; those who believed that advertising helps to reduce prices made more requests. The wording of some questions is likely to have biased results. For example 69.1% of respondents agreed that advertising "**can** educate consumers"; only 28.4% agreed that it "**will** confuse consumers." The two questions should have been worded similarly.

Doucette and Schommer, 1998

A 1998 study by Doucette and Schommer looked at the effects of age and medication knowledge on the public's desire for additional information on drug benefits, risks and costs following DTCA exposure.[74] This was a mail survey of a random sample of 360 households. The response rate was 42% (n=150), limiting generalizability. Older and less knowledgeable people were less likely to report a wish to seek additional information after exposure to a DTC prescription drug ad. Knowledge levels were based on self-reports only, and may have been inaccurate.

Physicians were the most strongly preferred source of information on benefits and risks of medicines. Pharmacists were the preferred source for cost information. Manufacturers tended to receive lower ratings as information sources, as did friends and family. This survey measured attitudes rather than behaviour. Consumers were asked their preferences, not whether they had searched for additional information following advertising exposure.

Maddox and Katsanis, 1997

Maddox and Katsanis carried out a random digit dialled survey of 165 English-speaking urban Canadians, randomly assigning respondents to one of two short scenarios on a hypothetical new 'breakthrough' prescription drug for colds, one of which involved

information obtained through advertising, the other information provided by a physician.[75]

The response was more positive to information obtained from a physician than from advertising. People randomized to the physician scenario were more likely to say they would seek additional information about the product and would ask for a prescription in the future than those randomized to DTCA. The latter frequently said they did not know if they would seek additional information, and were less likely to say that they would discuss the product with their doctor.

As this involves a speculative response to a hypothetical situation, the results should be interpreted with caution. Additionally, the results are unlikely to be generalizable to the Canadian population as a whole, as the survey was carried out in a single unidentified English-speaking city. The response rate was 41%, further limiting generalizability.

Experimental Interventions

Davis, 2000

Two studies published together explored the relationship between the degree of detail provided to consumers in risk information and their perceptions of the drug's safety and its appeal.[76] In the first study, 140 undergraduate and graduate university students were randomized to one of two descriptions of eight advertised drugs: an 'incomplete risk statement', taken directly from the advertising copy of print DTC ads (N=75); or a 'complete risk statement', including all side effects occurring in at least 3% of users (N=65). Product information was otherwise similar. The drugs were: loratadine (Claritin), doxazosin (Cardura), metronidazole (MetroGel), alendronate (Fosamax), sumatriptan (Imitrex), nabumetone (Relafen), itraconazole (Sporanox) and ipratropium (Atrovent) nasal spray. Respondents were asked to rate how likely they were to recommend or purchase each drug, based on a seven point scale. Those provided with incomplete risk information consistently judged drugs more favourably, and the difference was significant for six of the eight drugs.

The second study used five paired comparisons of complete and incomplete risk information, with information on drug benefits kept constant. The two versions of information were given different fictitious drug names, but both were based on existing information sources for the same product. The incomplete risk information was from a DTC ad. More complete information consisted of all risks found to occur in clinical trials at equal or greater frequency to the subset listed in the ad. In all five cases, respondents thought a product was safer if less risk information had been provided, and 78-98% said they would choose the drug with less complete description of risks. This study provides some insight into how consumers perceive drug risks based on the information provided in DTCA.

Christensen et al, 1997

Christensen et al. used several versions of a hypothetical print ad to assess elderly consumers' perceptions of risks and attitudes towards the advertised product.[77] The benefit information and fine print labelling information on the back of the ad were identical in all versions. However, the amount of detail on risks and the image of a person endorsing the product -- a doctor or a building contractor, represented by the same male model – varied between four versions. Different versions of the ads were distributed randomly to 131 volunteers over the age of 60.

The respondents judged the product as least risky if a contractor endorsed it and there was little risk information in the advertising copy. This reassuring non-medical scenario also produced the most positive response towards the product. If detailed risk information was provided in the advertising copy, respondents were more positive if a doctor endorsed the product, rather than a contractor.

The importance of images and advertising copy are highlighted in this survey. Participants had very different impressions of product safety and different degrees of trust in the product despite identical fine print risk information on the back of the ad. The

extent to which survey respondents read or understood this labelling information is unknown.

Other Survey Techniques

Mall or street surveys, clinics and convenience samples

Generalization of the results of the surveys described below to larger populations is limited by the methods used to select study participants. For example, men attending sexual health clinics are a self-selected population group, as are people shopping in a shopping mall or walking down a specific city street. However, these surveys provide insights into effects of DTCA not addressed in larger randomized surveys, and sample selection was independent of the measured outcome.

San Francisco Health Department, 2001

The San Francisco Health Department is carrying out a survey of 1000 men attending the city's sexual health clinics and has released interim results of interviews of the first 262 men included in the survey.[78] Gay men who reported seeing ads regularly for drugs to treat HIV/AIDS were more likely to also have unprotected sex than men who seldom saw or noticed seeing them, and 62% of the men surveyed thought that seeing ads for HIV/AIDS drugs affect a person's decision to have unprotected sex. These results are preliminary, but have been linked to unrealistic images used in ads for antiretroviral therapy, such as an ad for indinavir (Crixivan) showing four attractive men in hiking gear on top of a rocky mountaintop. "These medicines don't enable anyone with HIV to climb mountains," comments Jeffrey Klausner, an epidemiologist from San Francisco's health department. "The side effects make it impossible."[78] The U.S. FDA has written to all manufacturers of HIV/AIDS treatments as a result of the concerns raised by the San Francisco Health Department, advising them to stop using advertising images suggesting unrealistic treatment outcomes.[79]

Colmar Brunton, 2000

New Zealand's national drug benefit scheme, PHARMAC, commissioned a survey of young women, carried out by Colmar Brunton, to assess responses to an advertisement for cyproterone and estradiol (Diane-35).[80] This advertisement ran in New Zealand women's magazines in 1999-2000 (*She*, *Women's Weekly* and *Girlfriend*). This product was previously sold as a contraceptive in Europe, but its use has been restricted to treatment of severe acne because of concerns about liver toxicity.[81] There is also evidence of higher risks of fatal embolisms than with other oral contraceptives.[82] In New Zealand (as in Canada) its approved use is similarly limited to severe acne with signs of androgenization, and the New Zealand Ministry of Health sent out a safety advisory to physicians in March 2002 to strengthen warnings about venous thromboembolism.[83] The risk of a venous thromboembolic event (mainly deep vein thrombosis) is estimated at nearly four times that of the most commonly used oral contraceptives (odds ratio 3.9; 95% CI 1.1-13.4 versus levonorgestrel containing products)[84]

Two hundred women, aged 16-30, were included in the survey. A street-intercept method was used in downtown Auckland and Wellington, with interviewers approaching every third woman who appeared to be in the appropriate age range. The survey response rate was 30%, with 140 women participating in Auckland and 60 in Wellington. Women were initially shown the ad for 5-10 seconds then asked questions about their understanding of it. They were then shown the ad for an additional minute and asked more detailed questions.

- 28% remembered seeing the ad;
- 12% reported having 'ever used' Diane-35;
- 45% thought the ad gave them enough information to decide whether to take Diane-35;
- 27% thought the ad clearly states the risks and side effects.

The only risk mentioned in this ad is "Diane-35 has a similar side effect profile to other oral contraceptives. Some women should not use Diane-35." A complaint about this

advertisement, due to inadequate risk information provision, was since upheld.[49]

This is the only available research on consumer responses to an advertisement found to be in violation of national regulations, either in the U.S. or New Zealand. The results indicate that a substantial minority of the public may be misled into believing that the information provided is adequate for decision-making and accurately reflects product characteristics. In this case, the product in question is associated with serious risks. This survey is also of relevance to Canada as estradiol and cyproterone (Diane-35) has been advertised to the Canadian public.[85] The product is not available in the U.S.

Chandra and Sarpong, 1998

This is an unpublished report of a convenience sample of 200 U.S. university students with a mean age of 20.[86] Health professionals and students in a health field were excluded, and most respondents (70%) were women. A sample ad was provided with a brief written questionnaire. Although most respondents stated that prescription drug ads were informative (84.6%), more than two thirds judged them to be too complicated, hard to read, hard to understand or not designed for consumers. As in other U.S. consumer surveys, responses to more detailed questions contradicted more general questions. Female respondents were more likely to judge ads to be complicated and difficult to understand than male respondents.

National Consumers League Mall Survey, 1998a

This survey of 250 people was carried out over four days in 10 U.S. shopping malls.[87] Only people who had obtained a prescription drug within the last year were surveyed: 200 from the general public and 50 people over 65. The survey included a questionnaire about advertising awareness, attitudes and drug requests, and consumer responses to three formats of information materials that a pharmacist might distribute.

Over half of respondent (56%) said they had talked to their doctor about a medicine they heard about through an ad, and 42% had spoken to their doctor about a disease they heard about through an ad. Around 12% said their doctor had prescribed the drug. These higher

proportions, as compared to most U.S. consumer surveys, may reflect sample selection methods. Most respondents said the detailed information in prescription drug ads was easy to understand. However, most seniors (64%) thought the information was confusing and too technical.

Schommer et al. 1998

In this study, patients waiting for appointments at a university-based general medicine clinic were asked to view a 60 second televised ad for the non-sedating antihistamine fexofenadine (Allegra) and complete a questionnaire.[88] The aim was to assess 'rote learning' or information retention soon after seeing the ad. Of the 600 patients asked to participate in the study, 177 agreed and provided useable responses (29.5% response rate) to a questionnaire with 20 statements about the contents of the ad. On average 72% of the 20 items were answered correctly by respondents. Risk, benefit and neutral information were all well remembered. Only in one case did contradictory benefit and risk information affect responses: the ad stressed the product's major claim for 'non-drowsy allergy relief', but also included a risk statement that 1 in 100 people experience drowsiness. More than half (51.4%) disagreed that the drug provided non-drowsy relief and only 53.1% remembered that 1 in 100 became drowsy. Some respondents may not have forgotten the major claim; they may have been expressing reservations about it. This study only assessed memory and rote learning, not judgment or information quality.

Williams and Hensel, 1995

This study relied on a convenience sample of 132 people aged 60 and over, residents of retirement communities in a city in Ohio and community residents in a town in Pennsylvania.[89] Participants were asked about attitudes to DTCA and were given a print ad for a nitroglycerin patch for angina, along with a questionnaire on intent to seek additional information. More respondents said they would seek additional information from a physician than from a pharmacist or a friend. A positive attitude to DTCA, assessed before a person viewed the ad, was significantly associated with the decision to seek additional information after seeing it. Lower education level and worse health status

were associated with more favorable attitudes to DTCA.

Conclusion: Consumer Surveys

Although consumer surveys frequently rely on recall over long periods of time and hence may be subject to bias, this body of research is strongly consistent, suggesting that advertising is affecting behaviours. Between 5 and 19% of Americans have requested a drug from their doctor in response to advertising, and most appear to have received requested drugs.

Studies of consumer responses to specific ads suggest that the presentation of information strongly influences perceptions of product characteristics. A U.S. survey found that the public believed that products were safer if less risk information was provided; a New Zealand survey found that a significant minority of viewers believed an ad gave them the information they needed to make a treatment decision, although this ad was later judged to be illegal due to inadequate information. Between one-fourth and one-half of respondents to two surveys believe they are better protected by regulatory safeguards than is the case, and many cannot explain prescription-only status. This raises concerns that the public is taking action in response to ads without a clear understanding of the context in which advertising messages occur.

Although there is evidence that advertising influences consumer behaviours and that the content of ads affects perceptions, no research thus far has measured positive or negative health impacts.

2.4.4 Surveys of Health Professionals

Fewer surveys have been carried out of health professionals than consumers. Most are opinion surveys of doctors on DTCA and their experience of patient requests and other activities stimulated by advertising. On the whole, doctors' opinions of DTCA have tended to be more negative than those of consumers. Whether this reflects a paternalistic approach to the patient-doctor relationship, or the desire to protect patient-doctor relations

from commercial pressures, is controversial.[90 91] Only one survey of doctors has been published in the peer-reviewed medical literature, an opinion survey of U.S. family practitioners by Lipsky and Taylor.[18] Time magazine carried out a mail survey of doctors in 1998, and two additional unpublished surveys, one in Canada [75] and the other in the United States[92] are described in the literature. Table 2.24 lists the surveys of health professionals described in the medical and marketing literature with adequate description of sampling methodology to assess the generalizability of survey results. Many other market research surveys have been carried out, but no information is provided on sample selection or response rates, making it impossible to judge validity of results.

Four surveys of health professionals had response rates below 25% and thus are excluded: the U.S. physician survey by *Time* magazine (response rate 21%),[20] a published analysis of a 1995 Scott-Levin physician survey, [93] a survey of Louisiana pharmacists (response rate 18%),[21] and a Canadian Master's thesis examining physicians' attitudes (response rate 19.5%).[94] None of the authors investigated potential differences between respondents and non-respondents, and given the controversial nature of DTCA among health professionals, the likelihood of systematic differences between respondents and non-respondents is high.

Given the paucity of data on physician experiences with methodology adequately described, results of market research surveys in the U.S. and New Zealand are summarized. These surveys generally provide little detail on sampling techniques or response rates.

Table 2.24: Surveys of Health Professionals (N=3 included; 6 summarized)

Study	Main Outcomes Assessed	Methodology	No. of subjects
Random samples of U.S. health professionals			
U.S. FDA, 2003	▪ Most recent patient who initiated a discussion on a DTCA drug ▪ Attitudes to patient requests ▪ Pressure to prescribe	▪ Phone survey; response rate 46% ▪ 50% GP's, 50% specialists (dermatology, psychiatry, allergy/pulmonology, endocrinology)	500
Lipsky and Taylor, 1997	▪ Awareness, attitudes to DTCA ▪ Effects on patient/doctor relations ▪ Patient requests ▪ Hypothesized benefits & harms	▪ Mail survey of family physicians ▪ response rate 48%	419
Summarized studies that do not meet inclusion criteria (limited description of sampling methods)			
Pirisi, 1999; Spurgeon, 1999	▪ Attitudes to DTCA ▪ Patient requests ▪ Pressure to prescribe	▪ Family physicians identified as high prescribers of statins ▪ Phone survey ▪ Sampling methods not stated	199
IMS Health, 1997, 1998	▪ Attitudes to DTCA ▪ Patient requests ▪ Effect on doctor/patient relations	▪ Sample of participants in Physicians On-Line; may be a panel survey ▪ Methods not stated	5000 (1997) 2500 (1998)
IMS Health 1998	▪ Effects on managed care ▪ Attitudes to DTCA ▪ Patient requests	▪ Managed care organization executives ▪ Sampling method not stated	100
Scott-Levin 1992, 1998	▪ Attitudes to DTCA ▪ Patient requests	• Doctors in a variety of specialties • Sampling method not described; may be a panel survey	3700 (1992) >3000 (1998)
IMS/ New Zealand Doctor, 1998	▪ Attitudes to DTCA ▪ Effect on doctor/patient relations	▪ Fax survey of GP's, with a 30% response rate ▪ Sampling methods not stated	121

Random Samples of U.S. Health Professionals

U.S. FDA, 2003

The U.S. FDA's Division of Drug Marketing, Advertising and Communication surveyed a random sample of 500 physicians (250 G.P's, 250 specialists in dermatology, allergy/pulmonology, psychiatry and endocrinology) about their experiences with patient consultations affected by DTCA. [19] Most of the physicians (85%) said that their patients initiate questions about prescription drugs 'often' or 'all the time', and 92% could recall a recent encounter with a patient who had initiated a discussion about a medicine in response to DTCA (n=459). Table 2.25 presents the key findings.

Table 2.25: FDA physician survey: experiences in consultations affected by DTCA

Most recent consultation in which a patient initiated a discussion about a drug they had seen advertised	# physicians* (N=459)
Any beneficial effect on patient/doctor interaction	**187 (41%)**
Better discussion with patient	99 (22%)
Patient more aware of treatments	79 (17%)
New condition was discovered	11 (2%)
Patient sought treatment for serious condition	4 (1%)
Any problems created for patient/doctor interaction	**84 (18%)**
Time correcting misconceptions	34 (7%)
Drug not needed or patient did not have condition	22 (5%)
Patient wanted a drug rather than other treatment	8 (2%)
Pressure to prescribe	4 (1%)
Drug requests and prescribing	
Patient asked about a specific brand name drug	395 (86%)
Patient asked for a prescription *Physician provided a prescription*	237 (52%) *178/237 (75%)*
Patient asked for a prescription for a specific brand name drug *Physician prescribed the requested brand*	211 (46%) *120/211 (57%)*
Pressure to prescribe ('a little', 'somewhat' or 'very' pressured)	**216 (47%)**
Any pressure: request for a prescription (Rx) Any pressure: request for specific brand Rx Any pressure: NO request for brand Rx	140/237 (59%) 129/211 (61%) 52/148 (35%)
Somewhat or very pressured: request for brand Rx Somewhat or very pressured: NO request for brand Rx	65/211 (31%) 16/148 (11%)
Patient tried to influence treatment in a way that could harm him or her	**37 (8%)**

*Numbers calculated from percentages and denominators provided by the FDA presentation

As shown in Table 2.25, on the whole, the physicians' attitudes towards DTCA were more often positive or neutral than negative. When asked about the most recent consultation affected by DTCA, 40% felt DTCA had affected their patients and practice positively versus 32% who felt it had a negative effect and 28% no effect. The most common beneficial effect was on the discussion with patients or patient awareness of treatments. The most common problem reported was time taken up correcting patients' misconceptions, as well as the drug being inappropriate for the patient.

Interestingly, although 47% of physicians reported some degree of pressure to prescribe, only 18% reported any problems created for the doctor-patient interaction, and only 1% spontaneously mentioned pressure as a problem. However, the physicians reported pressure in nearly two-thirds of consultations in which a patient had requested a specific brand, and were more likely to report pressure in consultations in which a patient had requested a brand than in other consultations. They also provided prescriptions in most

consultations in which patients requested a prescription (75%), and reported more than half the time that they had prescribed the specific brand name drug the patient requested.

This survey leaves key questions unanswered due to its methodology. The emphasis on the most recent patient consultation affected by DTCA is useful, in that it was likely to be associated with less recall bias than a more general question about patient requests over a longer time period. However, this survey describes an uncontrolled case series. It only examines consultations affected by DTCA; it does not compare those consultations to other consultations not influenced by advertising. Therefore, little can be said about the direction of effect DTCA is having on patient-doctor interactions. Is it leading to more or less pressure to prescribe than in other consultations? Do physicians feel more or less positive about the patient-doctor interaction? Is there any interaction between physicians' reliance on promotion and their attitudes towards patient consultations affected by DTCA or willingness to prescribe?

An FDA talk paper accompanying the release of preliminary survey results claimed that: "The results confirm that DTC advertising, when done correctly, can serve positive public health functions such as increasing patient awareness of diseases that can be treated, and prompting thoughtful discussions with physicians that result in needed treatments being prescribed – often not the treatment in the DTC advertisement." [95] Without data comparing these to other consultations, or independent review of patients' medical records, such a claim seems premature.

Lipsky and Taylor, 1997

Lipsky and Taylor sent a mailed questionnaire to a random sample of the active members of the American Academy of Family Physicians.[18] They sent out 880 questionnaires and received 454 responses of which 419 were useable (48% response rate). Female doctors were underrepresented in their sample (83% male).

Overall, 89% did not feel that DTCA enhances the doctor/patient relationship and 71%

believed physicians are pressured to use drugs they might not ordinarily use. However, most (60%) also felt that DTCA encourages patients to take a more active role in health care. The respondents reported having received an average of 6.9 requests in the last 6 months (range 0-100). The most common reports were for requests of antihistamines, antihypertensives, H2 blockers, and lipid lowering drugs.

The survey included open-ended questions about the potential benefits and disadvantages of DTCA. The 364 potential benefits listed were grouped into five major categories:

- Better informed patients/ increased awareness;
- Patients recognize a problem earlier, increase in office visits;
- Patients take a more active role in health care;
- Promotes patient/doctor communication;
- Improves patient compliance and acceptance of treatment.

In total, 591 potential disadvantages were listed, of which 469 were grouped into 8 categories:

- Raises false hopes, a misleading or biased view;
- Increased cost for drugs;
- Creates unnecessary/ inappropriate demand;
- Creates conflict between patients and physicians;
- Confuses the patient, causes anxiety;
- Promotes self-diagnosis or self-treatment;
- Promotes superficial knowledge;
- Promotes an 'easy answer', a 'pill for every ill'.

Lipsky and Taylor's sample has been criticized in a report by the American Medical Association's Board of Trustees as not being representative of all U.S. primary care physicians because the population they sampled from were only active members of the American Academy of Family Physicians.[96] However, the response rate was better than other surveys of U.S. physicians (see below). It is also mainly an opinion survey, but

provides some indication of the experiences and attitudes of family doctors. Opinions of respondents may differ from non-respondents, however. Reporting of frequency of requests is unlikely to be accurate, as it is based on recall and doctors see many patients per week. However, the results of this survey do raise serious doubts about claims that DTCA enhances the doctor/patient relationship, given that 9 out of 10 doctors surveyed reported that it did not enhance this relationship.

Surveys with inadequately described sampling methodology

The following surveys do not meet study inclusion criteria because of the lack of adequate description of sample methodology. They are briefly summarized below because of the paucity of available research on physicians' experiences.

Pirisi, 1999; Spurgeon 1999

News reports were published in the *Lancet*[92] and the *BMJ*[97] of an as yet unpublished telephone survey of 199 U.S. primary care doctors, reported at a meeting of the American Association of Pharmaceutical Scientists in November 1999 and funded by Johnson & Johnson. The selection procedure is not described, but some of the doctors were selected because they are high prescribers of statins.

On average physicians reported that five patients per week asked them to prescribe a specific drug. The most frequently reported information sources were TV ads, followed by print ads and TV and print news stories. The information was judged to be only 'partially accurate' by 52% of the physicians and 'mostly accurate' by 42%. Thirty-eight percent reported very little pressure from patients 'informed by advertising, 47% a little pressure, and 6% a lot of pressure. Only 9% reported no pressure at all. More family physicians (42%) than internists (32%) said that they had prescribed medicines in response to patient requests.

IMS Health surveys

IMS Health has carried out a number of surveys of physicians participating in the Internet service Physicians On-Line, an ongoing physician panel, on their attitudes to DTCA. In 1997, 90% of a sample of 5000 doctors said that either the same number or more patients asked them for brand name drugs as during the previous year.[98] In this 1997 survey, 61% of physicians said they would like to see DTCA decrease or stop. [99]

In a similar 1998 survey of 2500 doctors participating in Physicians Online, the proportion wishing to see DTCA decrease or stop had increased to 65%.[100] Fifty-three percent of the 1998 respondents reported an increase in the number of consumers requesting prescription drugs in response to ads as compared to the same time one year ago. Fifty percent strongly or somewhat disagreed that DTCA contributes to a stronger doctor/patient relationships and only 21% agreed.

In 1998 IMS also surveyed 100 medical and pharmacy directors from managed care organizations on their opinions and experiences with DTCA.[101] Only 13.5% of the managed care executives thought that DTCA contributes to a stronger doctor/patient relationship. Nearly half of the managed care executives, 48%, said that they had experienced an increase in requests to include advertised drugs in their formularies..[102]

Scott-Levin surveys

The market research firm Scott-Levin also specializes in DTCA and carries out regular audits of doctors and consumers on their experiences and attitudes to DTCA.

In 1992, Scott-Levin surveyed 3700 doctors in 14 specialties on their experiences and attitudes to DTCA.[103] They reported an increase in the number of patients initiating discussions about prescription drugs and bringing in advertisements for drugs. In a 1989 Scott-Levin survey, 45% of doctors said that patients had requested a drug by brand name versus 83% in 1992. Most of the physicians said that they learned of DTCA campaigns from their patients, not from the sponsoring companies. Fifty-six percent were opposed to

DTCA but 84% said they would at least consider prescribing a drug a patient requested.

In a 1998 Scott-Levin survey of over 3000 doctors, more than 60% disagreed with the statement that DTC is a reliable source of information and that it gives the public information they can't get anywhere else. The most negative responses were from infectious disease specialists, cardiologists and pediatricians.[104] The physicians reported that sildenafil (Viagra) and finasteride (Propecia) were among the top 10 products patients requested, and that consumers were most likely to discuss drugs or conditions they'd seen advertised during a routine visit, rather than specifically planning a visit in response to DTCA.[105] The FDA's 1999 consumer survey similarly found that patients were more likely to report discussing advertised drugs in a consultation made for another reason, rather than making a doctor's appointment solely in response to DTCA.

IMS/New Zealand Doctor survey

In June 1998, IMS and *New Zealand Doctor*, a free weekly medical bulletin, carried out a fax poll of 400 general practitioners, with a response rate of 30% (N=121). The reported margin of error is +/- 8.7%. As in surveys of U.S. doctors, New Zealand GP's were on the whole negative:

- 75% either want DTCA to stop altogether or to decrease
- 16% want levels to remain the same
- 7% would like to see an increase
- 61% believe DTCA creates disharmony in doctor/patient relationship
- 62% believe DTCA is of no benefit to patients.[106]

Conclusion: surveys of health professionals

DTCA's effects on the work of physicians and other health professionals, and on the doctor/patient relationship, remains little studied. Market research companies have carried out many surveys, but these surveys primarily measure physicians' opinions, with only a few questions on experiences of patient behaviours stimulated by advertising. They generally cover past events over long periods of time, making them susceptible to recall

bias, and little information is provided on methods. Lipsky and Taylor's 1997 survey was carried out in 1994, before the relaxation of regulations governing U.S. television advertising, when population exposure levels were much lower than today. The FDA's physician survey measures physician experiences within an environment with heavy patient exposure to both broadcast and print DTCA, in 2001-2002. The approach used by the FDA minimizes the probability of recall bias because it asks about a specific encounter, the most recent consultation with a patient who mentioned a medicine in response to advertising. However, only preliminary results have been made public thus far. The FDA survey results suggest that although physicians' attitudes were more likely to be positive than negative towards DTCA-induced requests, they often reported pressure to prescribe, and this was most likely in consultations in which a patient had asked for a prescription for a specific brand-name drug. Physicians usually provided prescriptions to patients who requested them, although not always for the requested brand.

2.4.5 Retrospective Data Analyses

Table 2.26 describes studies that have used administrative and sales databases to examine the association between DTCA spending and drug prescribing and sales.

Table 2.26: Retrospective data analyses

Study	Main Outcomes Assessed	Methodology
National Institute of Health Care Management (NIHCM) 1999-2001 reports on DTCA & retail prescription drug spending		
Barents 1999	• Factors affecting growth in prescription drug expenditures • Drug classes responsible for spending increases • DTCA spending per class	▪ Data on DTCA from IMS Health and Competitive Media Reporting (CMR); ▪ Data on retail spending, prescriptions, from Scott Levin
Findlay, 2000	▪ Increase in retail drug spending in 1999 over 1998 levels attributable to top 25 DTCA drugs vs. other drugs	▪ Data on DTCA from IMS Health and CMR ▪ Data on retail spending, prescriptions, from Scott Levin
Findlay, 2001	▪ Increase in retail drug spending in 2000 over 1999 levels attributable to top 50 DTCA drugs vs. other drugs	▪ Data sources/ methodology same as above
Other reports		
Rosenthal et al, 2002	▪ Spending on DTCA vs other forms of promotion:1996-2000 ▪ Ad spending vs. sales 1996-2000	▪ Data from IMS Health and CMR ▪ 5 drug classes: antidepressants, antihistamines, statins, nasal sprays, PPI's
Zachry et al, 2002	▪ No. of diagnoses for conditions treated by DTCA drugs ▪ # Rx within drug class versus DTCA spending ▪ # Rx vs. DTCA spending	▪ Data from CMR for ad spending ▪ National Ambulatory Medical Care Survey (1992-1997) for diagnoses and prescriptions ▪ Time series analysis
PHARMAC, 2002	▪ DTCA spend for 4 subsidized drugs vs. sales and # Rx, 1999-2001 ▪ Volume & substitution effects	▪ Data on DTCA from IMS Health ▪ Spending and # of scripts, administrative data, New Zealand drug plan (PHARMAC)
Wosinska, 2001	▪ # Rx for advertised drugs ▪ Effects of DTCA by drug formulary status ▪ Product switching within class	▪ 1996-1999 data Blue Shield, ▪ # Rx for lipid-lowering drugs ▪ Data on DTCA and drug detailing from CMR
Eichner and Maronick, 2001	▪ DTCA spending vs. sales ▪ drugs for allergy, nail fungus, high cholesterol, depression	• DTCA data from CMR, prescribing data Scott-Levin • 1996-1998: 16 drugs -4 classes
Basara, 1996	▪ Increased prescribing and sales for Imitrex (sumatripan) vs. DTCA spending	• Four regional campaigns • Individual physician prescribing data from IMS Health • 7 month time series analysis

NIHCM: Effects of DTCA on U.S. Retail Drug Spending 1993-2000

The National Institute of Health Care Management (NIHCM), a non-profit foundation, published a report in July 1999 outlining factors affecting the growth in prescription drug expenditures in the U.S. between 1993 and 1998.[55] This report highlights the importance of growth in spending on new drugs within four heavily advertised drug classes: oral antihistamines, antidepressants, lipid lowering drugs and anti-ulcerants. NIHCM followed this report with two additional analyses specifically examining the relationship between DTCA and annual increases in retail prescription drug expenditures, published in 2000[107] and 2001.[108] As these reports follow one another as a progressively more detailed examination of the same phenomenon, they are discussed in chronological order below.

Barents 1999

U.S. retail spending on prescription drugs increased from $50.6 billion in 1993 to an estimated $93.4 billion in 1998, an 84% increase over a five-year period. Four categories of drugs accounted for 30.8% of this increase: oral antihistamines, antidepressants, lipid lowering drugs and anti-ulcerants. These categories include seven of the ten drugs most heavily advertised to the public in 1998.

Table 2.27 Increase in Spending in four Therapeutic Classes, 1993 to 1998

Drug category	Increase in expenditures 1993 – 1998 (U.S. $ billions)	% of total increase in prescription drug costs
Antidepressants	$ 5.0	11.8%
Lipid lowering drugs	$ 3.4	8.0%
Anti-ulcerants	$ 2.7	6.4%
Oral antihistamines	$ 1.9	4.5%
Total - four categories	**$13.1**	**30.8%**

Adapted from: Barents Group,1999, Figure A, p2

DTCA spending is highly concentrated. In 1998, U.S. $706.9 million, or 54% of total DTCA spending, went towards promoting ten products to the public. These ten drugs alone accounted for 22% of the total increase in retail pharmaceutical sales in the U.S. between 1993 and 1998.

Table 2.28 The 10 Drugs with Highest DTCA Spending in 1998

Drug	1998 sales US$ millions	Share of 1998 retail sales	Therapeutic category	Share in therapeutic category	Spending on DTCA US$ millions
Claritin (loratadine)	2,140.0	2.3%	Antihistamine	62.2%	185.1
Propecia (finasteride)	72.7	0.1%	Baldness	41.4%	92.0
Zyrtec (cetirizine)	454.9	0.5%	Antihistamine	18.6%	75.6
Zyban (bupropion)	183.8	0.2%	Smoking cessation	82.8%	64.4
Pravachol (pravastatin)	953.6	1.0%	Lipid lowering	18.3%	59.7
Allegra (fexofenadine)	432.0	0.5%	Antihistamine	13.6%	52.5
Prilosec (omeprazole)	2,945.0	3.2%	Ulcer/ reflux	44.7%	49.7
Zocor (simvastatin)	567.3	1.7%	Lipid lowering	30.1%	44.5
Evista (raloxifene)	99.8	0.1%	Osteoporosis	19.3%	42.3
Prozac (fluoxetine)	2,346.0	2.5%	Antidepressant	32.9%	41.1
Total above	**11,195 (12.0% of total sales)**	**12.0%**		**Mean=36.4%**	**$707 (53.9% of DTCA spend)**

Adapted from: Barents Group1999; Table 4, p13

From January to June 1999, the top five drugs advertised on television, by spending, were treatments for: allergy, baldness, obesity, and allergic rhinitis (two products); the top five drugs in print advertisements were for: allergy, type II diabetes, impotence and high cholesterol.[109]

Higher prices per prescription were responsible for 64% of the 1993-1998 increase in retail prescription drug spending, according to NIHCM, and the use of new, costlier drugs was identified as the primary factor driving this increase. In 1998, the average price of drugs introduced in 1992 or later was $71.49, as compared to an average price of $30.47 for drugs introduced before 1992.

Findlay, 2000

In a follow-up analysis of the effects of DTCA on pharmaceutical costs, NIHCM found that the top 25 drugs promoted directly to consumers were responsible for a U.S. $7.2 billion increase in U.S. retail pharmaceutical costs in 1999 over 1998 costs, or 40.7% of the total $17.7 billion increase in retail drug spending. They also found that doctors wrote 34.2% more prescriptions for these 25 products in 1999 than 1998, as compared to a 5.1% increase in prescribing volume for all other prescription drugs.[108]

Table 2.29 describes the contribution to drug sales of the 10 products with top DTCA spending, representing 41% of total DTCA spending. Only four of these products were also on the 1998 top 10 list for DTCA spending: loratadine (Claritin), cetirizine (Zyrtec), omeprazole (Prilosec) and fexofenadine (Allegra). However, the degree of concentration in DTCA spending is similar, as is the proportion of total prescription drug sales (11% vs. 12% in 1998) represented by this small number of drugs. Additionally, they contributed to the annual increase in U.S. retail spending to a similar degree (~20% versus 22%). This suggests a similar pattern of advertising spending as in 1998, highly concentrated on a few 'blockbuster' drugs.

Table 2.29 The 10 Drugs with Highest DTCA Spending in 1999

Drug	Indication	1999 DTCA Spending US$ millions	1999 sales US$ millions	Change in sales 1998-1999	Contribution to increased spending 1998-1999
Claritin (loratadine)	Allergy	137.1	2,591.1	+21.1%	2.6%
Prilosec (omeprazole)	Ulcer/reflux	79.4	3,649.4	+28.9%	4.1%
Xenical (orlistat)	Obesity	76.2	144.7	N/A*	0.8%
Zyrtec (cetirizine)	Allergy	57.1	551.5	+31.5%	0.8%
Lipitor (atorvastatin)	Lipid lowering	55.5	2,659.9	+55.7%	5.5%
Flonase (fluticasone)	Allergic rhinitis	53.5	489.5	+37.9%	0.8%
Nasonex (mometasone)	Allergic rhinitis	52.3	264.0	+116.1%	0.8%
Ortho tri-cyclen	contraceptive	50.1	431.5	+58.2%	0.9%
Glucophage (metformin)	Diabetes	43.1	1,157.8	+48.7%	2.2%
Allegra (fexofenadine)	Allergy	42.8	423.9	+50.0%	1.0%
Top 10 DTCA drugs		***647.1 (41% of DTCA spend)***	***12,363.3 (11% of total Rx drug sales)***	***Mean=50.0%***	***19.5%***

Adapted from: Findlay, 2000. Figure 3, page 4;
* launched in this period

Findlay, 2001

A follow-up NIHCM report in 2001 again examined the relationship between DTC advertised drugs and annual increases in retail drug sales.[108] In this report, Findlay examines the contribution of the 50 top DTCA drugs to sales. These 50 drugs represent almost all DTCA spending in 2000 (94.8%), and together they were responsible for U.S. $.9.9 billion, or 47.8%, of the $20.8 billion increase in retail spending over 1999 levels. They had combined sales of $41.3 billion, or 31.3% of total retail prescription drug sales.

Retail sales increased by 32% for these 50 drugs in 2000, as compared to an increase of 14% for all other drugs combined, and the number of prescriptions rose by 25%, as compared to a 4% increase in all other drugs.

Table 2.30 The 10 Drugs with Highest DTCA Spending in 2000

Drug	Indication	2000 DTCA spending US$ millions	2000 sales US$ millions	Change in sales 1999- 2000
Vioxx (rofecoxib)	Arthritis	160.8	1,518.0	+360.7%
Prilosec (omeprazole)	Ulcer/reflux	107.5	4,102.2	+12.4%
Claritin (loratadine)	Allergy	99.7	2,035.4	+14.9%
Paxil (paroxetine)	Antidepressant	91.8	1,808.0	+24.5%
Zocor (simvastatin)	Lipid lowering	91.2	809.4	+22.2%
Viagra (sildenafil)	Impotence	89.5	2,015.5	+31.2%
Celebrex (celecoxib)	Arthritis	78.3	618.7	+58.0%
Flonase (fluticasone)	Allergic rhinitis	73.5	1,120.4	+26.4%
Allegra (fexofenadine)	Allergy	67.0	113.2	+61.8%
Meridia (sibutramine)*	Obesity	65.0	652.7	-8.1%
Top 10 DTCA drugs		**924.3 (41% of DTCA spending)**	**14,793.5 (11% of total Rx drug sales)**	**Mean=+60.4%**

*safety concerns prompting a market withdrawal in Italy may have affected sales.

Table 2.30 above presents the contribution to sales of the top 10 drugs, by DTCA spending during 2000. The proportion of total DTCA spending on just 10 products was 41% in 2000, as in 1999, and these 10 products again represented 11% of the U.S. retail pharmaceutical market. The overlap between the year 2000 and 1999 'top 10' DTCA products was again 4 of the 10 products.

The three NIHCM reports summarized above indicate a strong association between annual increases in prescription drug spending and the most heavily advertised products. A small number of heavily advertised products contributed disproportionably to annual retail expenditures on prescription drugs, mainly through higher prescribing volume and sales, rather than through price increases. This is consistent with the expected direction of effect of DTCA, and suggestive of a causal effect. However, the authors were unable to distinguish between increased sales stimulated by DTCA alone, by promotion aimed at physicians alone, or by the combined effects of these two marketing techniques. Other factors may have also influenced prescribing volumes, such as publication of favourable

trial results, or formulary inclusion by large managed care companies.

Rosenthal et al. 2002

Meredith Rosenthal and colleagues compared industry spending on DTCA to spending on promotion aimed at physicians between 1996 and 2000.[3] They also examined data on sales versus DTCA spending for five heavily advertised therapeutic classes, antidepressants, antihistamines, lipid-lowering drugs, corticosteroid nasal sprays and proton pump inhibitors. Table 2.31 presents an overview of U.S. promotional spending over this time period.

Table 2.31: U.S. Spending on DTCA and promotion aimed at physicians: 1996-2000

	Promotional Spending (in US$ millions)				
	1996	**1997**	**1998**	**1999**	**2000**
Estimated spending on promotion to physicians*	9,503	11,261	12,663	13,643	15,029
DTCA spending	791	1,069	1,316	1,848	2,467
Percent of DTCA spending on television ads	28%	29%	50%	61%	64%
Total estimated promotional spending	10,294	12,330	13,979	15,491	17,496
Percent of promotional spending on DTCA	8.3%	9.5%	10.4%	13.5%	16.4%
DTCA spending as a percent of sales	1.2%	1.5%	1.6%	1.8%	2.2%
Total promotional spending as a % of sales	**15.8%**	**17.2%**	**17.1%**	**15.2%**	**15.6%**

Adapted from: Rosenthal et al, Table 1, p 500

*Promotion to physician recalculated to include an estimated 13.5% on meetings and events, as described by Rosenthal et al. (p. 499; Methods, range 12-15%) Rosenthal et al's Table 1 omits this category

Although the industry spent much more on promotion aimed at physicians than on DTCA, the proportion devoted to DTCA increased continually over this time period. By 2000, spending on DTCA had more than tripled over 1996 levels. In 2000, the industry as a whole spent nearly twice as much on print DTCA as on print advertising in health professional journals.

Rosenthal et al. examined advertising intensity within five drug classes: antidepressants, antihistamines, lipid-lowering drugs, corticosteroid nasal sprays and proton pump inhibitors (PPI's). They found that spending on DTCA as a proportion of sales varied much more per drug class than spending on promotion aimed at physicians. In 1999, the category with the highest DTCA advertising intensity (11.6% of sales) was nasal sprays.

In contrast, DTCA spending reached only 0.5% of sales for antidepressants. This was a 23-fold difference in advertising intensity. For promotion aimed at health professionals (omitting sponsored meetings and events), the highest advertising spending was also on nasal sprays, at 24.7% of sales. However, this was only a 2.8-fold difference in advertising intensity as compared to the category with the lowest spending among the five, lipid-lowering drugs (8.7% of sales).

Zachry et al, 2002

Zachry et al. carried out a retrospective data analysis to examine whether a relationship existed between prescriptions for an advertised drug, prescriptions for drugs within the same class, and frequencies of diagnoses for approved indications of advertised drugs and monthly advertising spending.[110] They combined data from the National Ambulatory Medical Care Survey (NAMCS) and information on monthly advertising spending obtained from Competitive Media Reporting. The NAMCS includes 195,577 consultations between 1992 and 1997, weighted to be representative of the U.S. population.

Zachry et al. only included drugs and drug classes advertised for at least 19 months within this time. From 1992-1997, 121 drugs within 48 drug classes were advertised to the U.S. public, with 80% of spending on full product advertising, and only 4.4% on 'help-seeking' or disease-oriented ads that make no mention of brand name. Nineteen of these drugs, within 5 drug classes, met the study inclusion criteria. The five classes were: antihistamines, antihypertensives, acid-peptic disorder drugs, benign prostatic hypertension (BPH), and lipid lowering drugs.

For lipid-lowering drugs, spending was significantly associated with diagnoses: for each $1000 spent on DTCA for lipid-lowering drugs, 32 additional diagnoses and 41 prescriptions were generated. For antihistamines, a strong substitution effect was observed within the class, with every $1000 spent on DTCA for loratadine (Claritin) associated with 24 additional prescriptions for loratadine (Claritin), 20 fewer for

terfenadine (Seldane) and 7 fewer for astemizole (Hismanal). No significant association was observed between spending on antihypertensives and BPH drugs and the number of diagnoses or prescriptions.

In two cases prescriptions for leaders within the class – loratadine (Claritin) and simvastatin (Zocor) – were positively associated with total spending within the class, as well as drug-specific spending.

The authors caution that causality cannot be assumed, and that DTCA expenditures accounted for a modest amount of variance (10-30%) associated with diagnoses and prescribing. However, this study represents the first published report to combine retrospective data on diagnoses and prescriptions with DTCA spending data. The differences the authors observed between drug classes are also consistent with market factors. For example, the majority of lipid-lowering drugs with strong sales performance are advertised to the U.S. public, and therefore both product-specific and class effects might be expected. However, most antihypertensives are not advertised to the public, and overall spending on DTCA within this class is lower than for lipid lowering drugs. This is consistent with the lack of association between monthly advertising spending and diagnoses or prescriptions within this class.

PHARMAC, 2002

In an unpublished report to the New Zealand Ministry of Health, New Zealand's public pharmaceutical management agency, PHARMAC, examined prescribing volumes and costs for four subsidized products that had been advertised to the New Zealand public between 1999 and 2001.[111] These were fluticasone (Flixotide), terbinafine (Lamisil), omeprazole (Losec) and eformoterol (Oxis Turbuhaler). This is the only analysis of the effects of DTCA on costs of publicly financed pharmaceuticals.

Table 2. 32: New Zealand DTCA spending for four products during 2001

Product	Total DTCA Spending (CDN $ equiv)	Print	TV	Radio
Flixotide (fluticasone)	$1,469,173	6%	94%	-
Lamisil (terbinafine)	$613,589	19%	81%	-
Losec (omeprazole)	$867,352	15%	75%	10%
Oxis Turbuhaler (eformoterol)	$998,006	12%	88%	-

Source: PHARMAC, 2002. Adapted from: Table 1, page 4

During the period from 1999 to 2001, the number of prescriptions grew for all four products. Table 2.33, below, provides information on the number of prescriptions per year and cost differences had prices remained stable (standardized to May 2002 prices).

Table 2.33: Increases in expenditure and script numbers from 1999 – 2001

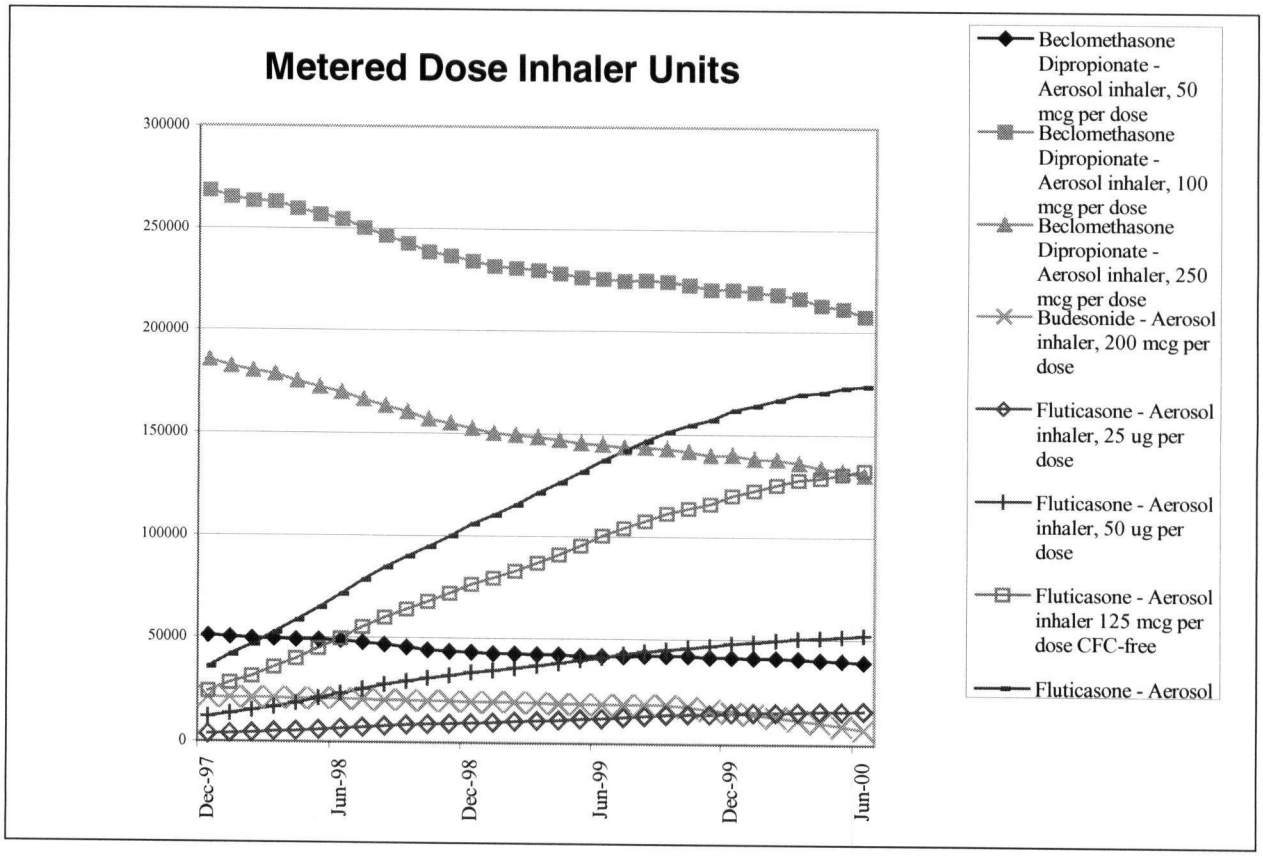
	No. of prescriptions/year			2001 vs. 1999	
Product	1999	2000	2001	% increase in no. of prescriptions	% increase in spending at May 2002 prices*
Flixotide (fluticasone)	184,608	216,021	269,584	46%	54%
Lamisil (terbinafine)	10,161	13,415	15,661	54%	64%
Losec (omeprazole)	294,888	337,076	327,583	11%	18%
Oxis Turbuhaler (eformoterol)	2,012	4,094	21,017	945%	704%

*May 2002 prices used as subsidy prices for some products changed during this period

Real growth in expenditure on these four products was more than NZ$3.66 million (CDN $2.94) from 1999 to 2001. This is a lower fiscal risk than might have occurred without other policies implemented by PHARMAC, including negotiated price reductions for fluticasone (Flixotide) in mid 1999 and a manufacturer surcharge for omeprazole (Losec) in April 2001, in both cases in response to increased prescribing volumes.

PHARMAC tracked shifts in prescribing volume for metered dose corticosteroid inhalers used to treat asthma in the period from January 1998 to June 2000.[112] They documented a substitution effect from less expensive beclomethasone inhalers, which are off patent and therefore not advertised, to fluticasone (Flixotide). Television advertising campaigns had encouraged patients to switch to fluticasone if their asthma was 'not controlled'. This substitution effect occurred in spite of a lack of reliable evidence of greater effectiveness or safety for fluticasone versus other steroid inhalers such as beclomethasone.[113]

Figure 2.1: Numbers of Corticosteroid Metered Dose Inhalers Dispensed, 1998-2000



Source: PHARMAC, 2000. Adapted from Graph 1, page 4

These data do not allow for attribution of a causal effect between DTCA and increased prescribing volume for fluticasone, as fluticasone inhalers were most likely also promoted heavily to physicians during this time period. These are also aggregated data on population prescribing patterns, which do not allow for examination of individual switching from beclomethasone to fluticasone versus differences in product choice for initial prescriptions for a steroid inhaler for asthma. Thus the extent of substitution of fluticasone for beclomethasone among individuals who incorrectly believed that the advertised product was superior to the steroid inhaler they were already using is unknown.

Wosinska, 2001

In an unpublished report, Marta Wosinska has analyzed the relative contributions of DTCA and promotion aimed at physicians on shifts in prescribing of cholesterol-lowering

drugs within a population insured by Blue Shield of California's PPO plan.[114] She analyzed data covering over 38,000 patients who filled a prescription for one or more cholesterol-lowering drugs between 1996 and 1999. Prescribing data were matched to monthly brand-level DTCA spending, obtained from Competitive Media Reporting, and monthly, brand-level spending on sales representatives and free sampling.

Preliminary results indicate a strong association between product choice and DTCA spending. However, the impact is diminished if physician detailing and free samples are taken into account, and the estimated impact of detailing is five times that of DTCA. She also found that although spending on DTCA strongly affects product choice, the effect for drugs that were on Blue Shield's formulary was three times that of drugs not on the formulary. Thus the effects of DTCA on product choice appeared to have been mediated by decisions related to formulary inclusion.

Eichner and Maronick, 2001

Eichner and Maronick compared DTCA spending and sales data from 1996 to 1998 for products within four heavily-advertised drug classes: antihistamines, lipid-lowering drugs, antidepressants and antifungal drugs for toenail fungus.[115] This is based on annual advertising spending and sales data obtained from Competitive Media Reporting and Scott-Levin.

Between 1996 and 1998, there was a 2.5-fold increase in prescriptions for three heavily-advertised antihistamines, loratadine (Claritin), fexofenadine (Allegra), and cetirizine (Zyrtec), a much greater increase than in overall drug prescriptions within this time period. This was not accounted for by substitution of these newer products for older antihistamines; the proportion of patients prescribed an antihistamine for allergy increased. The authors were unable to examine whether patients had previously used over-the-counter medications, or whether they were treating symptoms they had previously managed without medicines. For nail fungus treatments, prescriptions within the class increased by over 50% between 1996 and 1998, although DTCA spending

decreased within this time period. This could reflect awareness raising for the condition and/or other promotional spending. The authors also did not examine whether lagged effects occurred.

For lipid-lowering drugs, the authors found a stronger class than product-specific effect. The authors calculated the degree of correlation between product-specific DTCA spending and the product's market share within its class. Their results are generally inconclusive, especially in drug classes with several competitors. This is likely to reflect the many factors that remain unexamined, such as the date of a product's launch, product-specific characteristics (such as therapeutic advantages or disadvantages), and spending on promotion aimed at physicians.

Basara 1996

Lisa Basara used the launch of sumatriptan (Imitrex) for migraine in February 1993 as a test case to examine the effects of a DTCA campaign.[8] She used a time series analysis to look at the volume of new prescriptions before and after a seven month DTCA campaign. Data from four cities were used. Albany, Erie, Grand Rapids, Boise City. They were chosen because of similar demographics and physician prescribing levels. The four cities had a joint population of 1.1 million and 2419 doctors. Physician-specific data were available for 73% of the doctors through IMS, which buys these data from dispensing pharmacies. All physicians in the four regions with at least one dispensed prescription were included in the study.

The sumatriptan (Imitrex) advertising campaign did not include the product name, but it mentioned a 'surprisingly effective' new treatment for migraine and said to go see your doctor. As this was the only migraine therapy being actively promoted to doctors, such an approach was expected to pay off. Thus this is a study of the effectiveness of 'help-seeking' DTCA in generating sales.

The interrupted time series analysis included eleven months before the launch of the DTCA campaign, seven months during an active campaign, and four months afterwards.

The primary hypothesis tested was whether the number of new prescriptions would increase significantly after consumers were exposed to DTCA. Basara found the DTCA campaign to be a significant predictor of new prescription volume (p=.0006). She estimates that 1620 new prescriptions could be attributed to the seven-month campaign in these four cities. Extrapolating to the entire U.S. population, this campaign would have generated about $11.5 million for the company in new prescriptions, and nearly as much again could be expected in refills.

DTCA was entered into this analysis as a binary variable representing presence or absence of consumer-directed advertising within specific months, with lagged effects also included within the model. Basara's analysis explored whether a relationship was found between DTCA presence and increased prescribing volumes; she did not include differences in the amount spent on DTCA per month in her model and was therefore unable to estimate returns on advertising investment.

This is the only published study using a time series analysis of physician-specific data to assess the effects of a DTCA campaign. Promotion of this product to physicians preceded the DTCA campaign and continued afterwards. Thus, this analysis identified increases in prescribing associated in time with the DTCA campaign and probably attributable to it.

Conclusion: retrospective data analyses

The administrative data analyses described above indicate an association between heavily advertised products and increases in prescribing volume and drug costs. In other words, they strongly suggest that, as intended by manufacturers, DTCA does stimulate drug sales. The NIHCM reports have found a strong association between the most heavily advertised products and therapeutic classes, and large annual increases in retail prescription drug costs in the U.S. This occurred through an increase in prescribing volume for expensive heavily advertised products.

Zachry et al. found an association between monthly spending on DTCA and increases in

diagnoses for conditions treated by advertised conditions as well as for prescriptions for specific products. For lipid lowering drugs, both the drug class and individual products appeared to benefit. This is consistent with the pattern of advertising that has occurred within this class, with competing products advertised to the public. For antihistamines, increased prescribing for heavily advertised products was accompanied by a reduction for older products that are not being advertised to the public. This is similar to the pattern observed by PHARMAC in New Zealand, with a concurrent increase in prescription volume for fluticasone inhalers and a reduction in volume of beclomethasone inhalers. The experience in New Zealand suggests that some beclomethasone users (and their physicians) may have been unaware that the two products were essentially equivalent, except in price.

Wosinska found a strong association between monthly spending on DTCA and choice of lipid lowering drug within an insured population in California. However, when promotion aimed at physicians (drug detailing) was entered into the model, the association became weaker, and her results suggest that drug detailing remains a dominant means of shifting prescribing choice.

Taken together, the administrative database analyses suggest that DTCA does contribute to increased prescribing volumes for heavily advertised drugs. However, most of these analyses cannot separate out the effects of DTCA from promotion aimed at physicians, and therefore do not allow for calculation of the proportion of new prescriptions stimulated by DTCA versus those stimulated by physician-directed promotion, or of interactions between the two.

2.4.6 Effects of DTCA on Use of Health Care Services

Effects of DTCA on many aspects of health care service use remain largely unexamined, such as the decision to consult a physician, effects on managed care and formulary development, disease management, and the association between DTCA and direct Internet sales of prescription drugs. In some cases market research companies have

examined these outcomes. These reports generally contain few details on methodology, making it difficult to judge study validity. They are summarized below.

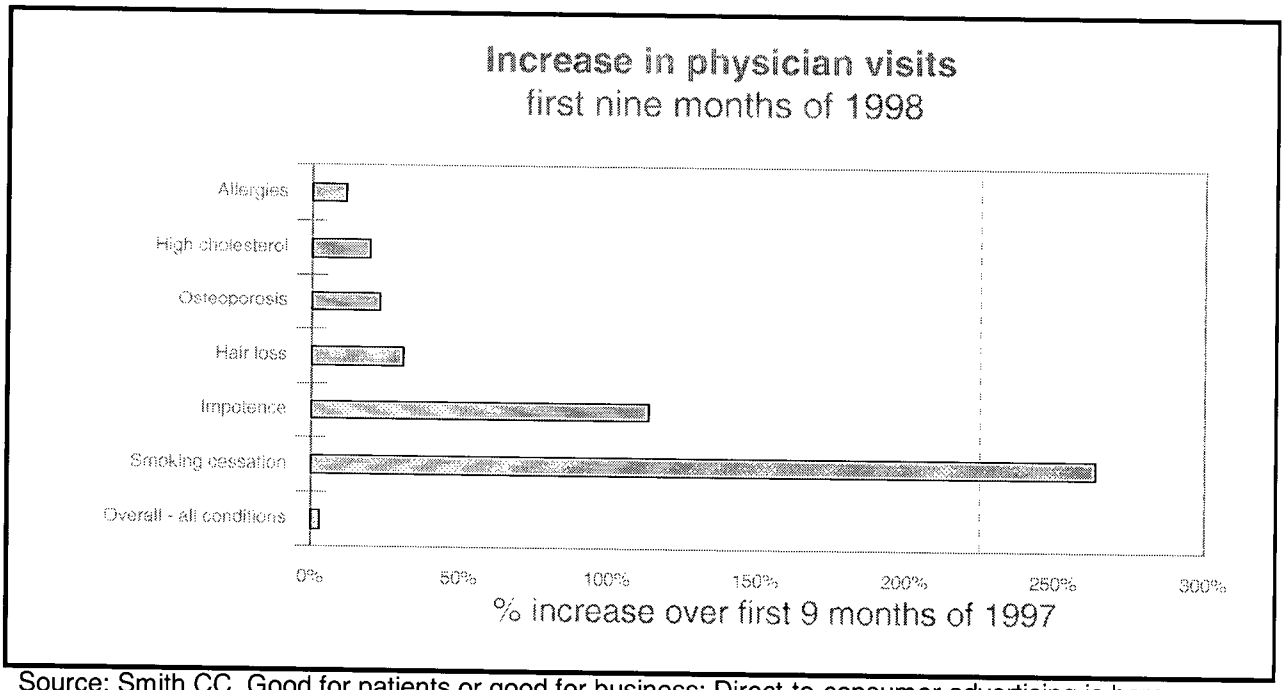
The Decision to Seek Medical Care

If DTCA is to result in increased sales, patients must visit their doctors for advertised conditions and/or request advertised drugs. During the first nine months of 1998, visits to physicians' offices in the U.S. rose by 2% overall. However, market research firms report that the number of visits for conditions targeted by DTCA campaigns rose much more dramatically,[116] as shown in Figure 2.2 on the following page. Figure 2.2 suggests that a mix of factors must be taken into account in assessing potential links between advertising spending and shifts in volumes of physician consultations. For example, although three of the top 10 DTCA drugs by spending in 1998 were allergy drugs, these drugs were also heavily advertised in previous years. This may explain the relatively small increase in volume of consultations for allergy. In contrast, large increases in frequency of visits for smoking cessation were probably associated with the launch of bupropion (Zyban). Figure 2.2 reports relative rather than absolute increases in frequency. Causality cannot be assumed and in some cases intense media attention, as with the launch of sildenafil (Viagra), was most likely responsible for a proportion of the increased consultation rate.

Scott-Levin reported that, between January and September 1998 U.S. doctors received 870,000 visits for male pattern hair loss, a 79% increase over the 485,000 visits for baldness during the corresponding 1997 period.** A drug was prescribed during 73% of these visits, as compared to 57% in the previous year. Thus, if Scott-Levin's estimates are correct, around 687,300 American men would have received drug treatment for baldness during this time, as compared to 276,450 during the corresponding period in 1997, a 250% increase.[117]

** This is a larger increase in visits for baldness than reported by HSCA, as described in Figure 2.2 below; the reason for the discrepancy is not known, neither authors report methods used to estimate frequencies.

Figure 2.2: Increased frequency of physician visits for selected conditions, first 9 months of 1998



Source: Smith CC. Good for patients or good for business: Direct-to-consumer advertising is here to stay, but who benefits? Health Services Corporation of America. HSCA Current Issue. Direct-to-consumer advertising and the Pharmacy. May 10,1999. [http://www.hasca.com/DTCAdver/htm/] Accessed January 2001

Following the launch of celecoxib (Celebrex) in the U.S. in January 1999, the number of patients visiting their doctors for osteoarthritis increased by 18%, to 4.8 million, compared to the same four month period in 1998.[118] During its first 13 weeks on the market, 2.5 million prescriptions were written for celecoxib, a record that has only been surpassed thus far by sildenafil (Viagra), with 2.7 million prescriptions in its first 13 weeks.

It is highly likely that the company's promotional campaign targeting both patients and doctors was responsible for this large number of prescriptions, given the lack of published documentation of a safety or efficacy advantage for this product at the time. No randomized controlled trials had been published comparing celecoxib to placebo or to other NSAIDs, and the drug's effect on the frequency of gastric bleeding remained unknown.[119] There was no evidence of an effectiveness advantage, and a meta-analysis of safety data for celecoxib and its close competitor, rofecoxib, indicated a higher risk of

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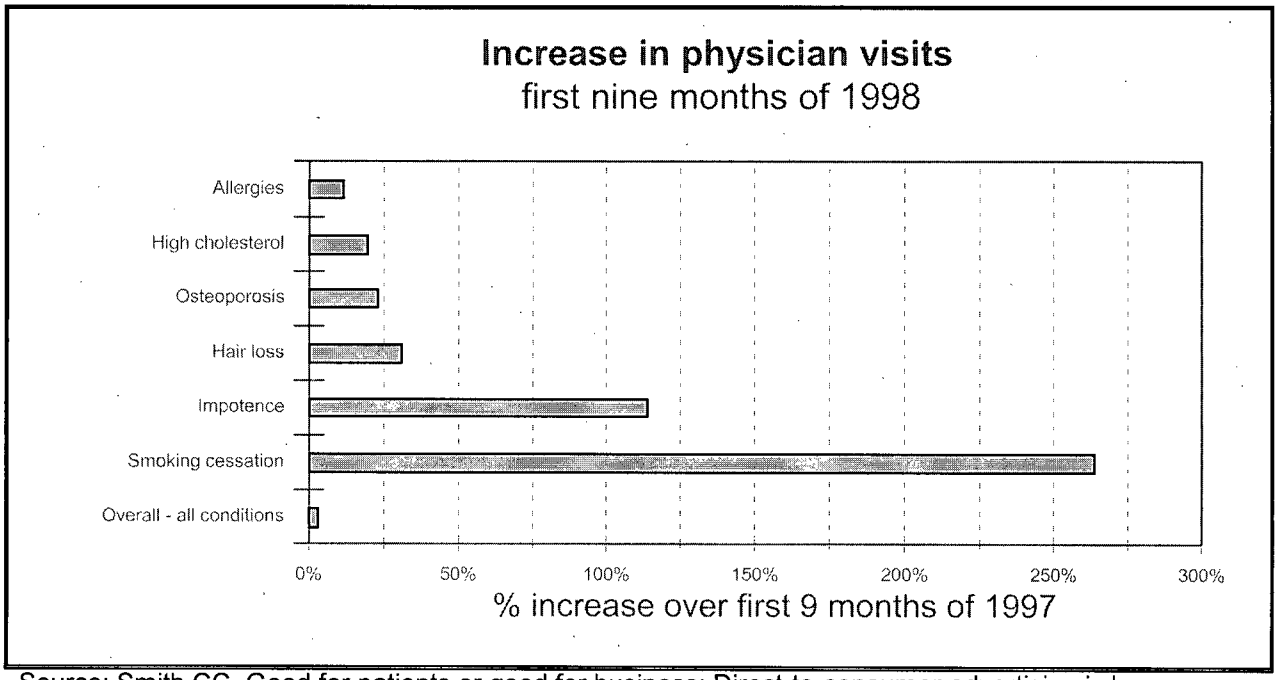

Source: Smith CC. Good for patients or good for business: Direct-to-consumer advertising is here to stay, but who benefits? Health Services Corporation of America. HSCA Current Issue. Direct-to-consumer advertising and the Pharmacy. May 10,1999. [http://www.hasca.com/DTCAdver/htm/] Accessed January 2001

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overall serious morbidity than older NSAIDs.[120] These safety results remain provisional as the trials involved higher than therapeutic doses.

In the first nine months of 1999, the number of doctor visits for urinary incontinence increased to 2.5 million from 1.7 million during the corresponding periods in 1997 and 1998, an increase of 47%. According to Scott-Levin's CEO John Ross, speaking at a conference on DTCA, Pharmacia & Upjohn's used their campaign for tolteridone (Detrol) to build a market for drug treatment of urinary incontinence, dovetailing their DTCA campaign with promotion aimed at doctors. Previously, the rate of drug treatment for urinary incontinence had been low.[121] Treatment is symptomatic and the effect appears to be modest. In 2000, two published randomized controlled trials had compared tolteridone, oxybutin and placebo, one of which assessed patients' subjective assessment of improvement. [122] This 12 week trial found no significant difference in the proportion of patients who believed that their bladder symptoms had improved, whether they were on placebo, tolterodine, or, oxybutin.[123]

The U.S. anti-obesity drug market went into decline following the discovery of cardiac adverse effects with the popular fen/phen combination (dexfenfluramine and phenfluramine) and the press coverage accompanying the withdrawal of both products in 1997. In April 1997, there were two million prescriptions for obesity drugs; in December 1997 the number had dropped to less than 400,000.[124] However, two new anti-obesity products have been launched in the U.S. since this withdrawal: sibutramine (Meridia) in January 1998, and orlistat (Xenical) in May 1999, fuelling a revival in sales of anti-obesity drugs. In the 12 months ending July 1999, doctors prescribed drug therapy for nearly two thirds of obesity visits. Most of the patients visiting doctors for obesity were women (77%) and most paid for their prescriptions themselves (78%). There is no evidence to date establishing the effectiveness of any drug treatment for obesity, including sibutramine and orlistat, in sustained long-term weight loss or on reductions in morbidity or mortality associated with obesity.[125]

Following the launch of sildenafil (Viagra), consultations for impotence more than doubled in 1998.[126] Patient visits for depression, another condition associated with DTCA, rose 10% to 19 million during the 12 months ending in November 1998.[127] One of the top ten drugs by DTCA spending during this time period was an antidepressant, fluoxetine (Prozac).

In 1997, six of the ten medical conditions accounting for increased office visits had been mentioned in DTCA campaigns.[128] In 1996, the therapeutic area leading DTCA was osteoporosis, with campaigns such as Merck's promotion of alendronate (Fosamax). Patient visits for osteoporosis doubled between 1995 and 1996, according to the market research company Scott-Levin's Physician Drug and Diagnosis Audit.[129]

These reports are descriptive and are based on audits of doctors' diagnoses and prescribing by market research firms. The samples may or may not be representative of U.S. doctors in general, as published reports in the pharmaceutical marketing press generally provide little detail on sampling methodology. However, these reports indicate a consistent association between more frequent consultations and the conditions associated with advertising campaigns. They are also consistent with reports of increased sales of drugs for heavily advertised conditions.

The Likelihood that a Requested Drug is Prescribed

A report by the market research firm Scott-Levin's physician drug and diagnosis audit indicates that requests for loratadine (Claritin) were honoured 86% of the time in 1997, and pravastatin (Pravachol) requests 90% of the time.[130] In 1998, nearly two thirds of consultations for impotence involved a request for a prescription. Eighty percent of the time this was for sildenafil (Viagra) and doctors honoured over 90% of patient requests.[118]

An antidepressant was prescribed during 93% of consultations for depression during the 12 months ending in November 1998, according to a Scott-Levin report.[119] Although the

proportion of visits in which patients requested a drug is not stated, several SSRI/SNRI antidepressants are heavily advertised to the public. DTCA, in combination with pharmaceutical promotion aimed at doctors, may be contributing to an impression that drug treatment is nearly always the best option available for depression, despite a lack of evidence to support the superiority of antidepressants over cognitive therapy in the treatment of mild to moderate depression.[131] These reports suggest that if patients request specific drugs, they are highly likely to receive them. This is consistent with the results of national U.S. consumer surveys reported above.

Drug Formulary Development in Managed Care

Drug formularies are limited lists of reimbursable drugs developed by health service or drug benefit providers. A formulary may have a single or several tiers. For example, it may include drugs that are fully or partially reimbursed, drugs that require prior authorization for reimbursement, etc. A drug may also be included on a formulary because a health provider such as a health maintenance organization (HMO) is able to negotiate better prices for the product through bulk purchasing, or because clinicians request its inclusion.

The aim of formularies is primarily cost containment, by avoiding the use of unnecessarily costly drugs when equivalent less costly alternatives exist.

Currently more than 80 million people in the U.S. are enrolled in some sort of managed care. [132] The move to managed care and to pharmaceutical payment primarily by third parties in the U.S. has contributed to a greater squeeze on manufacturers. In addition to convincing individual physicians to prescribe a newly launched drug, manufacturers now need to convince health service and benefit providers to include it on their formularies. One strategy is to create patient pressure for formulary inclusion through DTCA-induced requests. According to a *Financial Times* report on DTCA "Increased public awareness helps to get medicines on to managed care formularies and keep them there." [133]

Nearly 68% of the 2.6 billion prescriptions dispensed in the U.S. between June 1998 and June 1999 were paid for by managed care, according to Scott-Levin, a pharmaceutical market research company.[134] A survey of managed care executives and pharmacy benefit managers by the market research firm IMS Health indicated concern over the use of DTCA to influence formulary inclusion.

When Rocky Mountain HMO, based in Colorado, introduced a $10 to $15 co-payment with prescriptions of loratadine (Claritin), Schering-Plough, placed full-page ads in the local papers saying: "Claritin is covered by over 93 percent of the managed care plans in the country? Is your plan one of the 93 percent?"[135] This public relations counter-attack on user charges was predicated on brand recognition established through DTCA. Loratadine (Claritin) was the product with the highest DTCA spending in 1997 and 1998.

There are no published reports analyzing the influence of advertising-induced patient requests on formulary development. DTCA could lead to expanded formularies because of pressure from patient requests, or to more restricted formularies. Scott-Levin identified ten therapeutic classes with the highest number of plans reporting a restriction in 1998;[136] half of these were also among the ten drug classes with the highest DTCA spending (antifungals, pain medications, antidepressants, cholesterol reducers, and ulcer/reflux).[137]

Allan Korn, Chief Medical Officer for Blue Cross Blue Shield Association, points out that plans with flat co-payments may be especially vulnerable to DTCA for expensive products: "Imagine seeing sequential television ads for a Dodge Neon, a Chrysler 300M, a Mercedes, and a Bentley. At the end, an announcer says, 'It's your choice for a $25 copayment.' That's what we're doing with drugs."[138] U.S. managed care companies have responded to increased drug costs by increasing patient co-payments, with almost 70% offering a three-tiered prescription drug payment system (generics, brands on formulary, brands not on formulary) in 1999, as compared to 36% in 1998.[139]

Managed care companies are also affected by increases in use of physician services stimulated by DTCA. One managed care executive, pharmacy Vice President Pete Penna of Cigna Health Care, warned that managed care companies may remove commonly advertised drugs from formulary lists if DTCA continues to generate more informational visits to doctors.[140]

DTCA and Disease Management

Disease management is defined as a comprehensive, integrated approach to care for patients with specific medical problems. A disease management strategy is especially suited to chronic conditions, many of the same conditions targeted by products that are currently being heavily advertised to the public.

A 1999 review by Joel Lexchin examines the potential effects of DTCA on disease management.[141] In the absence of empirical research, both positive and negative effects are hypothesized. DTCA could lead to higher patient awareness of symptoms of specific diseases, newly available prescription drugs, and product characteristics. A positive effect on disease management has been hypothesized as a result. Increased compliance might also occur if patients see ads for drugs they are using, and feel more positive about the drug and/or are reminded to take their medications.

This assumes a similar approach to awareness and treatment of chronic diseases under disease management protocols and DTCA. However, disease management spans a range of treatment options, not just drugs. When drug treatments are recommended, cost-effectiveness is a key concern. As the rationale for choice of therapy includes both short and long-term effects on patient health, drugs with documented long-term benefits and with a more complete and longer term safety record would also be preferred. Most newly approved drugs meet neither criterion.

Lexchin raises concerns that DTCA could lead to patient requests for drugs other than those recommended under disease management protocols, as DTCA focuses mainly on

new expensive drugs. A primer on successful DTCA campaigns published in *Pharmaceutical Executive* suggests ten principles for successful DTCA. [142] These principles include disease chronicity, disease prevalence and under-diagnosis, factors of importance to disease management. However, the need to ensure adequate returns on advertising investments (ROI), based on price per patient times number treated, conflicts with cost-effectiveness criteria.

If disease management protocols recommend treatments other than those advertised to the public, this in turn could lead to patient dissatisfaction if requested drugs are refused, or could undermine the effectiveness of disease management if these requests are honoured in spite of a lesser contribution to therapy, higher expense, or both. If inappropriate prescribing results in more adverse effects, or if the therapeutic alliance between doctors and patients is undermined by tensions created by DTCA, disease management would be expected to suffer. These effects, both positive and negative, are speculative, as no empirical research studies have assessed the effects of DTCA on disease management.

Bypassing Prescription-Only Status: Internet Sales

One of the concerns expressed about potential health effects of DTCA is that viewers can directly buy advertised prescription drugs over the Internet without consulting a doctor. Armstrong and Asch carried out a search for Internet sites selling sildenafil (Viagra) in April 1999.[143] They found 86 sites that did not require a previous prescription or doctor's appointment, 77 of which were still operating 10 days later when they collected more data. Only 55% (42) provided any information on the product or required consumers to fill in an on-line medical evaluation. The 22 sites based outside of the U.S. (29%) were significantly less likely to ask for medical information from customers or provide information on treatment risks than sites based in the U.S.

Ex-U.S. president Clinton proposed legislation to regulate Internet prescription drug sales in early 2000.[144] Online drug stores would be required to obtain FDA approval and to comply with state pharmacy and medicine regulations, and fines up to U.S. $500,000

would be levied to anyone convicted of illegally dispensing prescription drugs. Most sites identified by Armstrong and Asch were located in the US. However, such legislation cannot eliminate direct Internet drug sales of DTC advertised products because sites outside the U.S. remain untouched. In 1999 one British Channel Island site estimated that it received 60-70 orders per hour for orlistat (Xenical).[133]

2.5 Discussion and Conclusions

How much is currently known about the effects of DTCA on health and use of health care services?

U.S. patients are requesting and receiving drugs in response to advertising

U.S. general population surveys based on random nationally representative samples indicate that a substantial minority of the public responds to prescription drug advertising by speaking with their doctors about advertised drugs and conditions, and 5-19% directly request drugs. Although these surveys are based on recall and self-reported behaviour and thus may be subject to recall bias, reports of requests in response to DTCA are consistent across studies. Based on these survey results, the U.S. General Accounting Office estimated in 2002 that 8.5 million people each year receive prescriptions in response to advertising in the U.S.[45]

Advertised products strongly associated with annual increases in drug costs

Additionally, the pharmaceutical industry's growing investment in DTCA in the U.S. over the last decade indicates that companies are obtaining adequate returns on rather considerable investments, i.e. that sales are stimulated through advertising of prescription drugs to the general public. The National Institute of Health Care Management found that DTC advertised drugs and drug classes were a major contributor to annual increases in U.S. retail pharmaceutical costs from 1993-2000. [107 108 55] The time series analysis of the sumatripan (Imitrex) campaign by Basara also indicates a positive effect on sales and returns on investment attributable to a DTCA campaign;[9] Zachry et al. found an association between DTCA spending and physician diagnoses and prescribing within

specific heavily advertised drug classes,[3] and Wosinska's analysis of prescriptions issued to patients covered by Blue Cross found a correlation between product choice and brand-specific DTCA spending.[114]

Effects on prescribing appropriateness have not been examined directly

Less is known about the appropriateness or lack of appropriateness of drug utilization following DTCA. It is possible to guess that DTCA results in increased use of the specific drugs that are advertised to the public. DTCA spending in the U.S. is highly concentrated, with only 10 products accounting for 40-50% of spending annually. These were largely new, expensive drugs for conditions affecting a relatively large target population. These characteristics would be expected in much future DTCA as well, because of the expense of large-scale advertising campaigns, particularly television advertising.

Studies of physician prescribing in relation to their sources of information on pharmaceuticals have shown a consistent association between less appropriate prescribing and higher reliance on drug promotion. [145] [146] [147] [148] [149] [150] [151] [152] No research has been carried out on the appropriateness of patients' use of drugs and reliance on DTCA.

The literature on the influence of drug promotion on doctors also raises concerns about the accuracy of self-reports of reliance on advertising. Avorn et al. found a large discrepancy between the degree to which doctors said they relied on commercial information sources and their prescribing of two products: vasodilators for dementia, and proxyprophene, a painkiller associated with greater risks but no difference in effectiveness as compared to alternatives.[153] Although the doctors said that they relied little on commercial information sources, many felt that the products were useful and stated that they would prescribe them in some circumstances. The scientific evidence did not support prescribing in either case; commercial information sources did. This was a non-random sample of physicians in the Boston area in the early 1980's, and may therefore not be broadly generalizable to North American physicians today.

The degree to which the general public might also under-report the influence of DTCA on their decisions to seek care or request drugs is unknown. Maddox and Katsanis commented more generally on consumer advertising that, "Despite the fact that 60% of consumers said that "advertising insults my intelligence" and 70% said they "don't believe a company's ad," there is no question that advertising works." The Kaiser Family Foundation found that people who had just viewed a TV ad were more likely to say they trusted the information – regardless of which ad they had viewed – than members of the public who had seen many televised DTC ads in the past, but had not just viewed an ad.[67] This suggests that TV ad viewers may temporarily suspend disbelief.

Stimulation of rapid use of new drugs raises health concerns

Most DTCA thus far has been for newly marketed drugs. When a drug is first marketed, information on its safety is generally limited to experience in a median of 1500 patients.[154] Information on efficacy is generally better known, but often only in relation to intermediate endpoints or surrogate markers. Often relatively little is known about clinical outcomes for drugs used to treat chronic conditions, including morbidity or mortality in the long term. Additionally, frequently few or no trials have been published comparing a new drug to alternative treatments for the same condition, as these are not required for regulatory approval. Richard Martin, research fellow at Southampton's Drug Safety Unit, comments that, "Without these data, it is often difficult to justify the increased costs compared to cheaper, established drugs of proven effectiveness." [154] A related concern is that regulatory standards for marketing approval may have been weakened by policies implemented to speed up drug approvals.

If most new drugs offered significant therapeutic advantages, then the benefits of stimulating increased use might outweigh harms. However, when it comes to drugs, newer is not necessarily better. Before 1992, the U.S. FDA classified new chemical entities according to therapeutic potential. Between 1978 and 1991, of 312 new chemical entities, only 50 (16%) were rated as important therapeutic advances, and 166 (53%) rated as conveying little to no therapeutic advantage.[155] Canada's Patent Medicines

Pricing Review Board judged only 25 (6%) of 415 new patented drugs introduced between 1996 and 2000 to be breakthroughs. A French independent drug bulletin, la Revue Prescrire, assessed the 2257 new drugs and new indications for existing drugs introduced in France between 1981 and 2000. They found evidence of significant therapeutic advantages for only 74 (3.3%); 1427 (63%) of these drugs "brought nothing new" and 58 (2.6%) were actually *worse* than existing alternatives. Thus all three assessments suggest that new, important advances are rare.[156]

Another question is whether some Canadians might be more vulnerable to potential harmful effects of DTCA than others. There have been no assessments of the differential impact of DTCA on the health of women, children, the elderly, minorities or different socio-economic groups. However, an analysis of cohort studies of 48 newly marketed drugs in Britain between 1982 and 1997 involving the experiences of more than 500,000 patients indicated that women were 60% as likely to experience a harmful drug reaction than men over the same duration of drug use.[157] This study actively followed up prescriptions of specified drugs in primary care by sending questionnaires to family physicians either six months or one year after an initial prescription. Only drugs for long-term use were assessed. Many drugs advertised to the public in the U.S. are also new drugs indicated for chronic use. The authors hypothesized that this differential effect, which occurred in all adult age groups and across different classes of drugs, was probably dose-related and due to women's smaller average size.

Of the 548 new drugs introduced to the U.S. public between 1975 and 1999, 2.9% were withdrawn for safety reasons and 8.2% acquired one or more black-box warnings, the strongest type of warning of a safety concern required by the U.S. FDA.[158] More than half of these withdrawals occurred within the first two years after market launch. With heavy promotion through DTCA campaigns soon after a product's launch, population exposure may soon become widespread. Nearly 20 million Americans were exposed to one or more of the five drugs withdrawn from the U.S. market between September 1997 and 1998. [159] Several products advertised to the U.S. public were later withdrawn for safety reasons,

including cisapride (Propulsid), troglitazone (Rezulin) and alosetron (Lotronex). Alosetron has since been reintroduced onto the U.S. market.

Most requested drugs are apparently prescribed, but results are provisional

Eighty percent of 1998 Prevention survey respondents and 84% of 1999 respondents who requested a drug in response to advertising said that their doctor prescribed the requested drug. Additionally, product-specific market research by Scott-Levin and IMS indicates a high proportion of prescriptions in response to requests, in some cases over 90%. However, these surveys may not reflect broader population trends, as sampling methodology is generally unstated.

Proponents of DTCA argue that the advertising simply stimulates a discussion between a patient and doctor about treatment needs, and not necessarily a specific prescription. For example, Alan Holmer stressed in a *Journal of the American Medical Association* editorial that, "the patient has been empowered with information, not prescribing authority" and that "since prescription drugs are available only under a doctor's supervision, there is little danger that advertising will lead to inappropriate use." [160] The assumption is that consumers are protected against harm because a doctor ultimately decides if a product is suitable.

If nearly all requested drugs are prescribed, however, the safeguard provided by prescription-only status may become seriously eroded. Philip Brown, publisher of the U.K. pharmaceutical bulletin *Scrip*, remarks that: "all the evidence suggests that in a free market, what the patient asks for, the doctor will prescribe."[161] Surveys of doctors and patients in primary care settings indicate a strong association between physicians' decision to prescribe and their perceptions of patient desire for a prescription even when they know the drugs are not indicated [162] [163] and even when the doctor's perception is wrong.[164] [165]

In a U.S. FDA survey, 75% of physicians said that they had provided a prescription to a

patient who requested one or more in response to advertising, although not always for the requested brand.[19] Beyond product-specific effects, DTCA may lead to increased overall prescribing volumes. Such effects remain speculative as they have not been directly measured.

Health effects are likely to involve a complex mix of factors

No research has been carried out on health outcomes in relation to specific DTCA campaigns. Anecdotal reports have raised concerns about deaths because heavily advertised drugs were inappropriately used instead of treatments of established efficacy. For example, a January 2000 news article reported that some U.S. patients had died from flu complications after being prescribed heavily advertised new antiviral drugs.[166] These drugs had not been shown to reduce serious morbidity or mortality, and there was limited experience in high-risk patients. Two patients died after being prescribed zanamivir (Relenza) when they developed bacterial infections as a complication of the flu and should have received antibiotics. Three patients died after being prescribed zanamivir but not receiving needed oxygen, I.V. fluids and hospitalization. Another patient recovered after receiving a second heavily advertised flu drug, oseltamivir (Tamiflu), when he should have received antibiotics for a serious bacterial infection. Whether patients requested these drugs is not known, as they are being promoted both to patients and physicians. A Canadian website advertising oseltamivir (Tamiflu)[167] presented this class of drugs as revolutionary new treatments and referred to the millions of flu deaths during the 1918 pandemic. A reader could easily assume that the drugs would be helpful in serious, life-threatening illness.

A similar type of concern was raised by the San Francisco Department of Public Health when their survey of men attending STD clinics found that those with higher exposure to DTCA for AIDS drugs were more likely to have reported engaging in unprotected sex within the last month. [168] In this case, the concern was that unrealistic images of treatment success in ads for antiretroviral drugs had convinced gay men to be less concerned about prevention than they might have been otherwise. Kaiser Family Foundation found that

people who had seen an ad for an oral anti-asthma drug not only gained information but also misinformation from the ad: they were more likely than non-viewers to believe that a pill could be helpful for an acute asthma attack, an incorrect assumption with potentially dangerous consequences.[67]

These are isolated examples, but they suggest that an assessment of the health impacts of DTCA is complex, involving not only the treatments people obtain following exposure to advertising, but also a range of other health-related behaviours potentially affected by advertising, such as decisions to undertake disease prevention measures, to use non-advertised treatments, or to seek emergency care.

Effects on doctor-patient relationship are unstudied

Effects of DTCA on the doctor-patient relationship remain largely unknown. The hypothesis that exposure to advertising leads to a more informed patient, better able to be a partner in decisions about care, remains untested. After over 10 years of exposure to DTCA and to patient requests stimulated by DTCA, U.S. physicians continue to have a largely negative opinion of this form of advertising. In the only survey of physicians in the peer-reviewed literature, Lipsky and Taylor found that nearly 9 out of 10 family practitioners believed that DTCA had a negative effect on the doctor/patient relationship.[18] A majority of New Zealand physicians are also opposed to DTCA. An editorial in *the Lancet*[169] blames medical paternalism for this opposition, whereas editorials in *Journal of the American Medical Association*[170] and the *British Medical Journal*[171] suggest that advertising is negatively affecting doctor-patient relationships.

An adequate information base for shared informed decision-making?

The goal of shared decision-making in clinical care is receiving increased attention in the medical press. Coulter et al. stress the need for scientifically reliable information to support treatment decisions, presented in a form that is acceptable and useful to patients.[172] In a study published last year, they used patient focus groups and academic specialists to assess the quality of information materials U.K. patients have available to support decision-making. The authors found that many patient information materials on

ten common conditions: "omit relevant data, fail to give a balanced view of the effectiveness of different treatments, and ignore uncertainties." A variety of organizations had produced these materials, including patient groups, health service providers and pharmaceutical companies.

How DTCA affects consumer knowledge, education and ability to participate effectively in health care decisions may be guessed to a large extent from its content. This is product-specific information produced with the aim of stimulating sales. Consumers are unlikely to be educated about competing products for the same condition, especially products that are no longer under patent, and they are unlikely to receive education about the limits to drug therapy. An analysis of the educational content of 10 years' worth of print DTCA in the U.S. found that 9 of 11 basic elements of information on the drug and the condition it treats were usually lacking.[31] Similarly, another systematic analysis of magazine advertising found that most ads included only vague claims of benefits, and that a substantial minority included patient or physician testimonials and/or financial incentives to use a specific product.[29] Earlier studies had found that risk information presentation was often inadequate.[34 36]Additionally, New Zealand's MedSafe and the U.S. FDA have found many ads to violate legislative requirements for accurate, balanced information, including repeat violations by the same company and for the same product.

The U.S. public reports a more positive attitude than physicians when asked general questions about prescription drug advertising. More detailed questions, particularly about completeness and balance of benefit and risk information in ads, solicit less enthusiastic responses. A survey of patients' hypothetical response to their doctor's refusal to prescribe a requested drug found that people who thought that only the safest and most effective drugs could be advertised to the public were more likely to contest a refusal.[65] This study raises concerns that patients' actions may be affected by false assumptions about the degree of regulatory protection against harm. Over one-fourth of people surveyed by the FDA thought that only the safest drugs could be advertised to the public, although no such limit exists. [61]

Dr David Kessler, former FDA Commissioner, asked whether it is in the public interest, "to make a mediocre drug the drug of choice based on marketing and not science?" Kessler's opposition to DTCA as Commissioner was credited with delaying liberalization of broadcast ads; he has since become more supportive of DTCA.[173] Hoffman and Wilkes[171] suggest that DTCA focuses primarily on 'me-too' drugs in competitive categories. Marcia Angell, ex-editor of the New England Journal of Medicine, similarly comments that "...the less important the drug; the more marketing it takes to sell it. Important new drugs do not need much promotion. Me-too-drugs do." [174]

Effects on compliance remain unknown

One claimed benefit of DTCA is in improving compliance with treatment recommendations. This has not been adequately tested. The results of *Prevention* magazine's survey are frequently cited: *Prevention* asked survey respondents who had a prescription for a drug they saw advertised whether seeing the ads reminded them to refill prescriptions. [56] Most said no, but among those who said yes (5-8% of the sample), it is impossible to know how many people actually took their medicine or went out for a refill, or whether these actions would be expected to improve health status. For some drugs there would be a clear benefit, for others not, and in some cases more regular use of a symptomatic treatment (particularly beyond that required by symptoms) can lead to unnecessary harm.[56]

A solution for under-treatment or a cause of over-treatment?

Another hypothesized beneficial effect of DTCA is in helping people to seek and receive appropriate care at an earlier stage of disease progression.[175] For example, only a minority of men with heart disease are being treated for elevated cholesterol, and many people with clinical depression are not receiving treatment, either drug or non-drug.

Evidence of more frequent physician visits for advertised conditions does not distinguish between people who require care and for whom treatment is likely to be beneficial, and people for whom there is little evidence of benefit. Although men with heart disease who could benefit from lipid-lowering drugs do not always receive them, many women and

elderly people are also prescribed these drugs for primary prevention despite a lack of evidence of a beneficial effect on morbidity or mortality in these population groups. If DTCA increases the use of lipid-lowering drugs, does it primarily affect the under-treated, the over-treated, or both? Similarly, there are many anecdotal reports of antidepressant use by people without psychiatric diagnoses, for whom no systematic evidence exists of a health benefit. Studies could be designed to evaluate the effect of DTCA both on appropriate and inappropriate care. However, no such study has been carried out thus far.

Because of the need to recoup advertising investments and target large audiences, DTCA may lead to unnecessary medicalization of healthy life stages, and increases the frequency of prescription drug use among people with mild health problems or who are essentially healthy. This was discussed in an editorial in the *British Medical Journal*, reproduced as Appendix 2.2.

Reports by market research companies in the U.S. indicate that physician visits for the conditions associated with advertised drugs increase during an advertising campaign. No studies have been carried out on the appropriateness of these visits. For example, are people who require treatment visiting their doctors for the first time? Or are people with milder symptoms and/or conditions less amenable to drug treatment visiting doctors? In some cases, as for example the increase in patient visits for male pattern baldness during the campaign for finasteride (Propecia), DTCA contributes to use of health care services for cosmetic rather than health concerns.

Conclusion

Evidence of benefits to health or health care quality is lacking

In conclusion, many gaps remain in our knowledge of outcomes of prescription drug advertising to the public. In 1991, when the U.S. General Accounting Office reviewed the literature on DTCA, there was little experience with this form of advertising. Over the next 11 years, the amount of public exposure to DTCA, especially in the US, grew

enormously. Surveys of the U.S. public and physicians report widespread behavioural changes in response to advertising, specifically that patients are responding to ads by going to their doctors, discussing advertised drugs and conditions, requesting advertised drugs, and receiving prescriptions.

A recent synthesis report, again by the U.S. General Accounting Office, estimates that at least 8.5 million Americans per year request and receive prescription drugs in response to advertising. "If the increase in utilization is based on false claims, that's very troubling," commented U.S. Senator Susan Collins, one of the legislators who had requested the review.[176] Regulatory reviews indicate that such false claims are common, and that the amount of population exposure to misleading claims is highly dependent on the strength of regulatory controls.[45] Systematic analyses of advertising content suggest broader concerns beyond the minority of advertisements found to violate U.S. law: celebrity endorsements, statements about how many people have used a product, vague emotional claims and free trial offers are unlikely to provide the type of information the public needs to make informed health care decisions.

DTCA appears to affect prescribing behaviour and drug costs. However, knowledge of DTCA's effects on health and on the quality of health care services remains elusive. No reliable evidence exists to support hypotheses of potential health benefits or to exclude potential harm.

Appendix 2.1 – Search strategies

MEDLINE, EMBASE, CINAHL AND HEALTHSTAR

1. exp advertising/
2. direct-to-consumer.tw.
3. dtca.tw.
4. (advertis: or advertiz).tw.
5. exp marketing of health services/
6. or/1-5
7. exp drug industry/
8. exp prescriptions, drug
9. prescription drug.tw.
10. ((drug or pharmaceutical) adj1 industr:.tw.
11. or/7-10
12. 6 and 11
13. exp Patients/
14. consumer:.pm. or patient:.tw. or consumer:.tw.
15. or/13-14
16. 12 and 15
17. limit 16 to yr=1980-1999

CURRENT CONTENTS 1996-PRESENT

1. dtc:.mp.
2. direct-to-consumer.mp.
3. consumer:.mp.
4. or/1-4
5. advertising.mp.
6. drug marketing.mp.
7. marketing.mp.
8. or/6-8
9. pharmaceutical.mp.
10. 4 and 8
11. 9 and 10

PAIS, ECONLIT, CBCA*

1. explode 'Drugs-' in DE
2. direct-to-consumer
3. dtc
4. explode 'Consumer-' in DE
5. 2 or 3 or 4
6. 1 and 5
7. explode 'Advertising-' in DE
8. explode 'Pharmaceutical-industry' in DE
9. 7 and 8
10. 6 and 9
11. 10 and (py=f1980-1999)

ABI / INFORM

(prescription drugs) and advertising and consumer

INGENTA

Ti:[Consumer Advertising or DTCA](tka)

Appendix 2.2

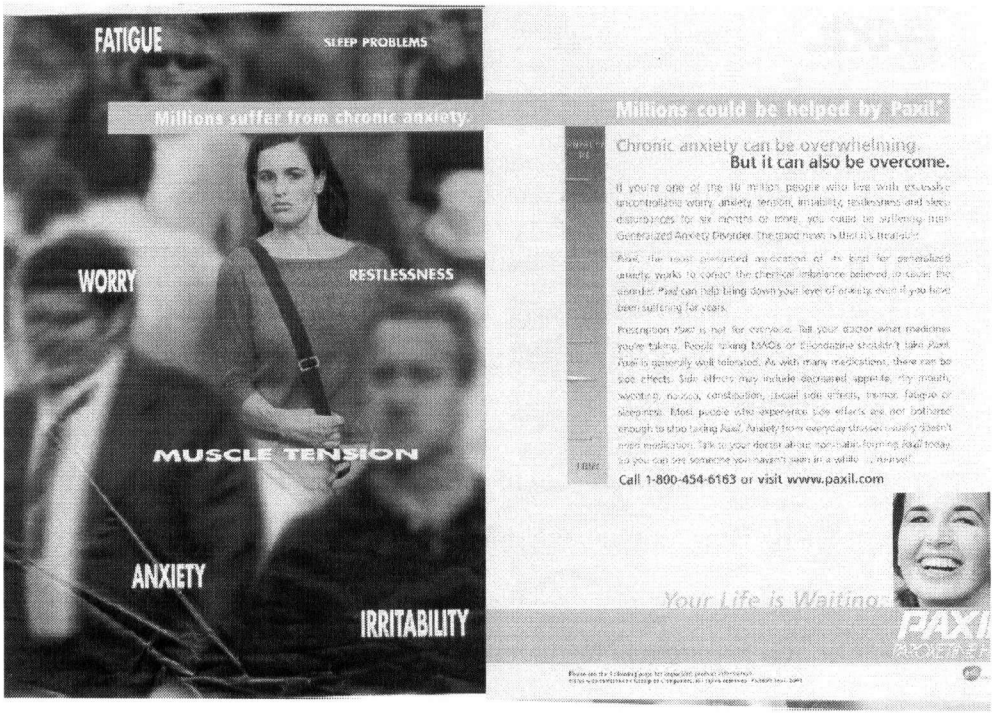
Direct to consumer advertising is medicalising normal human experience

Barbara Mintzes

BMJ 2002;324:908-9 (Reprinted with permission from the British Medical Journal, BMJ Publishing Group)

In October 2001, GlaxoSmithKline ran an advertisement in the *New York Times Magazine* for paroxetine (known as Paxil in the United States). A woman is walking on a crowded street, her face strained, in a crowd otherwise blurred. The headline reads, "Millions suffer from chronic anxiety. Millions could be helped by Paxil."

No doubt many New Yorkers felt anxious in the aftermath of the attack on the World Trade Center, experiencing symptoms highlighted in the advertisement, such as worry, anxiety, or irritability. At what point does an understandable response to distressing life events become an indication for drug treatment—and a market opportunity?



Kawachi and Conrad describe medicalisation as a "process by which non-medical problems become defined and treated as medical problems, usually in terms of illnesses and disorders," decontextualizing human problems and turning attention from the social environment to the individual.[177] They point out the negative consequences, chiefly the extension of the sick role and diversion from other solutions.

Does direct to consumer advertising of prescription drugs, currently allowed only in the United States and New Zealand, broaden the domain of medicine beyond justifiable bounds?

Promotion of drug use among healthy people

Liz Coyle of the market research firm IMS Health suggests instead that "Consumers often ignore, or choose not to treat, symptoms that seem `minor' or that are not in acute stages," and that advertising "can help them improve their health and avoid more serious, costly conditions down the road." She is describing US disease oriented advertising for hair loss, menopause, obesity, osteoporosis, and acne.[178] New Zealand's pharmaceutical industry similarly claims that direct to consumer advertising "encourages people to seek medical attention for conditions or symptoms that might otherwise go untreated, including asymptomatic diseases." [179]

Charles Medawar of Social Audit UK argues that the most dangerous effect of direct to consumer advertising is to encourage healthy people to believe they need medical attention. He quotes Lewis Thomas: "The new danger to our well-being, if we continue to listen to all the talk, is in becoming a nation of healthy hypochondriacs, living gingerly, worrying ourselves half to death."[180]

Many advertising campaigns focus on fears of death or disability. In Better Homes and Gardens (April 2000), Merck, manufacturer of alendronic acid, told older US women, "See how beautiful 60 can look? See how invisible osteoporosis can be?" The

advertisement urges women aged 60 or older to go for a bone density test, citing a nearly 1 in 2 chance of having osteoporosis, leading to broken bones and dowager's hump—"no matter how healthy you look on the outside." Bone mineral density testing is a poor predictor of future fractures[181] but an excellent predictor of start of drug use. [182] For healthy people, benefits may not outweigh risks: in pre-marketing trials 1.5% of users of alendronic acid experienced oesophageal ulcers.[183]

Relatively healthy people are targeted because of the need for adequate returns on costly advertising campaigns. Consistently, around 40% of spending on direct to consumer advertising is on only 10 drugs, mainly new, expensive drugs for long term use by large population groups. In 2000, they were drugs for allergy, ulcer/reflux, anxiety, obesity, arthritis, impotence, and high cholesterol levels. Morais suggests that manufacturers assess whether a product-specific campaign is worth pursuing based on numbers of potential patients, the "persuadable" percentage, the proportion of doctors who will prescribe, and the value per patient (return per script multiplied by the duration of use).[184]

Advertising campaigns can lead to shifts in the pattern of use of healthcare services. The Dutch Health Inspectorate reported dramatic increases in consultations for toenail fungus after a three month unbranded media campaign. In 1998, during a campaign for finasteride (Propecia), visits to US doctors for baldness increased by 79% compared with 1997 levels, to 850 000 (Scott Levin, press release, 31 November 1998).[185]

Even when the focus is on prevention of serious disease, many advertising campaigns cast too wide a net. Lipid lowering drugs, for example, reduce mortality in men with heart disease yet there is underprescribing in this population group. However, it is more lucrative to promote primary prevention as many more people are affected, despite the lack of significant reduction in mortality.[186] In Chatelaine magazine in October 2001, Pfizer used the tagged toe of a corpse to promote cholesterol testing among women in their 50s without heart disease. [187]

Companies are under intense pressure to garner and retain market share, leading to what the World Health Organization has called "an inherent conflict of interest between the legitimate business goals of manufacturers and the social, medical and economic needs of providers and the public to select and use drugs in the most rational way." [188] Doctors with greater reliance on promotion prescribe less appropriately,[189] and the patients who are exposed more to direct to consumer advertising request more advertised drugs. These requested drugs are usually prescribed, often despite doctors' reservations about treatment choice. [190]

Both critics and supporters of direct to consumer advertising agree that it is likely to expand drug treatment in healthier populations. This can occur through broader disease definitions, based on physiological measures rather than on clinical events; through promotion of drugs for disease prevention; and through prescription drug use for symptoms previously treated with over the counter remedies or non-drug approaches.An additional effect, observed in the United States at a population level, is substitution of newer for older drugs among those already receiving treatment.

Newer drugs are not necessarily better

Evidence on clinical outcomes is often inadequate when drugs first come on to the market, at times leading to false impressions. COX 2 inhibitors, for example, were widely believed to be safer than other non-steroidal anti-inflammatories when first launched. An assessment of the full experience of serious adverse events in comparative trials clearly demonstrates the contrary.[191]

This type of comparative information does not reach the public in direct to consumer advertisements. In a 10-year analysis of advertising in US magazines, 91% of advertisements omitted information about the likelihood of treatment success and 71% failed to mention any other possible treatments.[30]

A powerful cumulative effect

With more than $2.5bn (£1.8bn; &2.9bn) spent on direct to consumer advertising in the United States last year, the cumulative message may be stronger than any individual campaign. A market researcher estimated that in late 1999, Americans on average saw nine prescription drug advertisements a day on television. To an unprecedented degree they portrayed the educational message of a pill for every ill—and increasingly an ill for every pill.

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Chapter 3

How should the effects of DTCA be modeled?

Chapter 2 reviewed the available evidence on the content and quality of DTCA, and on its effects on health and health care services. There are considerable gaps in the research evidence, particularly in terms of how much is known about the effects of DTCA on health and on the quality of health care services. Many key claimed outcomes remain untested, such as effects of DTCA on compliance, and on the appropriateness or inappropriateness of prescribing decisions and diagnoses. Additionally, the design of many studies limits the conclusions that may be reliably drawn from them, as is the case for instance in consumer and physician surveys that rely on recall over long period of times or that do not include a comparison group.

Both the patient and physician must play a part if patient-directed advertising is to result in a shift in prescribing decisions. However, the effects of DTCA are unlikely to occur in isolation; patient-directed prescription drug advertising is one of a range of social and medical influences on prescribing decisions in primary care.

This chapter begins with a discussion of the research evidence on two related phenomena hypothesized to affect prescribing decisions: physician-directed drug promotion, and physicians' responses to patient expectations of prescriptions. Both can provide additional insight into how DTCA might be expected to affect prescribing, given what is already known about these related non-medical influences on prescribing. This research provides a useful starting point for hypotheses about the likely effects of DTCA on prescribing decisions and on patient-doctor interactions, and complements the research directly examining effects of DTCA (described in Chapter 2).

Two main types of conceptual models are relevant to DTCA research: economic theories focusing on the role of advertising within the pharmaceutical marketplace, and health services research models that focus on DTCA's effects on patient/doctor interactions prescribing decisions. Four papers have outlined potential approaches to analyzing

DTCA using economic or health services research models. These are described below. Although this study uses a health services research framework, economic analyses are also relevant in that they situate DTCA as a marketing tool that reflects the needs of companies operating within the pharmaceutical marketplace. Thus economic analyses can assist in the understanding of characteristics of patient-directed advertising and DTC-advertised products, as well as the relationship of DTCA to other forms of pharmaceutical promotion.

DTCA is likely to be only one of a number of influences on patient care-seeking behaviours and prescribing in primary care. Thus, models that examine different factors influencing health service utilization, such as that developed by developed by Anderson and Newman[1] provide a useful framework for the examination of effects of DTCA in primary care. This model is relevant to DTCA research because it includes both individual and broader social determinants of health car services, and provides a means to tease apart medical and non-medical influences on health service use.

In summary, this chapter begins with a review of empirical research that is not directly about DTCA, but is relevant to the conceptualization of its effects on patient-doctor interactions and prescribing decisions. Given some of the methodological weaknesses and gaps in the existing body of evidence on outcomes of DTCA, theoretical analyses carried out by other researchers to recommend more appropriate methodologies for DTCA research are also highly relevant to this study. The chapter concludes with a review of these analyses, and develops the groundwork for the conceptual framework used for the current study, which is described in Chapter 4.

3.1 Promotional and social influences on prescribing decisions

Patients do not obtain prescription drugs in isolation, and companies only carry out DTCA as part of a larger marketing campaign that also involves physician-directed promotion. To place this literature in context, it is useful to examine what is known about the effects of physician reliance on pharmaceutical promotion. This literature is summarized below in section 3.1.1. Additionally, section 3.1.2 reviews the research on

social influences on prescribing, including the interplay between patient expectations of a prescription and prescribing decisions.

3.1.1 Effects of drug promotion on physicians' behaviours

Between 1972 and 1998, 11 studies in Belgium, the Netherlands, the United Kingdom and the United States examined the association between the information sources primary care physicians use and the quality of prescribing decisions.[2 3 4 5 6 7 8 9 10 11 12] These studies are briefly described in Table 3.1. In all of these studies, physicians who relied to a greater extent on information from the pharmaceutical industry were found to prescribe less appropriately than physicians with less reliance on commercial information. Prescribing appropriateness was measured in various ways: avoidance of unnecessarily hazardous or costly products; more frequent prescribing of generic drugs; appropriate treatment recommendations for specific hypothetical cases; and not being overly 'prone' to prescribe for common conditions. Additionally, some studies examined prescribing rates for specific drugs such as benzodiazepines, psychoactive drugs in general, and an antibiotic, chloramphenicol.

These studies span a large time period and a range of geographic areas, and in some cases there are methodological concerns, for example regarding response rates, measures of prescribing quality and/or reliance on self-report. However, they consistently describe a similar direction of effect, linking greater reliance on promotion to poorer prescribing quality, across a range of outcomes related to prescribing appropriateness.

Results of related research support these findings. A study of 103 primary care group practices in the U.S. found a significant association between lower drug costs and policies to restrict contact with sales representatives.[13] Prescribing by medical specialists, similarly, is influenced by drug promotion. For example, Schwartz et al. compared initial prescriptions for newly admitted psychiatric patients during 12 week periods in which residents attended 'drug lunch' sales visits as compared to 12 week periods in which such lunches had not taken place, at the same clinic. This study relied on retrospective analysis of prescription records as compared to 'drug lunch' topics. Patients were more

significantly likely to receive prescriptions for 12 of 13 promoted products during the period following sales visits than during control time periods, and the relationship remained highly significant after adjusting for multiple comparisons.[14]

Table 3.1: Studies of Influences of Promotion on Prescribing in Primary Care

Study, Country	N	Outcome assessed	Information sources	Conclusions	Comments
Becker et al 1972, USA	37	Appropriate prescribing for common illnesses, knowledge	Journal ads, detailers	Better prescribing with less use of journal ads (p<.05); negative attitudes to detailers (p<.01)	Prescribing assessed by expert panel; Response rate 84% (in county)
Linn et al 1972, USA	107	Psychoactive drug prescribing	Commercial Information	More likely to prescribe for everyday problems (p<.05)	Random sample; response rate 55.6%
Mapes, 1977, UK	54	Prescribing of drugs with poor safety profiles	Commercial information	Less safe prescribing with greater reliance on commercial info	Database cohort of 900 practitioners who started in 1970; 116 selected (random?), 47% response rate
Haayer 1982, NL	116	Appropriateness of prescribing for 8 case histories	Commercial information	Less rational prescribing with greater reliance (p<.05)	Appropriateness for symptoms/disease; effectiveness & safety of treatment; right dose & duration; 116/148 GP's in area (78% response)
Ferry et al 1985, USA	143	Knowledge of drug treatment for the elderly	Journal ads	If ads seen as more important, lower test score (p=.0067)	Expert panel devised questionnaire and scoring; stratified random sample of 607 (24% response rate)
Blondeel et al, 1987 Belgium	358	8 case histories + 4 week prescribing review (#Rx & quality);	detailers; commercial information	Better quality prescribing (p<.05) less volume(p<.01) if less detailers seen; poorer w/ reliance on commercial info (p<.05);	Quality assessed by expert committee; evidence-based prescribing, given patient characteristics in simulated cases and prescribing review; representative sample of Flemish GPs
Bower et al, 1987, USA	317	generic prescribing; recognition of 10 common generic names	Detailers, journal ads	More generic prescribing w/ less reliance on detailers (p<.05), more knowledge of generics w/ less reliance on ads (p<.05)	GPs randomly selected; responses from 317/501 eligible (63%)
Cormack et al, 1992, UK	37	benzodiazepine prescribing	Commercial information	Low prescribers more sceptical (p<.005)	Data on prescribing from Prescription Pricing Authority; GP sample from those attending annual refresher course & willing to participate;
Berings et al, 1994, Belgium	128	Mean number of benzodiazepine prescriptions	detailers; commercial information	Those w/ positive attitudes (p<.1) & who saw more detailers (p<.1) prescribed more benzodiazepines	More recent graduates prescribed fewer benzodiazepines; random sample of 450 GPs from two provinces (28% response rate)
Caudill et al, 1996, USA	446	Relative cost of prescribing based on treatment choices for three case scenarios	# detailers seen, information use	Frequency of use was significant (p=.02) independent positive predictor of cost	Four choices offered for each scenario, choices equal in efficacy but widely varying costs; cases developed by academic internists; (28% response, mail survey)
Powers et al 1998, USA	78	Rx for hypertension	# of detailers seen	More frequent prescribing of ACE Inhibitors, calcium channel blockers if more detailers seen	Abstract only; prescription audit (~4000 Rx) compared to physician survey results on frequency of interactions w/ reps

*based on Lexchin J. Table of studies on effects of drug prescribing on promotion. [unpublished] 2001. www.drugpromo.info/

A systematic review by Wazana, published in the *Journal of the American Medical Association* in 2000, supports these results.[15] Following a thorough literature search, Wazana identified 29 empirical studies published in the 1980s and 1990s on the impact of interactions between physicians (and medical residents) and the pharmaceutical industry. Most of these studies found that interactions with the industry were associated with negative outcomes. These included:

- an inability to identify inaccurate claims about medicines;
- rapid adoption and prescription of new drugs;
- requests for formulary inclusions of drugs without additional therapeutic advantages;
- irrational prescribing behavior;
- increased prescribing rate;
- less cost-effective prescribing: fewer generics, more new medicines without demonstrated advantage.

Only one positive outcome was identified in one study: residents' knowledge of treatment protocols for complicated illness after attending lunchtime rounds by sales representatives. However, they were also more likely to prescribe inappropriately for milder forms of the same illness.[16]

The most compelling testimony of the power of promotion to drive prescribing behaviour towards less appropriate therapy is in the treatment of hypertension. For primary hypertension, the preferred treatments are diuretics and beta blockers, which are known to reduce cardiovascular morbidity and mortality, as was noted in the fifth report of the U.S. Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure.[17] In spite of these recommendations, prescribing rates for diuretics decreased by 50% and beta-blockers by 40% between 1993 and 1995, while prescriptions for calcium channel blockers grew by 13%.[18] Calcium channel blockers are less effective and more expensive, but they are newer heavily advertised drugs and are still under patent, whereas diuretics and beta-blockers were largely off-patent and hence not advertised. A five-year trial of high-risk patients with hypertension confirms the

superiority of thiazide diuretics over more expensive calcium channel blockers and ACE inhibitors in preventing cardio-vascular events.[19]

A study of pharmaceutical advertising intensity of drugs for hypertension in the *New England Journal of Medicine* from 1985 to 1996 (210 issues), found that the proportion of advertising pages used to promote calcium channel blockers increased from 5% in 1985 to 27% in 1996, whereas pages devoted to beta blockers decreased from 12% in 1985 to none in 1996, and diuretics similarly decreased from 4% in 1985 to none in 1996.[20] This study did not examine advertising content, only the number of pages of advertising per drug and whether or not it belonged to one of these four classes of antihypertensive drugs.

Sullivan compared outcomes for two antibiotics in the treatment of acute ear infections among patients in a health maintenance organization. [21] One is heavily advertised, azithromycin (Zithromax). The other, amoxicillin, is off-patent and therefore is not advertised to patients or physicians. The Centers for Disease Control (CDC) guidelines recommend amoxicillin as a first-line treatment. Sullivan used administrative databases to compare the success rate and total costs of treatment with these two antibiotics. Patients were classified as treatment failures if they needed a second antibiotic. The failure rate for amoxicillin was 21% and azithromycin 19%; the difference was not statistically significant. The cost per cure, which included the second antibiotic when needed, was U.S. $9 for amoxicillin versus $39 for azithromycin. In this example, health outcomes were similar for an advertised and non-advertised drug, but cost differences were dramatic.

In the most extensive evaluation to date of the relationship between promotional expenditures and drug sales, De Laat et al. analyzed the influence of drug promotion on sales in the Netherlands, combining monthly data on marketing expenses, for detailing, advertising and direct mail, and sales of prescription drug, for the period from 1994 to 1999.[22] The authors used data obtained from IMS Health, a market research company. This covered 11 therapeutic classes, representing 58% of the total market in sales, and

55% of promotional expenses. They found a significant association between higher marketing outlays and lower price elasticity*, which proved to be robust over time. Thus they surmised that marketing makes physicians less sensitive to price when making prescribing decisions, an effect that is "unambiguously bad for welfare". They also found a statistically significant positive effect of marketing expenses on sales, with a 1% marketing increase resulting in a 0.3% increase in sales ($p<.0001$). Approximately 35% of this sales growth occurred at the expense of competitors' sales and the remaining 65% was due to market growth.

De Laat et al. also examined promotional spending by product age. They found that spending grew rapidly to a peak during the second year post launch, with rapid decline thereafter. By 10 years post-launch, on average, spending was only about 20% of that at year two. This pattern of intense promotion soon after market launch is similar to that occurring with a range of different types of marketed products, from new models of cars to computer software.

A recent survey of U.S. physicians indicates that attitudes towards promotional visits by pharmaceutical sales representatives are generally positive. From March to October 2001, the Kaiser Family Foundation carried out a mail survey of a nationally representative sample of 2608 U.S. physicians to examine physician interactions and attitudes towards pharmaceutical promotion[23]. Although only 15% (95% CI 12-18) considered information from sales reps to be 'very useful', another 59% (95% CI 56-62) believed it was 'somewhat useful'. Similarly, 9% (95% CI 6-12) believed the information provided to be 'very accurate' and an additional 72% (95% CI 69-75) answered that it was somewhat accurate as opposed to 'not very accurate' or 'not at all accurate'. Nearly two-thirds of the physicians had accepted meals, tickets to entertainment events or free travel from industry representatives and nearly all had received free samples.

The Chair of the American Medical Association's Council on Ethical and Judicial Affairs, Dr. Leonard Morse, believes such interactions are educational and ethically

* the percent change in quantity sold in response to a percent change in price

sound: "If you think those people are coming to doctors' offices to make a buck and profit, then the attitude is completely wrong. They're coming because they're bringing learned information the doctor wouldn't otherwise get."[24]

These generally positive attitudes towards the usefulness and accuracy of information from sales representatives contrast sharply with published evaluations. For example, a U.S.-based study found that 11% of statements by sales representatives were factually inaccurate, even when the representatives were aware that they were being recorded, and that all inaccurate statements were favourable towards the promoted drug.[25] Additional studies in Australia and Finland similarly indicate that sales representatives frequently overemphasize product benefits and omit risk information.[26 27 28] In France, an ongoing monitoring study carried out since 1991 via an anonymous physicians' network has found that sales representatives failed to mention any risk information – including side effects, contraindications and interactions – in about three quarters of visits. [29] The amount of time physicians spend with sales representatives can be considerable, as a group of general practitioners in Italy found when they evaluated this systematically. On average the doctors had 435 visits per year from sales representatives, amounting to 58 hours.[30]

Information reaching physicians through pharmaceutical advertising is similarly often of poor quality. A 1992 study by Wilkes et al. used expert peer reviewers, who reviewed articles submitted to 10 leading U.S. medical journals, to evaluate 109 ads in those journals.[31] The reviewers judged 57% of the ads to have little to no educational value and believed that in 44% of cases, reliance on the information in the ad would lead to improper prescribing. Over 90% of the ads were not in compliance with at least one FDA criterion; most often (in 68%) this was due to minimization of harmful drug effects. Such deficiencies are widespread. Herxheimer et al. examined advertisements in leading medical journals in 18 countries.[32] They found that important warnings and precautions were missing in half of the advertisements and around 40% lacked information on harmful effects and contraindications. Informational content was poor both in developing and industrialized countries, with Finnish ads least likely to mention harmful effects (1% of ads).

Many advertising claims are presented only in vague, qualitative terms, making it difficult to estimate the probability of benefit. An Australian study examined 1504 claims in 174 advertisements appearing in a three-month sample of six popular Australian medical journals and bulletins.[33] Fewer than 8% of the ads contained quantitative information about treatment outcomes, and those that did usually stated the information in relative rather than absolute terms. In Canada, Lexchin looked at a sample of ads in 38 issues of four Canadian and one American medical journal: 50% presented results only as relative risk reductions, 9% provided enough information to calculate absolute risk reductions and the rest did not quantify likely treatment outcomes.[34] The presentation of drug effects in terms of relative risk reductions alone has been found to exaggerate impressions of benefit[35] and physicians' willingness to prescribe a drug.[36] Gutnecht examined how research results were presented in ads in a six-month sample of four journals (three U.S. and one Canadian). [37] He found 43 quantitative presentations of data, in 33 of 187 ads (17.6%). Rarely was the reader provided enough information to judge the validity of the data: most did not state whether subjects in trials were randomized, just over half did not state if they were blinded to treatment allocation, few confirmed that all subjects were accounted for and none mentioned comparability of treatment groups.

There are no published studies examining the interaction between physicians' reliance on drug promotion, and patient behaviours in response to DTCA. Such interactions are likely. For example, if physicians receive free samples from sales representatives for DTCA products requested by patients, they may be more likely to provide the requested medicine than if they do not have free samples available, or only have a sample for a competitor. Additionally, physicians are exposed to the general media, and similar images and messages in DTCA and physician-directed promotion could reinforce one another. These suggestions remain speculative. Companies analyze the effectiveness of different combinations of marketing techniques, but such research is not publicly available.

3.1.2 Social influences on prescribing decisions

In a commentary on 'what constitutes good prescribing?'[38] Barber points out the need for attention to grey areas when assessing prescribing quality, particularly in terms of juggling respect for patients' choices with evidence-based criteria for maximizing effectiveness, minimizing risk, and prescribing the least expensive of equivalent choices. He discusses the increasingly common view that compliance with patient choice, for example for brand-name drugs rather than generic equivalents, or for antibiotics for viral infections, is a feature of poor prescribing. This view conflicts with ideals of shared informed health care choices. At a minimum, physicians should listen to patients' desires and make sure that their choices are based on full information. Rather than striving to make all of their prescriptions evidence-based, physicians should set themselves a compromise level of perhaps 80% that meet prescribing appropriateness criteria. As an example to illustrate this dilemma, Barber discusses his regret at having switched a dying man from a costlier to a less costly sleeping pill, against his wishes.

Inappropriate prescribing in response to patient wishes is well documented, particularly in studies of antibiotic prescribing for viral infections. [39] Barber's commentary highlights the difficulties physicians often face in juggling conflicting desires to be caring and empathetic towards their patients, and yet to avoid providing treatments that are unnecessary or unnecessarily expensive. These conflicting pressures exist even in the absence of patient-directed pharmaceutical advertising.

In many cases, however, physicians misinterpret their patients' desires. Britten and colleagues carried out a qualitative study of 35 consultations in 20 general practices in England.[40] They audiotaped consultations and interviewed both the patients and physicians about the consultation and prescribed medicines, and compiled a list of categories of misunderstanding in relation to prescribing. These were often based on inaccurate assumptions and unvoiced patient preferences. "In particular," the authors note, "doctors seemed unaware of the relevance of patients' ideas for successful prescribing and of the fairly widespread aversion to taking medicines." For example, in some cases patients were consulting primarily because they wanted a diagnosis, whereas

physicians assumed that they wanted a prescription. This study highlights the complexity of patient/doctor communication and in particular its relationship to improvements in medicine use.

A more recent qualitative analysis of patients' decisions about whether or not to take antihypertensive drugs highlights the active role of patients in decisions on medication use.[41] The authors carried out in-depth interviews of a sample of 38 patients who received repeat prescriptions of antihypertensives in two U.K. urban general practices. Most patients mentioned explicitly mentioned balancing their reservations against the potential benefits of using antihypertensives. These perceived risks and benefits sometimes differed markedly from established pharmacological effects: for example many patients said they took antihypertensives because they made them feel better, although this perception is at odds with the asymptomatic nature of most hypertension. Reservations were often related to the perception that the use of a medicine was a signifier of ill health, rather than with specific adverse effects of antihypertensive therapy.

Similarly, measures of compliance often fail to take patient perspectives into account. In one study of the effects of patients' recall of physicians' instructions on compliance, researchers discovered on further investigation that 16 of the 54 included patients (30%) rejected the physician's diagnosis.[42] An earlier examination had only examined patients' recall. Upon re-analysis, patients' memory appeared to be strongly affected by whether or not the patient agreed with what the physician had said.

In another qualitative study, U.K. primary care patients were interviewed in their homes before a consultation and results were matched to interviews with physicians after the consultation.[43] Only 4 of the 35 patients had fully voiced their concerns and desires to their physicians. Psychosocial concerns and concerns related to patient autonomy were most often left unmentioned.

These studies highlight the social nature of the interaction between physicians and patients, including prescribing decisions and medicine use. They suggest that patients and

physicians' perceptions of a consultation frequently differ. Additionally, patients' compliance with physicians' recommendations may be strongly affected by their own opinions about their health conditions and the type of care that is needed.

Physicians' perceptions of patient expectations of a prescription

DTCA is likely to be one of a number of influences on patient expectations of a prescription medicine in primary care. Thus one related body of research is on the influence of patient expectations on prescribing. Britten and Ukoumunne compared primary care patients' expectations of a prescription with physicians' perceptions of those expectations and decisions to prescribe.[44] Physicians' perceptions of patient expectations of a medicine were the strongest predictor of the decision to prescribe. In 22% of consultations physicians provided prescriptions when they did not believe they were indicated 'on purely medical grounds'. This U.K. study took place in an environment without patient-directed prescription drug advertising. However, it highlights the influence of physicians' perceptions of patients' hopes on prescribing decisions, as well as their ambivalence about the medical need for some of the prescriptions they provided.

A similarly designed survey in primary care in Australia confirms these results.[45] If physicians believed that patients expected a medicine, they were ten times as likely to provide a prescription to those patients, compared to other patients (odds ratio = 10.1; 95% CI 5.3 – 19.6). Physicians were usually correct about patients' expectations (182/255 patients, or 71% of the time). As in the U.K. study described above, physician perception of patient expectations was a stronger predictor of prescribing decisions than patient expectations. Similarly, a German study found that if physicians believed a patient expected a medicine, they provided a prescription in nearly 100% of cases. However, in this study the physicians were correct only 41% of the time. [46]

These studies highlight the strong social as well as medical component to prescribing decisions, whether conscious or not. When physicians prescribe a medicine in response to perceived patient wishes, they are communicating the belief that a patient's symptoms represent a medical problem, as well as the offer of a solution. Michael Montagne

describes a symbolic component to the use of medicines: "The ritual of interacting with a physician and receiving a prescription is a symbolic act. The act of taking a medication (whether self-directed or prescribed by someone else) fulfills an ingrained habit; the need to take something when confronted with illness."[47] Officially the physician is the "gatekeeper" for access to prescription-only medicines and has sole legal responsibility for prescribing decisions; unofficially, many ambiguities exist in this gatekeeper position, even in the absence of DTCA.

One of the most contentious areas in which patient pressure is perceived to affect prescribing is in the unnecessary prescribing of antibiotics for respiratory infections encountered in primary care. These conditions are usually self-limiting and do not require antibiotic treatment. Macfarlane et al. compared prescribing decisions to patient expectations for 787 U.K. patients with acute symptoms of lower respiratory infections who consulted 76 family physicians.[48] Both patients and physicians filled in a questionnaire following the consultation. Nearly 9 out of 10 patients believed that antibiotics would help their symptoms, and over a quarter of those patients asked for a prescription. Patients who expected antibiotics were much more likely to receive them than those who did not (85% vs. 41%, $p<.0001$). Physicians prescribed antibiotics to 74% of the patients, although for 126 of these patients (22%) they believed that the antibiotic was probably or definitely not indicated, and in 44% of cases they said that non-clinical factors influenced their decision to prescribe. Over half the time this was because of perceived patient pressure, and in these cases the physician was much more likely to judge that the antibiotic was not indicated (63% of consultations with patient pressure).

In contrast, in a study in metropolitan Toronto, Miller et al. found that physicians generally felt that patient demand had little effect on their prescribing decisions.[49] However, they were more likely to cite perceived patient desire as a factor influencing prescribing in consultations in which they were uncertain about treatment decisions.

A U.S. study of consultations for children with ear, nose and throat problems, most of which were likely due to viral infections, similarly found that the most consistent

predictor of antibiotic use was physicians' perceptions that parents wanted antibiotics.[50] The physicians were also significantly more likely to diagnose the infection as being bacterial when they thought parents wanted antibiotics (70% vs. 31%). In this study, physicians overestimated parents' desires for antibiotics.

These results are relevant to studies of DTCA for several reasons. Physicians said that they prescribed some medicines that they believed were not indicated 'on purely medical grounds' or because of 'non-clinical factors', often because they perceived patients to expect a prescription. In the case of two studies of antibiotic prescribing, both the diagnoses provided to patients and prescriptions were influenced by physicians' perceptions of patient expectations.

These types of influences on prescribing occur in environments without DTCA. They are likely to exist in different environments, including those with DTCA. Thus in environments with DTCA, patient desires or expectations of a prescription are unlikely to be solely attributable to patient-directed advertising. This suggests that DTCA may lead to changes in the frequency of a type of interaction that is already occurring between patients and physicians, rather than a qualitatively different interaction, although the types of patient expectations, products and conditions involved may differ.

Research on antibiotic prescribing also suggests that patients' expectations of future treatment are strongly influenced by previous care. Little and colleagues followed up 716 patients who had participated in a randomized controlled trial testing of antibiotic prescribing for sore throats to see whether they had returned to see their doctors again for sore throat during the next two years. In the initial trial, patients without antibiotics had similar complication rates to those receiving them, suggesting that antibiotics were usually not needed. Those who received antibiotics, however, were more likely to consult physicians' again for sore throat during the following two years: adjusted hazard ratio 1.39 (95 % confidence interval 1.03 –1.89). As the two groups were randomized, there is no reason to believe that these patients experienced more sore throats. However, they

appear to have been more likely to define sore throat as a condition requiring medical treatment.

This study highlights the inability of individual patients to know whether their sore throat resolved because they were taking antibiotics or because it was a self-limiting condition and they got better with time. It also suggests that the belief that a medicine is needed for a specific health problem is influenced by previous experience of medical care, and not only by cultural factors or pre-existing health beliefs.

Models of patient-physician interactions in primary care

Three key models of patient-physician interactions in primary care are often described:

- The paternalistic model, in which physicians diagnose and decide on treatment recommendations and inform the patient;
- The informed choice model, in which physicians are seen primarily as a source of information and the patient ultimately decides, and
- The shared decision-making model, in which information exchange is two-way and the physician and patient jointly decide on treatment.[51]

The current preferred model – perhaps in theory more than practice – is shared informed decision-making. However, when it comes to overprescribing of antibiotics in primary care or prescribing of 'medically unnecessary' drugs in response to perceived patient expectations, a clash of ideals exists. In these cases, how is it possible to reconcile the ideal of shared informed decision-making with the ideal of evidence-based prescribing? Butler and colleagues[85] suggest that a paternalistic model, in which the doctor decides, is inappropriate even for respiratory tract infections in primary care, because four key assumptions are not met:

- A single best treatment exists;
- Physicians know the best treatments available and consistently apply them;
- Physicians are best able to evaluate trade-offs between different treatments and make treatment decisions;

- Because of their professional concern for the welfare of their patients, physicians have a legitimate investment in each treatment decision.

They argue that evidence exists that antibiotics sometimes help (although they do not address the need to weigh inconsequential benefits against risks of antibiotic resistance), that inappropriate prescribing is rampant, and that physicians often prescribe for social reasons such as bringing closure to a consultation. In other words, according to Butler et al., physicians should not be trusted to make prescribing decisions alone as they often make poor choices.

The informed choice model, in which the patient receives the information and then decides, is inappropriate both because patients may not consider the broader social implications of antibiotic resistance and because they may prefer not to be burdened with decision-making when they feel unwell. Additionally, this model does not adequately reflect physicians' legal responsibility for prescribing decisions, Butler et al. argue in favour of open, two-way discussions based on full information. They believe that prescribing of antibiotics for viral infections cannot be addressed unless patients obtain full accurate information, but not full responsibility, for prescribing decisions.

It is possible to reduce unnecessary antibiotic prescribing by providing patients with information explaining appropriate conditions for use. Macfarlane et al. randomized patients with acute bronchitis who were judged not to need antibiotics immediately into two groups.[52] All were provided with a prescription to fill only if they got worse, and received verbal assurances that most bronchitis resolves without antibiotics. Half also received an information booklet explaining conditions for antibiotic use. Antibiotic use was reduced by one fourth in the patients who received the booklet (risk ratio 0.76; 95% CI 0.59-0.97, p=0.04).

One limitation with the model of shared informed choice is in the type and quality of information available to the public. Coulter and colleagues used two types of panels, of clinical experts and of patients with targeted conditions, to review U.K. patient health

information materials.[53] The panels found that the materials were often patronizing and unbalanced, and did not contain basic information readers needed to judge their relevance. For example, nearly a third lacked a publication date. Very few contained references or discussions of the strength of research evidence. The authors concluded that, "there was a dearth of information designed specifically to support patient involvement in treatment options."

This issue is especially relevant to research on DTCA. As described in Chapter 2, proponents of DTCA hypothesize that it empowers patients to participate in shared informed choice, whereas critics believe that it creates pressure on physicians and interferes with mutually supportive therapeutic encounters. DTCA's ability to promote shared informed decision-making can be judged on the basis of content and information quality, applying standards similar to those applied by Coulter and colleagues to patient leaflets. In other words, the information should be accurate, balanced, complete, and should include background information that allows the public to judge the relevance of claims. DTCA fails to meet these requirements in two key ways. Firstly, there is a conflict between advertisers' aims to promote use of a specific product and the patient's need for unbiased comparative information as a basis for shared informed health care choices. Secondly, both the regulatory experience and published research on advertising content suggest that DTCA frequently fails to meet predetermined criteria for information accuracy and completeness, criteria, as is described in Chapter 2, Section 2.4.1.

3.1.3 Relevance of these findings to research on DTCA

Studies of the influence of pharmaceutical promotion on prescribing decisions, and on physicians' prescribing in response to patient expectations of a prescription, highlight the many non-medical factors affecting diagnoses, and treatment choices. DTCA is not the only commercially motivated influence on prescribing decisions. Although product-specific spending in some cases exceeds physician-directed promotion, as a whole the pharmaceutical industry spends much more on promotion aimed at physicians than on DTCA. Nor is DTCA likely to be the only source of patient expectations for prescriptions in primary care. Thus DTCA is expected to influence the frequency of prescribing

choices influenced by drug promotion and by patient requests for medicines. Whether or not patient-directed advertising also causes fundamentally new patient-doctor interactions is unknown, but it is likely to amplify these existing effects.

The research evidence on physicians' reliance on commercial information sources and prescribing decisions provides a generally pessimistic view of the likely effect of DTCA on prescribing appropriateness, as there is no *a priori* reason to believe that promotional information would have opposing directions of effect on physicians and patients. The research evidence on the influence of perceived patient expectations on prescribing decisions additionally suggests that if physicians are aware that a patient desires a specific medication, they are likely to provide it, particularly in situations involving uncertainty about optimal treatment.

Additionally, studies on physician perceptions of patient expectations for a prescription provide a model for collecting and comparing information from patients and physicians covering a single consultation. This framework allows for a direct comparison between patient expectations and desires, and prescribing decisions. The focus is primarily on patient and physician behaviours during a single surveyed consultation, rather than on their intentions or memory of past events. Thus this type of design is less prone to recall bias or to difficulties in distinguishing between stated intentions and behaviour changes than the methods used in most DTCA consumer surveys thus far. It is also able to distinguish between prescriptions initiated by patient requests, and those initiated solely by physicians.

As is described in Chapter 2, DTCA consumer surveys have mainly relied on telephone interviews of random samples of the U.S. population that collect information about past events, often over long periods of time. Other evidence, from administrative and sales data, cannot clearly distinguish between sales stimulated by DTCA and those stimulated by physician-directed promotion or other factors.

3.2 Theoretical approaches to measuring DTCA

Four papers have examined how to best measure the effects of patient-directed pharmaceutical advertising on health and health care services. These papers address both the question of appropriate research design and the most relevant existing conceptual frameworks. The following section reviews these papers as a background to the development of the framework used in the current study (described in Chapter 4). Three of the four articles were commissioned background papers presented at a meeting convened by the U.S. Department of Health and Human Services Office of the Assistant Secretary for Planning and Evaluation in May 2001. [54] The aim of this meeting was to discuss which frameworks and methods were best suited to DTCA research on health care use, costs and outcomes. The fourth paper was an economic evaluation commissioned by Health Canada as part of the same impact assessment of DTCA as the research carried out for this dissertation.[55] A briefer version of the paper is published in the *Journal of Health Services Research and Policy*.[56] These four papers examine two main approaches to assessing the effects of DTCA: economic analyses and health services utilization research.

3.2.1 Economic analyses

The role of DTCA within the pharmaceutical marketplace

In a paper on determinants and effects of patient-directed prescription drug advertising, Frank and colleagues suggest ways to study the patterns and effects of DTCA in light of the unique characteristics of the prescription drug market.[57] They explicitly focus on the actions of manufacturers as well as other players, including patients, physicians and managed care organizations.

The prescription drug market differs from the market for other consumer goods in that the person who chooses what will be used does not buy the product. With a shift to third party payment and only 27% of U.S. drug costs paid for out-of-pocket in 1998, as compared to 93% in 1965, increasingly, as Frank et al. note: "he who consumes does not pay." [57]

In light of the fact that pharmaceutical benefits have been among the fastest-growing cost components for managed care and other health plans in the U.S., those plans have increasingly sought new ways to manage these risks. Many health plans impose formulary restrictions, and some require physicians to share the financial risks for pharmacy costs. Thus, U.S. physicians have moved from working within a financially insensitive fee-for-service payment system to a more cost-sensitive managed care system. This shift is one of the factors frequently cited as contributing to the rise in DTCA in the U.S. [58]

Frank et al. suggest applying a profit maximization framework to the choices companies face in terms of price, marketing spending, and the mix of marketing techniques that maximize profit over time. Applying Dorfman and Steiner's model,[59] they hypothesize that the optimal marketing to sales ratio reflects the ratio of marketing demand elasticity to price elasticity of demand. *Marketing demand elasticity* is defined as the percent change in quantity sold given a 1% change in marketing efforts; the *price elasticity of demand* is the percent change in quantity sold in response to a percent change in price.

Given the characteristics of the pharmaceutical marketplace, the influence of marketing efforts (marketing demand elasticity) is expected to be large early in a product's life cycle, and the influence of price is expected to be smaller. During the mature phase of its life cycle, the two are expected to converge, and when a product goes off patent they are expected to reverse. In other words, firms find it profitable to advertise new drugs heavily very soon after product launch, then to taper off, with little to no advertising expenditure but increased price competition once the products are off patent.

This analysis highlights the importance of patents to marketing decisions. Frank and colleagues are not alone in stressing the importance of patents to the pharmaceutical marketplace. De Laat et al., a team of Dutch researchers who examined the effects of pharmaceutical promotion, went so far as to suggest that, "[t]he pharmaceutical industry may be viewed as a product of the patent system."[22]

Table 3.2 presents a summary of the research questions Frank et al. propose, relating both to effects within the pharmaceutical marketplace and to impacts on consumer health and information needs. Their hypotheses span positive, negative and neutral effects on patients' health and appropriateness of use of health care services and prescription drugs.

Table 3.2: Key research questions proposed by Frank et al.

Question	Hypothesized DTCA characteristics
What are the characteristics of advertised products?	Drugs used in primary care vs. in hospital Low risk, easy-to-use (similar to OTC drugs) Large target audience: chronic and common illnesses,
	Hypothesized DTCA effects
Is there an overall shift in promotional spending associated with use of DTCA?	If DTCA becomes less expensive due to deregulation; promotional mix would be expected to change; Composition of marketing media could shift over time
How does DTCA affect price elasticities?	If DTCA is informational, advertising would enhance price competition; If DTCA is persuasive it would not
What is the impact on entry barriers?	DTCA could lead to reduced competition within a class if it is a barrier to market entry; Prohibiting advertising could decrease competitiveness by removing a means for entrants to gain market share
What are the effects on demand?	Shifts in demand for advertised brand Shifts in demand for drug class Differences in demand by physician incentives Differences by health plan formulary arrangement
How do 3rd party payers respond?	Shift formulary position; Increase co-payments
What is the effect on appropriateness of care?	Previously untreated get needed drugs Demand increases by those unlikely to benefit
	People are matched differently to specific treatments; receive more (or less) appropriate treatment

A number of approaches are suggested to investigate the characteristics of advertised products and their place within the pharmaceutical marketplace. Variables of interest include types of treated condition, ease of use, safety profile, types of physicians who prescribe specific drugs, share of hospital vs. outpatient sales, size of market, existence of generic and OTC substitutes, whether a product was a market leader in its class, the time elapsed since launch, and time to patent expiration. Additionally, studies of the level and composition of DTCA outlays for advertised drugs can provide insight into the relationship between different marketing strategies and product characteristics.

Frank et al. suggest using administrative databases and individual claims data to measure effects on consumer demand, looking at both continuous and discrete changes over time. The latter could be combined with 'natural experiments' in regulatory policy, such as the

U.S. FDA 1997 regulatory change affecting broadcast advertising. This type of dramatic shift allows for comparisons of the period before and after policy change. Impacts on prescribing appropriateness could be examined using indicators developed from existing treatment guidelines, knowledge of co-morbidities of users and contraindications.

They hypothesize that in general advertising would improve appropriateness of medicine use because consumers would obtain additional information and greater understanding of the product. This does not take into consideration the empirical studies carried out thus far on content of U.S. DTCA, nor of regulatory reviews in the U.S. and New Zealand, which suggest that misinformation is common (See Chapter 2).

This hypothesis also reflects an underlying unstated assumption: that newer drugs are better than older alternatives. Within Frank et al.'s profit maximization model, firms are expected to concentrate DTCA spending on new products. A systematic evaluation of over 2200 new drugs launched onto the French market between 1981 and 2000 found that only 74 provided important therapeutic advantages over available treatments; most were 'me-too' drugs without therapeutic advantages.[60] Similarly Canada's Patented Medicines Pricing Review Board judged that between 1996 and 2000, only 6% of 415 new patented products were 'breakthrough' medicines.[61] These analyses suggest that newer drugs cannot be assumed to be better than older alternatives.

Frank et al. also recommend the use of treatment guidelines together with knowledge of patient characteristics, co-morbidities and concomitant treatments to measure effects of DTCA on treatment appropriateness. Evidence-based treatment guidelines provide a useful 'gold standard' for treatment appropriateness. However, if guideline developers have a vested interest in the promotion of specific products, they may introduce a bias into the interpretation of the evidence. A cross-sectional survey of authors of clinical guidelines, published in the *Journal of the American Medical Association* in February 2002, found that conflicts of interest were commonplace and usually involved the drugs considered in the guidelines.[62] In most cases there were no formal procedures for authors of guidelines to declare these conflicts or to exclude themselves from parts of the

guideline procedures. This study did not examine whether vested interests affected the degree to which guidelines reflected the research evidence.

A review of five cholesterol-testing guidelines found that in four of the five cases, guideline recommendations did not reflect the research evidence.[63] The authors identified reliance on clinical experts in guideline development as a key factor associated with divergence from the evidence. This example is especially relevant to DTCA, as cholesterol-lowering drugs are heavily advertised to the U.S. public, and ad campaigns frequently promote cholesterol testing. In another example relevant to DTCA, guidelines for general practice treatment of gastro-oesophageal reflux disease (GERD) published in the *British Medical Journal* in 2001 were written by clinicians with close connections to AstraZeneca, the manufacturer of the leading proton pump inhibitor, omeprazole (Prilosec in the U.S., Losec in Canada). These guidelines were developed at a workshop sponsored by AstraZeneca, and the company participated in the preparation of the manuscript.[64] The recommendations favoured first-line use of proton pump inhibitors to treat GERD. Thus in these cases Frank et al.'s assumption is not met; clinical guidelines do not necessarily provide a standard for treatment appropriateness that is reliable and/or independent of companies' aims to maximize sales.

Frank et al. also hypothesize that products will be advertised if they are easy to use and are associated with few serious risks. However, a short time since product launch is associated both with the probability that a drug will be advertised to the public and, inversely, with the extent of knowledge of harmful effects. For example, an analysis by Lasser et al. of new chemical entities launched from 1975 to 1999 found a 20% probability that new serious risks would be discovered post-launch, leading to a 'black box' warning on the label or to market withdrawal. Half of the labeling changes occurred within seven years; half of the market withdrawals within the first two years post launch.[65] Thus, assessment of characteristics of advertised products is likely to be confounded by timing of advertising campaigns in relation to market launch. Additionally, published reports of randomized controlled trials often contain incomplete information on the adverse event experience of trial participants.[66]

Frank et al. appear to assume that manufacturers will choose to advertise prescription drugs to the public if they are generally similar to over-the-counter (OTC) products. In some cases, this appears to be true: low-sedating antihistamines for allergy such as loratadine (Claritin) and fexofenadine (Allegra) are among the drugs with the highest product-specific DTCA spending in the U.S. These products have OTC status in Canada. The U.S. FDA recommended that manufacturers seek OTC status, but thus far the companies have chosen not to do so, presumably because it is more profitable to maintain prescription-only status.[67] This situation raises interesting questions about the potential role of DTCA in supporting manufacturers' sales through increased consumer demand, without the price competition that might be expected to follow a switch to OTC status. However, many other drugs advertised to the U.S. public do not fit the classic profile of OTC drugs. For example, drugs such as troglitazone (Rezulin), a treatment for type II diabetes, and sibutramine (Meridia), an obesity drug, have been advertised to the U.S. public after they had been withdrawn from markets in other countries for safety reasons. Other examples of DTC-advertised drugs that were later withdrawn for safety reasons include cisapride (Propulsid) and alosetron (Lotronex).[68] Alosetron has since been reintroduced in the U.S., but under restricted conditions.

In the case of troglitazone and cisapride, market withdrawal was preceded by a number of labeling changes that increased the complexity of administration, such as in the former case requirements for frequent monitoring of liver enzymes and for the latter a long list of other drugs to avoid because of interactions. Thus, in these cases, DTC advertised products would not be characterized by ease of use, as compared to most drugs provided to outpatients. Similarly infliximab (Remicade) is advertised to the U.S. public in spite of a requirement for intravenous administration.

The strength of the model proposed by Frank et al. is in its attention to the characteristics of the pharmaceutical market and market pressures on competing firms; the weakness of their model is primarily in the inclusion of untested assumptions about clinical characteristics of DTC advertised drugs and of effects of DTCA on consumer welfare, some of which directly contradict the results of empirical studies.

Modeling the effects of DTCA on consumer welfare

In another exploration of the applicability of economic models to DTCA research, Morgan and colleagues investigate the use of economic theories of advertising to predict the consumer welfare and cost consequences of DTCA.[56] Rather than simply assuming that DTCA is informational advertising, they examine whether or not DTCA fulfills the assumptions underlying economic theories of informational advertising.

Like Frank et al., Morgan et al. begin with the premise that firms engage in promotional activities with a single aim: the pursuit of profits. Therefore investments are made in advertising if they are expected to induce a transfer of wealth from consumers (and third party payers) to producers. Some marketing campaigns may not increase profits, but these are generally short-lived, as profit-maximizing firms do not continue to invest in activities that fail to provide adequate returns.

Is this improvement in producer welfare accompanied by an improvement in consumer welfare? Consumer welfare would be expected to improve if advertising conveys accurate information about the availability, cost, uses and quality of a product. Therefore, although consumers may pay more for an advertised product, they would also receive better value because the additional information provided by advertising would lead them to choose the products most appropriate to their circumstances.

Theories of non-informational benefits for advertising have also been proposed.[69] For example when the purchase of a good is associated with increased social status, as in the case of luxury automobiles or designer label clothing, then advertising may increase the status-enhancing characteristics of the product. In most cases this does not readily apply to prescription drugs, as one does not normally wear a medicine or leave it in the driveway for the neighbours to admire.

Status enhancement can also have negative consequences for rationality of treatment. For example, in tropical countries the marketing of antidiarrhoeal drugs through their image as potent modern pharmaceuticals creates a significant barrier to appropriate treatment of

childhood diarrhea, given the lack of efficacy of these products in preventing dehydration, the most serious consequence of diarrhoeal disease.[70] Oral rehydration therapy, the most potent 'cure' in terms of saving children's lives, does not benefit from a similarly enhanced image of potency, as it can be produced at home with commonly available ingredients.

Many other less dramatic examples exist of the image enhancement of medicines through advertising. The use of celebrity endorsements in advertisements is an example of advertisers' attempt to develop a link between product use and enhanced social status.[71] Can the enhanced image of a prescription drug through its association with a star improve medical care or consumer welfare? If it is the most effective and safest treatment available for a specific condition, and is no costlier than alternatives, then consumers with that condition will benefit from using it regardless; if it is less effective or safe, or more expensive than equivalent alternatives, a hockey star's endorsement is unlikely to create better outcomes or improve the cost-effectiveness of treatment.[†]

Morgan and colleagues stress that whether advertising is beneficial or harmful to consumers hinges on its role: is it primarily informational or persuasive? If its role is primarily to provide objective information about the uses and quality of a product, then consumers' appraisals will be more accurate after exposure than before. Theories of informational advertising assume that advertising does not shift core consumer preferences, but helps consumers to find the goods to best meet their inherent needs. Truth in advertising is a necessary precondition. This requires either effective regulation or correction by market mechanisms. The latter case would consist of situations in which it was more profitable to advertise truthfully than deceptively, or in which companies could suffer financial losses if they carried out deceptive advertising campaigns.

Economic theory does not rule out misleading or fraudulent advertising as a means of pursuing profits, just as it does not rule out the possibility of bias in privately funded

[†] Some might argue that the status-enhancing effects of celebrity endorsements could enhance the placebo effect of medicines and thus lead to health benefits. This suggestion has not been empirically tested, and if the primary aim of therapy is the placebo effect, more cost-effective (and safer) alternatives exist.

research.[72] In both cases, such investments would be stopped if they became unprofitable, for example if the perpetrators were detected and punished with sufficient frequency and severity to affect the firm's profitability. The regulatory experience with DTCA in the U.S. indicates that repeat violations – both by company and by product – are common, suggesting that the adverse effects of regulatory actions on a firm's profitability are minimal.[73]

It can be highly profitable for companies to misrepresent pharmaceutical product characteristics, as is illustrated in a recent U.S. court case involving Parke Davis' promotion of gabapentin (Neurontin), to physicians.[74] The company is alleged to have promoted this secondary epilepsy treatment for more than a dozen medical conditions for which it was not approved, including attention deficit disorder in children, neurological pain, and bipolar disorder. Documents released in this Massachusetts court case indicate that Parke Davis adopted this marketing strategy, rather than carrying out the clinical trials needed to obtain approval for new indications, because the product would soon lose patent protection.[75] An internal whistle-blower, David Franklin, reported that he was told to tell physicians that early results from clinical trials showed that the product was highly effective for many off-label uses, although no data existed to support these statements. He was also advised by managers not to mention published reports of adverse effects in children. Tactics to extend the product's use were apparently highly profitable: in 2001 sales of gabapentin reached U.S. $1.7 billion, mainly for unapproved indications.[28]

Morgan et al. list three conditions that must be satisfied in order for market mechanisms to ensure truth in advertising. The target audience must:

1) have predetermined preferences concerning product characteristics;
2) be able to detect false claims about these characteristics;
3) be able to selectively reward only those firms whose products have the characteristics portrayed in advertising.

If consumer product preferences can be shifted by subjective and emotive appeals, firms that are attempting to maximize profits would be expected to respond by supplying ads

with these types of appeals. Although decisions about medical treatment are ideally based on scientific standards of safety and efficacy, pharmaceutical advertisements that rely on emotional appeals and celebrity endorsements are common,[21] suggesting that companies have found that such advertising works.

Market mechanisms are most likely to ensure that advertising claims truthfully represent product characteristics if consumers can detect false claims and selectively reward only truthful advertising. This could occur, for example, if they can verify whether products have advertised characteristics before purchasing them. In this case, consumers will choose not to buy a product that does not live up to advertising claims. However, a consumer cannot judge the qualities of a medicine by examining it before purchase. The look, feel or smell of a bottle of pills tells one nothing about its characteristics as a medical treatment and, in the case of prescription drugs, even if it did, this would be no help to the patient, who does not get to examine the bottle before purchase.

Consumers can, at least in theory, create conditions supporting only truthful advertising in the case of frequent repeat purchases, if they can verify marketing claims through personal experience with the product. In this case, truthful advertisers would generate more sales than advertising that created unrealistic expectations. However, if a person takes a medicine and feels better, it may be due to a placebo effect, or the natural history of disease, or the medicine. Patient demand for antibiotics for viral infections is an ongoing example of the inadequacy of individual experience as a tool to judge the effectiveness of medicines. Furthermore, if a drug is taken, even repeatedly, to prevent future illness or to treat a risk factor for disease, the user would not expect to experience a change in perceptible symptoms. This makes it even more difficult for a patient or prospective patient to tell if a drug has the advertised effect.

In symptomatic treatment of chronic discomfort or commonly occurring acute illnesses, the consumer is better able to tell whether a drug has helped, thus reinforcing truth-telling by refusing repeat purchases of drugs that do not live up to marketing claims. As Morgan points out, this is the traditional domain of OTC drugs.

It can be especially difficult for a consumer to judge advertising claims concerning minor differences between a product and its competitors, in terms of whether these represent a therapeutic advantage or not. Additionally, equivalent products may differ in cost, but patients may have little incentive to pursue products with price advantages if they do not pay for their own medicines.

In most cases, the only way that a consumer would be able to judge the truth of an advertiser's claims is if he or she has full access to (and can understand) the results of scientific studies of the drug's safety and efficacy, as well as the expertise with which to place these results in context and to compare the characteristics of this product to other treatments for the same condition. This presupposes specialized medical and pharmacy expertise – the type of training usually obtained by physicians and pharmacists – and/or access to accurate independent evaluations of the scientific literature on the product's characteristics and its role in treatment. It also presupposes open access to the results of unpublished trials provided to regulatory agencies in applications for market approval, particularly for newer drugs for which few published reports may be available.[76] In Canada, this information is considered confidential and is unavailable to the public.[77] Table 3.3 below presents an overview of the types of information consumers would need in order to judge the value of individual drug treatments.

Table 3.3: Key types of information needed for drug treatment choices

Information needed for drug treatment choices:
The probability of benefit versus the probability of harm in individual patients
How this treatment option compares to other available drug and non-drug alternatives
Price, especially in relation to therapeutically equivalent alternatives
Additional required information:
• The probability that the pharmaceutical is effective for specific treatment outcomes, ranked in importance to patients' health (i.e. mortality, serious morbidity,
• The speed at which it becomes effective
• Any differences in effectiveness in different population groups (men, women, elderly, children, patients with co-morbidities etc)
• What happens if a patient takes too much or too little (therapeutic window)
• Interactions with other pharmaceuticals or foods
• Drug class allergies
• Adverse effect profile, including type, frequency of serious and non-serious events, reversibility
• Differences in vulnerability to adverse effects across different types of patients
• Contraindications to use
• Mode of application (pill, injection, etc.)
• Administration schedule
• Duration of use

*Adapted from: de Laat et al., 2002[22]

Many barriers exist to public access to this type of information but it is theoretically feasible to make it available, and models of accessible technically complex information exist in consumer reports for a range of products such as electronic equipment. Education on the principles of pharmacotherapy is also feasible, both within the educational system and outside of it. However, in this type of scenario, the public would have ready access to detailed, accurate information on all available medicines. This raises questions about what additional *informational* role pharmaceutical advertising could play.

Given that consumers generally cannot tell whether advertisers' claims are true under current conditions, reliance on traditional market mechanisms is unlikely to protect the public against misleading advertising. This is also borne out empirically by the historical experience in the pre-regulatory era, in which spending on drug advertising was primarily aimed at the public, and ineffective – and at times harmful – products were often promoted as panaceas.[78]

This inability of market mechanisms to protect the public against misleading claims, together with the potential for toxicity of prescription-only drugs, is the basis for the legislated responsibility of health authorities for the regulation of prescription drug advertising. An argument made in favour of DTCA having an informational role is that it is more highly regulated than other forms of advertising, leading to a higher degree of accuracy.[79] However, recent U.S. regulatory history provides ample evidence that pharmaceutical ads aimed both at physicians and the public are often inaccurate and that the public and physicians rarely receive corrections of inaccurate information.[26 80]

Morgan also examines the extent to which firms have incentives to advertise three types of prescription drugs to the public: breakthrough products that represent significant therapeutic advances; competitors without established advantages ('me-too' products); and lifestyle drugs.[55] Morgan suggests that for breakthrough drugs for serious conditions, firms have little to no additional incentive to carry out full product advertising targeting consumers (i.e. ads with product name and health claims) as opposed to general disease-oriented advertising highlighting the condition treated by the medication. The

development of a breakthrough treatment for a serious disease is an uncommon event, and information on such products is rapidly disseminated within the medical community. Physicians are highly likely to prescribe them to patients with the relevant condition, making sales less dependent on brand-specific patient requests.

The incentive for full product advertising is highest for products vying for market share within a specific therapeutic class. This includes 'me-too' products without established therapeutic advantages over competitors. Firms also have an incentive to advertise drugs for 'lifestyle' conditions to the public, as many people would not otherwise recognize these conditions to be "medical problems" requiring drug treatment.

Market research approaches to assessment of outcomes of DTCA

The frameworks proposed above were developed by academic researchers interested in tracking the effects of DTCA, and in determining whether its effects on health service use and patient health are beneficial or harmful. The pharmaceutical industry also has an interest in tracking the effectiveness of advertising campaigns in terms of effects on sales volumes. Yuan, of IMS Health, a U.S. pharmaceutical market research company, describes a variety of approaches used to track the effects of DTCA campaigns, from panel surveys to semi-experimental controlled comparisons of different regions with different advertising exposure.[81] These approaches to DTCA research methodology were presented at the U.S. seminar on DTCA research described above. In selecting appropriate models to track effects on sales, she emphasized the need to detect the lag structure for a specific product. How long does it take for a new promotional campaign for a prescription drug to affect sales? This depends on the frequency of patient visits for a specific condition, both in the case of physician-oriented promotion and DTCA.

Yuan describes the use of sub-national test and control regions, matched in terms of socio-economic status, seasonal patterns, managed care environments and population structure. Sales are compared in the pre-DTCA and post-DTCA evaluation period, allowing for an appropriate lag time. The aim is to test a hypothesis of a systematic difference in product sales between the pre- and post-DTCA period. This approach is

similar to one used in the only published analysis of the effectiveness of a DTCA campaign for a single product, Basara's evaluation of the sales impact of a DTCA campaign for sumatriptan (Imitrex), in which she found an effect on prescription rates.[82]

Although the aim is primarily to track sales, the type of modeling used by market research companies, and their attention to moderating effects such as lag times, could also be incorporated into administrative database research.

Summary: economic analyses and market research

Yuan provides a practical means for pharmaceutical companies to know whether or not their advertising campaigns are promoting sales. This framework is more restricted than the economic analyses described above, in that it makes no attempt to measure effects on consumer welfare or prescribing appropriateness. However, knowledge of the magnitude of DTCA's effects on drug sales is a critical component in understanding potential effects on health care services. The main drawback is the limited public availability of some of some of the detailed spending and sales data needed for these types of analyses.

Frank et al. and Morgan suggest approaches to the analysis of DTCA that have much in common, in that they both assume that the manufacturer's aim is to stimulate sales and maximize profits. However, a key difference is in the underlying assumptions made about the effect of consumer-directed advertising on consumer welfare. Frank et al. assume that DTCA will benefit the public by providing previously unavailable information, whereas Morgan asks whether market mechanisms can ensure that the information in DTCA is accurate. He finds such mechanisms lacking, both on theoretical and empirical grounds.

Frank et al. and Morgan's papers highlight the need to situate pharmaceutical advertising as a marketing tool and to understand it within the framework of manufacturers' imperatives for profit maximization, as well as pharmaceutical product lifecycles. Although the focus of this study is primarily clinical rather than economic, an understanding of market mechanisms makes it possible to develop realistic hypotheses about the nature and likely effects of DTCA. It also identifies useful directions for policy-

oriented research. As Morgan points out, market mechanisms cannot be relied on to ensure information accuracy in DTCA, making the role of regulation more important. This suggests the need for research to assess the adequacy of different regulatory approaches, in terms of their effects on information accuracy, appropriateness of drug use, public understanding and health and cost outcomes.

3.2.2 Health Services Utilization Research Models

DTCA's role as a determinant of use of health care services

Schommer and Hansen have explored the applicability of different types of theoretical models of determinants of health services utilization to research the effects of DTCA.[83] They ground this approach in a public policy decision-making perspective. In other words, the aim of research to estimate the effects of DTCA should be both to measure the contribution to equity and efficiency, and to plan policy responses that would contribute to the development of more equitable and efficient health care services. DTCA's primary aim – to increase product sales—is taken as a given.

Two types of theoretical frameworks are explored -- health behaviour theories and decision-making theories. Both aim primarily to model an individual patient's response to advertising exposure. The main difference is in whether DTCA is assumed to play a primary role, or whether it is modeled as one co-variate among others.

Health behaviour theories begin with an analysis of individual beliefs, expectations, motives, values and other characteristics and introduce the variable of interest – in this case DTCA – as a moderating or mediating variable. A mediating variable is a *necessary* intervening variable: x cannot lead to z unless y is present as a mediator. A moderating variable, on the other hand, causes a shift in effect, but is not a necessary intervening factor: in the presence of y, x leads to a different value in z. Schommer and Hansen stress the need to establish whether DTCA acts as a moderator or a mediator. Are its effects merely *quantitative* or is it also a cause of *qualitative* change? If the latter were true, DTCA would have effects that would not occur without exposure to prescription

drug advertising, such as new types of patient-doctor interactions, or patterns of medicine use not previously observed.

Schommer and Hansen review the existing theoretical models that could be applied to studies examining the role of DTCA, briefly summarized in Table 3.4. All of these models are applicable to some aspects of research on DTCA. Among the behavioural models, cognitive representation theories and decision-making theories focus primarily on the individual, whereas health service utilization models examine the individual's actions within a broader social context including not only health beliefs and attitudes, but also institutional and environmental factors. Agency theories also focus explicitly on social relationships, including disparities in power and position, but usually on a more limited scale, and diffusion of innovation theories primarily emphasize a broader social overview, in which the spread of medical technologies is analyzed in a similar way to adoption of other types of technological change.

The authors suggest first carrying out exploratory studies to identify key outcomes of interest, then designing studies around health behaviour models in order to determine the degree to which DTCA affects patient and physician behaviours. If clear evidence exists that DTCA is an important explanatory variable for health-related behaviours, they then suggest applying decision-making models.

Schommer and Hansen point out that DTCA is not the only variable affecting physician-patient relationships, prescribing, health care utilization and health outcomes. "... the most important way to investigate effects into DTCA is to view it within larger contexts and link the research problem to the explicit decision problem faced by policy makers." One example would be the use of a decision-making model to study whether consumer responses differ depending on how product risks are presented in an advertisement. If differences were found, these could be used to refine regulatory standards for risk information provision.

Table 3.4: Theoretical models for examining the role of DTCA

Type of models	Description	Applicability to DTCA
Cognitive representation models	Individuals'perceptions of illness and health seen as differing from biomedical disease models - health beliefs - locus of control: individual agency predicts behaviour - protection motivation theory: threats, fear key motivators - behavioural intention: intentions predict behaviours - social learning theories; self-efficacy, sense of control seen as key factors.	DTCA modeled as a co-variate, affecting public expectations about drugs, diseases, patient and physicians roles.
Decision-making theories	Persuasion theory. two types: rational, information-based, and/or peripheral, cues such as credibility, source, rewards. Other approaches: - attitude strength = determinant of role in decisions - information processing; format - hierarchies of effects theories; degree of involvement key to receptivity - adaptive decision-making (attempt to resolve multiple goals; minimize effort)	Content analysis and testing of consumer responses to DTCA; effects of DTCA on both patient and physician decision-making.
Agency theories	Focus on situations in which one party is an 'agent' for another, such as patient-doctor relationship; focus on adverse selection, hidden information, moral hazard	Effects of DTCA on patient-doctor and patient-payer relationships.
Health Services Utilization models	Relationships among personal/familial, societal and institutional factors predict the use of health services. Key factors: need; predisposing factors (beliefs), enabling factors (finances, access), societal and institutional organization Definition of equity and efficiency: patterns of health care use closely determined by need; less of an influence from other factors.	DTCA is viewed as an external factor influencing perception of need or health beliefs; more as a co-variate than a primary predictor of outcomes
Diffusion of innovation theory	Models rate of adoption of new technologies: perceived attributes of technology; how decisions are made; communication channels; nature of social system and extent of promotional efforts	DTCA could change rate of adoption of new technologies; this may be positive (important innovations) or negative (overadoption).

Focus on individual ↕ Focus on social interactions

Their framework is general and does not include an examination of the applicability of different models based on existing research evidence. However, clarification of the potential role of DTCA as a moderator or mediator of individual health behaviours is useful, as is the strong focus on a public policy perspective.

For some hypothesized outcomes, such as effects on patients' decisions to seek medical care, DTCA is likely to act as a moderator (increasing frequency), rather than a mediator (a necessary determinant). For others, such as direct patient requests for advertised

medicines or certain shifts in belief about the characteristics of advertised medicines and treated conditions, DTCA may act as a mediator.

From a public policy perspective, Schommer and Hansen's examination of theoretical frameworks points out the inherent limitations of approaches that focus entirely on individual patient responses, and neglect the interaction between environmental factors, patient and physician characteristics. Cognitive representation models, for example, are likely to be useful for studies that measure specific shifts in individual beliefs and behaviours associated with different levels of exposure to DTCA. They are less likely to be useful to examine the effect of DTCA on a health care system or drug use at a population level.

In terms of examining DTCA's effects on prescribing decisions in primary care, the most relevant models are health services utilization models, which examine individual beliefs and behaviours within a broader social context. The paper by Bero and Lipton, [84] described below, is an example of the application of this type of approach to DTCA research. Whereas Schommer and Hansen discuss the applicability of different models at an abstract level that avoids references to empirical studies on DTCA, Bero and Lipton tie their recommendations for a conceptual model for DTCA research much more closely to the existing empirical evidence.

Effects on patients and physicians: from a shift in attitudes to action

Bero and Lipton[84] outline a model of the potential effects of DTCA, beginning with a shift in patient and physician attitudes as a result of exposure to advertising, which in turn leads to a shift in behaviours and hence in the pattern of drug prescribing and use and eventually may affect health outcomes. The main approach suggested is to identify key variables and establish how they might best be measured in order to test for the existence of a causal chain. Bero and Lipton recommend measurement of population exposure levels and systematic analyses of advertising content as a necessary first step towards assessing the impact of exposure. This includes both an understanding of which products

are being advertised to the public, and the emotive and informational messages contained in DTC ads.

Bero and Lipton's model highlights the need to separate out the effects of DTCA on patient and physician *attitudes* from effects on *actions*, as well as to examine effects on the patient/doctor relationship separately. They highlight a number of possible effects on prescribing quantity and quality, as well as effects on health care plans and physician groups. For example, patient requests for advertised non-formulary drugs could result in changes in drug formularies or in the structure of co-payments, although there has been no systematic research to date on these types of policy responses.

Other hypothesized effects on health service utilization include increases in physician visits and use of diagnostic tests, or decreases in use of health care services (physicians, hospitals and emergency departments) if health problems are managed more effectively with requested advertised drugs.

Bero and Lipton identified six areas in which little data exists on the effects of DTCA:

- Patient/physician relationships
- Prescribing quality or appropriateness
- Physician group and health maintenance organization (HMO) actions in response to DTCA
- Health care costs and utilization
- Adherence to drug therapy
- Patient health outcomes.

Bero and Lipton correctly state that: "The causal link between exposure to advertising and patient health outcomes and health services utilization has not been established." The steps that have been studied – such as advertising quality or patient and physician attitudes – have generally been studied in isolation, and without attention to their relative importance in comparison to other influences on prescribing decisions, such as promotion aimed at physicians or cultural factors affecting the doctor/patient interaction. DTCA

needs to be contextualized as one of a number of influences on prescribing decisions, and its importance understood *relative* to other contributions to patient and physician-decision making.

Additionally, any empirical investigations of these influences should employ strong methodological designs, ideally randomized controlled trials (RCTs) or meta-analyses of RCTs. If RCTs are not feasible, the next level of evidence is from well-designed controlled trials (non-randomized), and cohort or case-control studies. Multiple time series with and without interventions may also be of value, as are descriptive studies, case reports and expert opinion. However, such studies generally cannot be relied on to support inferences regarding causation. Bero and Lipton also suggest applying Hill's criteria on causation to look at factors such as the strength, consistency and biological (in this case, social and economic) plausibility of study results.[85] The underlying message is that conclusions should not extend beyond what can be supported by the underlying evidence. As was described in Chapter 2, there are methodological weaknesses to the studies of behavioural change in response to DTCA that have been carried out to date; as a result, most claimed outcomes of DTCA are based on inadequate empirical research.

Bero and Lipton also suggest that an approach used by Avorn and colleagues to measure the influence of promotion on physicians[86] is also relevant to DTCA. Avorn et al. believed that physicians often underestimated the extent to which their prescribing was influenced by drug promotion. In order to test this hypothesis, they identified a set of 'commercial myths', ideas about drug treatments that were not supported by scientific evidence. In a 1982 survey of Boston area physicians, Avorn et al. found that most physicians who held advertising-oriented beliefs, and who reported that they prescribed accordingly, were unaware that they were strongly influenced by non-scientific information sources. Only 3% described drug advertising as a very important influence on their prescribing practices. However, 71% believed that impaired cerebral blood flow was a major cause of senile dementia and 49% believed that propoxyphene was a more potent painkiller than available alternatives such as aspirin. Neither of these 'commercial myths' was supported by scientific evidence.

Similarly, a recent survey of over 400 British general practitioners (GP's) and hospital physicians found that the information sources the physicians relied on in theory were not those most often used in practice.[87] When they were asked where they'd heard about the last new drug that they had prescribed, both GP's and hospital physicians mentioned a pharmaceutical sales representative more often than any other information source, although sales representatives were infrequently mentioned in response to a more general question about where they obtained information about new drugs.

As Bero and Lipton point out, studies on the influence of drug promotion on physicians are highly relevant to DTCA research. Both physicians and patients may underreport the degree to which they rely on advertising as an information source. Measurement of patients' behaviours and beliefs are more likely to provide an accurate assessment of the influence of DTCA than self-reported advertising influence.

Bero and Lipton stress the need to establish a clear causal chain from advertising exposure to effects on the organization and quality of health care services and on patient health outcomes. In Table 3.5, they identify the limits in existing approaches to measuring outcomes of DTCA, and question the validity of methods associated with a strong potential for confounding and recall bias.

Table 3.5: Limits of Methods used to study DTCA

Outcome	Type of Measurements	Limits
Extent of DTCA	Pharmaceutical industry spending	Confounding with physician-directed spending
Exposure to ads	Cross-sectional surveys	Recall bias
Content of ads	Cross-sectional content analysis	Sample selection Measurement validity
Patient attitudes	Cross sectional surveys	Recall bias
Patient demand	Cross sectional surveys	Recall bias
	Hypothetical scenarios	Context – other influences (confounding Intent, not action, measured)?
Physician attitudes	Cross sectional surveys	Recall bias
Prescribing quantity	Sales data,	Other influences on sales (confounding)
	Physician behaviours (recorded from patient surveys)	Recall bias

Adapted from: Table 1, Bero and Lipton, 2001[84]

Their recommended approaches to future research include in-depth qualitative analysis of recorded or videotaped patient-doctor interactions, chart review to assess appropriateness of prescribing, case-control studies of users vs. non-users of specific advertised drugs, cohort studies comparing groups with different exposure levels, and links between primary data collected from surveys and administrative data sets.

One aspect of this model is less well developed: measurement of health effects. The only specific outcome measure suggested is patient adherence to therapy. This is an intermediate or surrogate measure that may or may not ultimately be tied to health outcomes, depending on treatment goals, prescribing appropriateness, and drug class. For example, a case-control study found that NSAID users hospitalized for gastric bleeds were better adherers than similar patients not experiencing serious adverse effects.[88] If drugs are used for lifestyle purposes such as elimination of facial hair or for mild allergic rhinitis, better adherence is unlikely to bring health benefits. Conflicting effects — positive, negative or neutral in different contexts — suggest that adherence is unlikely to be a useful general predictor of health outcomes. Additionally, an advertising campaign might simultaneously promote better adherence in users of the advertised product but worse adherence in users of alternative treatments for the same condition. In this hypothetical scenario, measurement of effects on adherence only of the advertised drug could provide an incomplete picture of the effects of the advertisement.

3.3 Relevance of these models to the current study

The available body of empirical evidence on effects of DTCA on health and health care service use is limited, and much available research is hampered by inadequate methodology. Many claimed outcomes of DTCA are not supported by reliable research evidence. Given the rapid growth of DTCA and the highly polarized pharmaceutical policy debates it has provoked, this inadequate research base is problematic. Thus the attempts to outline appropriate conceptual models and research methodologies for DTCA research, as described above, are an important step towards improving the understanding of outcomes of DTCA.

One of the principles that emerges from the methodological approaches examined above is the need to ground assumptions underlying hypotheses about the effects of DTCA in existing research evidence. For example, Bero and Lipton emphasize the need to focus research on *actions* of patients and physicians, rather than their *opinions,* and the need for attention to the strength of research methodologies when drawing conclusions about effects of DTCA. Bero and Lipton's suggestion to incorporate Hill's criteria for causation into assessments of the effects of DTCA presumes that DTCA is not an isolated phenomenon, and that ideas such as 'biological plausibility' (or social and economic plausibility) can be used to develop hypotheses about the likely outcome of this form of pharmaceutical marketing, based on what is known about outcomes of other similar phenomena, such as physician-directed pharmaceutical marketing techniques. Additionally, hypotheses about physician responses to DTCA would be grounded in the existing body of knowledge on the determinants of physician prescribing decisions.

Economic evaluations of the role of advertising within the pharmaceutical marketplace can also assist in grounding questions about DTCA's effects on health and health care service use within models that also explicitly recognize the aims of advertising campaigns. Firms carry out advertising campaigns in order to increase sales and maximize profits; these campaigns are likely to reflect the constraints and opportunities of the pharmaceutical market in which they operate.

As noted above, Schommer and Hansen highlight the need to situate DTCA as a likely co-variate affecting patient and physician behaviours in primary care, specifically introducing the important distinction between variables that act as moderators and mediators. One model noted by them that has been extensively used in health services research stands out as being especially relevant: Andersen and Newman's behavioural model of health service utilization.[1] Although Bero and Lipton do not explicitly refer to this model, the approach they recommend is very similar, in that they situate DTCA research within a broader context of factors that affect patient's decisions to seek care and use prescription drugs.

3.3.1The Andersen-Newman model: applicability to DTCA research

Andersen and Newman developed a behavioural model of health service use in the late 1960s to assist in policy development to promote more equitable access to healthcare.[1] By focussing on the range of factors known to be associated with decisions to use health care services in addition to direct health needs, their approach allows for explicit modeling of the context in which individual patients move from exposure to advertising to requests and use of advertised medicines. Within this type of approach, DTCA would be modeled as one of a number of factors that can influence the degree to which use of health care services does or does not reflect medical needs.

The original aim of Andersen and Newman's model was to improve understanding of why health care services are used and to create operational definitions allowing for measurement of equity of access to care. The more equitable the access to medical care, the greater the role played by medical need and related demographic characteristics, such as age and gender, which are consistent predictors of health care use across settings. Given the consistency of this predictive value, these factors are believed to represent additional unmeasured aspects of need for health care services.

It is possible to measure the degree of equity of access to care by looking at the relative contribution of these factors as compared, for example, to other individual characteristics such as income, education, location of residence and race. These inter-relationships are complex, as differences in socio-economic status are associated both with differences in medical need and in access to services.[89] In essence the approach developed by Andersen and Newman allows for modeling of multi-factorial effects on patterns of individual and community use of health care services.

This behavioural model has been extensively used in health service utilization research since the early 1970's. It provides a flexible framework that has application as a basis for planning of interventions to address identified inequities. A systematic review identified 139 empirical studies of use of medical care services, published between 1975-1995, which relied primarily on Andersen and Newman's model as a conceptual framework. [90]

One example of the application of this model is the Australian longitudinal study on women's health, which examined use of general practitioner services within the framework proposed by Andersen and Newman,[91] combining survey data with data from linked administrative databases. Use of GP services was determined primarily by medical need, but the researchers also identified barriers to access to care among rural women, s reflected by lower levels of service use among those identified to be at higher need.

Andersen and Newman's initial model looked at people's use of health care services as a function of:

- **Predisposing** factors, such as age, gender, health beliefs and the social structure;
- Factors that **enable or impede** use, such as income level, availability of services in the community, and the presence or absence of financial barriers to access;
- Medical **need** for care. This is measured both as perceived need (self-assessed) and evaluated need (physician-assessed).

Over time, the model has been refined and extended, for example separating out population characteristics that predispose or enable individuals to seek care from characteristics of the health care system and the external environment, as well as incorporating feedback loops between individuals' experience of health care service use and subsequent care-seeking behaviours.[92]

Because this model was developed to examine equity of access to care, the initial outcome variable was use of services. However, when it comes to health care use, more is not necessarily better.[93] Access alone was replaced by *effective* and *efficient* access, with effective access measured as use leading to improved health status or consumer satisfaction with services, and efficient access measured by the level of improvement in health status or satisfaction relative to the amount of health care services used. This required drawing a conceptual distinction between consumer behaviours – use of health care services – and positive or negative outcomes of that use. This separation is of particular relevance to the modeling of patient behaviours stimulated by DTCA, as it

allows for the modeling of DTCA as one of several co-variates affecting patient decisions and care-seeking behaviours in primary care.

3.4 Conclusion: DTCA Research in Context

As is described in Chapter 4, the conceptual framework used for this study is an adaptation of the health services utilization model developed by Andersen and Newman. This allows for modeling of the effects of DTCA within the broader context of other influences on patient's decisions to seek care, and on patterns of prescription drug use within primary care settings. The focus is on measurement of patient and physician behaviours within primary care settings, rather than opinions or intent. Bero and Lipton recommended a similar approach,[84] and this is supported by existing knowledge on the influence of pharmaceutical promotion on prescribing decisions.

Little of the survey research on DTCA described in Chapter 2 acknowledges the existence of a body of research examining outcomes of physician-directed promotion. These are two types of marketing techniques are carried out by the same companies to promote sales of the same products. They could differ in their characteristics and effects, given the difference in target audience. However, these hypothesized differences should be empirically tested, rather than simply being assumed to occur. Currently, results of research on physician-directed promotion provide the best available proxy measure of DTCA's likely effects, in the absence of direct empirical research.

The other relevant body of research is the effect of patient expectations and desires for prescriptions, and physicians' perceptions of those desires, on prescribing decisions. For example, research by Britten and Oukummune,[44] and Cockburn and Pit[45] provides a useful model for the comparison of patient and physician influences on prescribing decisions within primary care consultations. This research strongly suggests that even in the absence of DTCA, physicians frequently prescribe medicines to patients because they believe that their patients desire them, even when they do not believe the prescription is warranted.

The design of these studies is also relevant to DTCA as matched patient and physician questionnaires covering the same consultation allow for separate measurement of patient and physician influences on the prescribing decision. One criticism leveled at administrative database analyses of sales of DTCA-advertised drugs is that they do not adequately distinguish between prescriptions generated as a result of DTCA and physician-directed promotion.

The current study differs from most of the approaches to research on DTCA described above in its starting point: for researchers in the U.S., DTCA is now a given. Regulatory requirements and market pressures may shift over time, but this form of pharmaceutical promotion is unlikely to disappear. State legislatures may bring in some restrictions, and there may be some pressure to limit advertising of publicly funded drugs, but these measures remain limited, relative to the policy options available in countries where DTCA is currently forbidden. Nearly all U.S. commentators consider the policy option of prohibition of DTCA to be unrealistic, given the strong constitutional protection for commercial free speech.

The context for this study is a discussion of potential legislative change to introduce DTCA in Canada. Thus the key underlying question is whether the net effect of DTCA on health and health care services is positive, negative or neutral. The focus is on one key potential outcome: DTCA's effects on prescribing decisions in primary care.
This survey cannot directly examine the health implications of prescribing decisions stimulated by patient requests for advertised medicines. However, it provides one step along the pathway to such research evidence, especially when combined with existing knowledge of the contribution of DTC advertised drugs to medical care, and the ability of advertising messages to accurately convey this contribution.

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Chapter 4

Conceptual Framework: Effects of direct-to-consumer advertising on prescribing in primary care

As discussed in the previous chapter, the framework I have used for the comparative patient-doctor study builds on Andersen and Newman's behavioural model of health care service utilization, which provides a context for examining patients' decisions to request advertised drugs.[1] Advertising is expected to be one of a range of influences on patients' decisions to seek medical care. Andersen and Newman's model, originally developed to examine barriers to access to health care services, allows the effects of DTCA to be modelled within the context of individual and environmental influences on patterns of use of health care services.

This study addresses a gap in the research evidence on DTCA: the relationship between patients' advertising exposure, requests for medicines and prescribing decisions in primary care. The aim is to examine the link between DTCA exposure and prescribing decisions in primary care settings in order to better understand both the type of effect DTCA is having on primary care, and the proportion of prescribing decisions that are currently affected by DTCA, in other words to estimate the magnitude of effect. In designing this study, one key aim was to separate out the effects of patient-directed drug promotion from effects of physician-directed promotion. In environments where DTCA is legal, the same drugs are promoted to patients and physicians.

As was discussed in Chapter 3, studies of physician perceptions of patient expectations of a prescription provide a model for the use of matched patient and physician questionnaires in order to separate out patient and physician influences on a single prescribing decision.[2] A similar design, based on matched patient and physician questionnaires, is used in this study.

Additionally, a key aim of this study is to examine the potential effects of a legislative change that is under consideration in Canada: introduction of full legal DTCA. Thus a

comparison between U.S. and Canadian primary care settings provides one means to examine the difference between current DTCA influences in Canada – primarily through cross-border exposure—and the type of influence that might be expected following legal change to allow DTCA. The U.S. is an imperfect model for what Canadian health care might look like with full DTCA, as there are many differences between the U.S. and Canadian health care systems and approaches to regulation of pharmaceutical promotion. However, it does provide some insight into expected differences.

The aim additionally is to develop a conceptual model that is consistent both with existing research on DTCA, as described in Chapter 2, and with research on related influences on prescribing decisions, such as physician-directed drug promotion and patient expectations of prescriptions in primary care.

4.1 Behavioural model of patient requests for medicines in primary care

Figure 4.1, below, outlines a conceptual model of shifts in health care utilization, and specifically of requests for medicines in primary care, in response to DTCA. This model is based on an assumption that both patients' individual characteristics and the external environment, including the presence, quantity and content of DTCA, have potential effects on their behaviours.

The aim is to contextualize the pathway from advertising to shifts in health care use within a broader framework that encompasses the range of factors contributing to patients' decisions and ability to seek and obtain medical care. DTCA is hypothesized to be one of many individual and environmental factors affecting patient behaviours rather than an isolated determinant of care-seeking behaviours. This conceptual model is an adaptation of Andersen and Newman's behavioural model of health care utilization.[1]

Patient behaviours are hypothesized to reflect both individual characteristics and the external environment, with the most important external factors influencing response to DTCA consisting of the advertising environment and the health care system.

If exposure to advertising is to affect product-specific sales, patients must respond by requesting medicines; and physicians must prescribe requested drugs. The primary outcomes assessed in this survey are patient requests for medicines and prescriptions in response to requests. This approach allows for the identification of a subset of prescribing decisions initiated by patients following exposure to advertising. These consultations and prescribing decisions can then be compared to other patient consultations with the same physician that did not involve patient requests for advertised medicines.

As described in Chapter 2, one drawback of many U.S. DTCA surveys is the lack of comparison group, making attribution and the direction of effect of DTCA difficult to gauge. This survey includes several levels of comparisons:

- between consultations in which a patient has requested an advertised medicine and other patient consultations with the same physician on the same day(s);
- between patients in a U.S. environment with full DTCA and in a Canadian environment with less exposure to advertising
- between patients with higher and lower advertising exposure within each setting.

Determinants of patient behaviours

Individual characteristics

Predisposing factors

As shown in Figure 4.1, exposure to advertising messages is postulated to be one predisposing factor among others affecting care-seeking behaviours. The relationship to health beliefs is interactive, as pre-existing health beliefs are expected to affect patients' response to advertising, and advertising messages frequently aim to affect patients' health beliefs both subliminally – for example through the use of emotive imagery – and directly, by providing medical explanations for common symptoms.[21] Factors such as sex and age are independent determinants of patients' predisposition to seek health care services. However, advertising campaigns are often targeted to patients with specific demographic characteristics, and thus sex and age could affect exposure levels as well as the degree of identification with specific advertising messages. In other words, an

interaction or effect modification might occur between demographic characteristics and advertising exposure. For example, a ten-year systematic analysis of US print advertising found that, in ads targeting one sex, women were more than twice as likely to be targeted as men. [3] Another analysis of television advertising found that they were more likely to portray negative images of older than younger adults.[4]

Enabling (or impeding) factors

Patients' access to health care services and to prescription medicines is affected by their socio-economic status, and by their access to health care insurance, including specifically drug insurance, and/or their ability to pay for medicines out-of-pocket. U.S. patients without health insurance face barriers to access both to physicians who might prescribe a drug and to the medicine itself.

There are many reasons that patients may have long-term relationships with a specific primary care physician. Some reasons are neutral, in terms of patients' opinions of the physician. For example geographical proximity or the preferences of other family members may play a large part in decisions to continue to consult a specific physician. In other cases, the length of patients' relationships to their physicians reflects overall level of trust in the physician, and/or comfort with a physician of a specific age or gender. These factors may also affect patients' level of comfort in requesting prescription drugs. Additionally, respondents in some DTCA surveys have said that they would visit another physician if their physician refused to prescribe a drug they requested. [5] [6] These consultations would be expected to be either first-time visits to a physician or to reflect relatively short-term doctor/patient relationships.

Perceived need

Patients are unlikely to request advertised medicines unless they perceive these products to be potentially beneficial to their health. This is likely to depend on the reasons they are seeking care, self-perceived health status, and whether they identify themselves as having an advertised health condition. The latter is a dual measure both of advertising exposure and health status, and includes both patients who already had the diagnosis before seeing

advertising, and those who – rightly or wrongly – identify their own symptoms with an advertised condition.

Another aspect of perceived health need is patients' belief that the advertised medicine is likely to be helpful to them. This depends on exposure to advertising messages and on prior beliefs and knowledge, in addition to a patients' health status and previous diagnosis with conditions for which treatments are advertised.

External environment

Two key aspects of the external environment are expected to affect patients' decisions to request advertised medicines: the advertising environment and the organization of the health care system.

Advertising environment

The advertising environment is a result both of market factors affecting companies' decisions to use specific marketing techniques, including DTCA, and decisions about which products to advertise within specific media, as well as the content of specific advertising campaigns. These factors are expected to reflect companies' determination of those marketing situations involving the highest expected marginal revenues, as well as specific characteristics of the pharmaceutical marketplace, as described above.

This can shift over time, reflecting product life cycles as well as broader market trends. For example, Pfizer's advertising campaign for sildenafil (Viagra) in the U.S. began in the first year with images of older couples (the "Let the Dance Begin" advertisements) and with televised advertisements in which Bob Dole spoke of impotence associated with surgery for prostate cancer. [7] In 2002, with two competitors in the pipeline and the need to garner larger market share, the company featured images of men in their 40's, not 70's, accompanied with a suggestion that they speak to their doctor no matter how occasional the problem and a free trial offer. [8]

Additionally, regulatory factors affect both the content and form of advertising. This includes both legislation and regulatory policies outlining the types of content that are

required and prohibited in pharmaceutical advertising, and monitoring and enforcement procedures. In both countries with legal DTCA and those without, the strength of enforcement procedures can have a profound effect on advertising content. Additionally, whether or not ads are pre-screened, codes governing content, the proportion found to be in violation of regulations, the period of delay before such ads are withdrawn, and whether or not corrections are required, can all affect the extent to which the public receives advertising messages that have been judged to be inaccurate or misleading.

Sometimes the simple introduction of a new administrative procedure can dramatically change the extent to which misleading advertising reaches the public. In November 2001, the US Food and Drug Administration introduced a requirement for letters of violation to be checked by the agency's legal counsel before they were sent to a company. The newly appointed chief counsel had previously represented pharmaceutical companies against the FDA.[9] In the ensuing months, the number of letters sent to companies to advise them to stop running ads that contravened regulations dropped dramatically, and the average time period from the first airing of an advertisement to regulatory action increased.

There are also dramatic differences in the content of New Zealand and U.S. DTC ads, although the same companies are advertising many of the same products in the two countries. Fewer details on product risks are included in New Zealand, although New Zealand ads are pre-screened and U.S. ads are not.[10]

The content of advertising and the messages received by the public are also expected to reflect national laws and monitoring and enforcement procedures. Issues such as whether ads are pre-screened and the strength or weakness of regulatory codes are also relevant. For example, ads in the U.S., with direct government regulation and requirements for 'fair balance' of benefit and risk information, differ from ads in New Zealand, with pre-screening, industry self-regulation and much less detailed risk information requirements. Additionally, although pre-screening might be expected to increase the accuracy and detail in an ad, a self-regulatory pre-screening procedure based on more limited requirements does not necessarily do so. The degree of public exposure to DTCA can also differ enormously among countries where such advertising is illegal, reflecting

differences in administrative policies on enforcement. Policies concerning correction of misinformation, sanctions or other measures to prevent repeat regulatory violations can also affect the messages reaching the public. As discussed in Chapter 2, such corrections are rare in the U.S., and companies do not face sanctions for repeat violations.

In addition to advertising for prescription drugs, companies may engage in other activities that result in public exposure to promotional information about a product, such as press and public relations activities and sponsorship of patient groups.

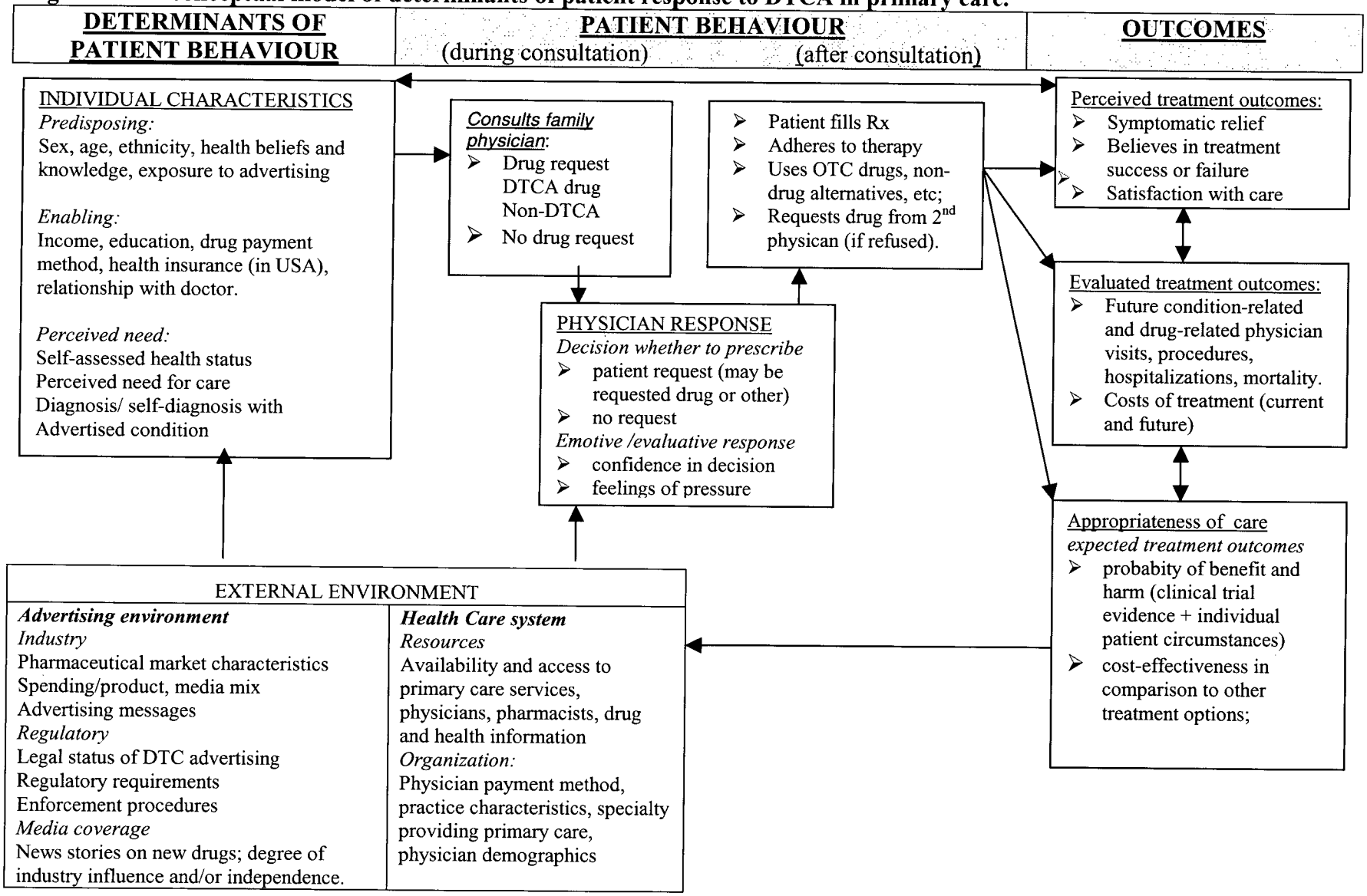
Health Care System

A patient's access to primary health care services and to medicines are also affected by the resources available for these services, how they are financed, and whether or not a society has policies that ensure equity of access to care.

Additionally, the way that physician practices are organized, for example in clinics with a range of different health professionals present, versus in individual offices, can affect access to care and the quality of available services. Physician remuneration method may affect the likelihood that a physician provides a prescription,[11] length of consultations and types of services provided. Referrals to specialists may be easier or more difficult to obtain. Pharmacy services may also vary depending on whether pharmacists are reimbursed for counseling and/or for medication review in addition to dispensing. Patients may or may not have access to independent medicines information and to approved product labeling when they receive a prescription.

The organization of health care services may contribute to the type of relationship patients have with physicians, for example whether they receive care from a single family physician over a long time period, or see a number of different physicians. This can affect both the ease with which patients may or may not ask for advertised medicines, and also potentially the likelihood that a patient whose request is refused simply asks another physician for the same prescription.

Figure 4.1: A conceptual model of determinants of patient response to DTCA in primary care.



distinguish between different causes. This is especially problematic for drug treatments that are used for prevention of future disease, such as antihypertensives or lipid lowering drugs, or for drugs that provide symptomatic relief for conditions known to be associated with a considerable placebo effect, such as treatment of depression and anxiety.

Evaluated health outcomes differ from perceived outcomes in that, at a minimum, a clinician's judgment is involved. Ideally, evaluated health outcomes also include objective measurements. For examples, patients may be followed over time and mortality rates or future hospitalizations and use of outpatient health care services measured. However, evaluated health outcomes may also be subject to bias if patients who obtain and use advertised drugs differ in disease severity from patients who use other treatments. For example, if patients with milder depression are more likely to initiate treatment in response to television advertising than patients with more severe depression, they would also be less likely to be hospitalized in the future for depression. This would especially be true if older non-advertised products were reserved for patients with more serious disease. In this case it would be difficult to know whether a measurement of future use of health care services reflected outcomes of drug treatment or underlying patient population characteristics related to treatment selection.

It is possible to measure and adjust for obvious differences in population characteristics, such as age or previous disease diagnoses. However, these types of adjustments are subject to limitations. For example, large, long-term observational studies of hormone replacement therapy (HRT) for disease prevention indicated a protective effect on heart disease.[12] When well-designed randomized controlled trials were carried out to test this effect, they found no protective effect; on the contrary HRT increased the rate of adverse cardiovascular outcomes.[13] [14] The results of observational studies probably reflected unmeasured systematic differences in cardiovascular risk among women who were and were not prescribed HRT in normal clinical practice. In this case, an effect attributed to the drug was eventually found to be an artifact of population differences.

The current survey could not assess either perceived or evaluated health outcomes, given the limited time frame, a single consultation, and the lack of access to patient medical records or to

Patient behaviour and physician response

As described in Figure 4.1, patients' individual characteristics, including predisposing and enabling factors, as well as their external environment (market and health care system) are expected to affect whether or not they consult physicians and request advertised drugs, as well as whether they fill prescriptions, take prescribed medicines, and/or visit another physician if a request is refused.

Physicians' decision to prescribe is also affected by a range of factors, in addition to whether or not the patient requests a drug in response to advertising. Needless to say, the physician's judgment of the patient's health status and whether or not a medicine is needed should play a major part in this decision. The external environment – both the health care system and market factors – are also expected to have a direct influence on physicians' prescribing decisions. This includes for example physician-directed promotion and the presence of free samples, physicians' exposure to DTCA, their ease of access to independent information sources, and the presence of various incentives or disincentives to prescribe specific products, such as their inclusion on a managed care formulary.

The chain of events that lead from patient exposure to advertising to a prescription for an advertised drug are described in Figure 4.2, below. The aim is to tease out in greater detail the sequence of interactions between advertisers, patients and physicians that are examined in the current study.

Treatment outcomes

Three types of outcomes of health care use are hypothesized within this model, as described in Figure 4.1:

- perceived health outcomes
- evaluated health outcomes
- appropriateness of care.

If a person uses a medicine and then feels better (or worse), this may reflect the drug effect, the placebo effect, or the natural history of disease. On an individual basis, it is difficult to

follow-up evaluations. As is described in Chapter 2, thus far the health outcomes of DTCA remain unexamined although they are the key to any evaluation of benefits versus harm of this form of pharmaceutical marketing.

Measures of appropriateness of care are based on expected treatment outcomes. These are indirect measures of the probability of benefit or harm from a specific treatment. Clinical trial evidence, together with information on relative costs of different available treatments, can be used to judge the appropriateness of treatment decisions for patients with specified characteristics. This is similar to the recommendation by Frank et al., discussed in the Chapter 3, to use clinical guidelines as a proxy for treatment outcome.[15] The advantage of this approach is its reliance on evidence from randomized controlled trials, rather than observational evidence, in order to judge treatment appropriateness, as well as attention to the quality and applicability of clinical trial evidence. In other words, it should involve explicit attention to the strength and quality of available evidence, reflecting the criteria presented by Hadorn[16] and discussed in Chapter 1. A focus on treatment appropriateness also avoids the pitfalls of perceived treatment outcome, in which it is difficult to separate out drug effects from disease or placebo effects. It is, however, an indirect measure based on previous research rather than observed patient outcomes.

Physician confidence in treatment choice is one proxy for treatment appropriateness. It is subject to a number of limitations, as physicians may not have access to full information on the pros and cons of available treatment options, and they may have preferences based on clinical experience or pharmaceutical promotion that conflict with the research evidence. However, although not a perfect measure of appropriateness, this does provide an indication of the degree to which physicians believe that specific prescriptions are or are not appropriate for the patient who receives them. This is relevant to the *prescription-only* status of medicines that are advertised to the public through DTCA. If public exposure to advertising is hypothesized to shift the locus of control over prescribing decisions from the physician to the advertiser (via patients who are convinced through advertising that a specific treatment will help them), then physicians' confidence in treatment choice would be expected to decline.

4.2 How is DTCA expected to influence primary care patients?

Figure 4.2 below describes the likely pathway of effect from public exposure to product sales. The aim was to further tease out the factors likely to be associated with DTCA-influenced drug requests and prescriptions. Several key steps are required, involving first the patient and then the physician:

- *The patient* is exposed to advertising messages. This exposure includes product-specific advertisements as well as cumulative messages about the benefits of drug therapy and the ubiquitous suggestion to 'ask your doctor' about specific drugs.
- *The patient* moves from *awareness* to *identification* with an advertising campaign by perceiving her or himself to have a condition treatable by an advertised drug.
- *The patient* believes the advertised drug is a viable treatment option.
- *The patient* directly or indirectly asks a physician for a prescription for the drug.
- *The physician* agrees to prescribe the drug in response to the patient's request. This can reflect a variety of physician opinions, ranging from the view that the drug provides optimal treatment to reservations about treatment choice.
- If *the physician* refuses to prescribe a desired advertised drug, a patient's request may still influence therapy if *the physician* prescribes another drug in the same class, chooses drug therapy rather than a non-drug approach, or if *the patient* goes to another doctor for the prescription.
- *The patient* must fill the prescription. In the case of drugs for chronic use, this includes obtaining and filling repeat prescriptions over time.

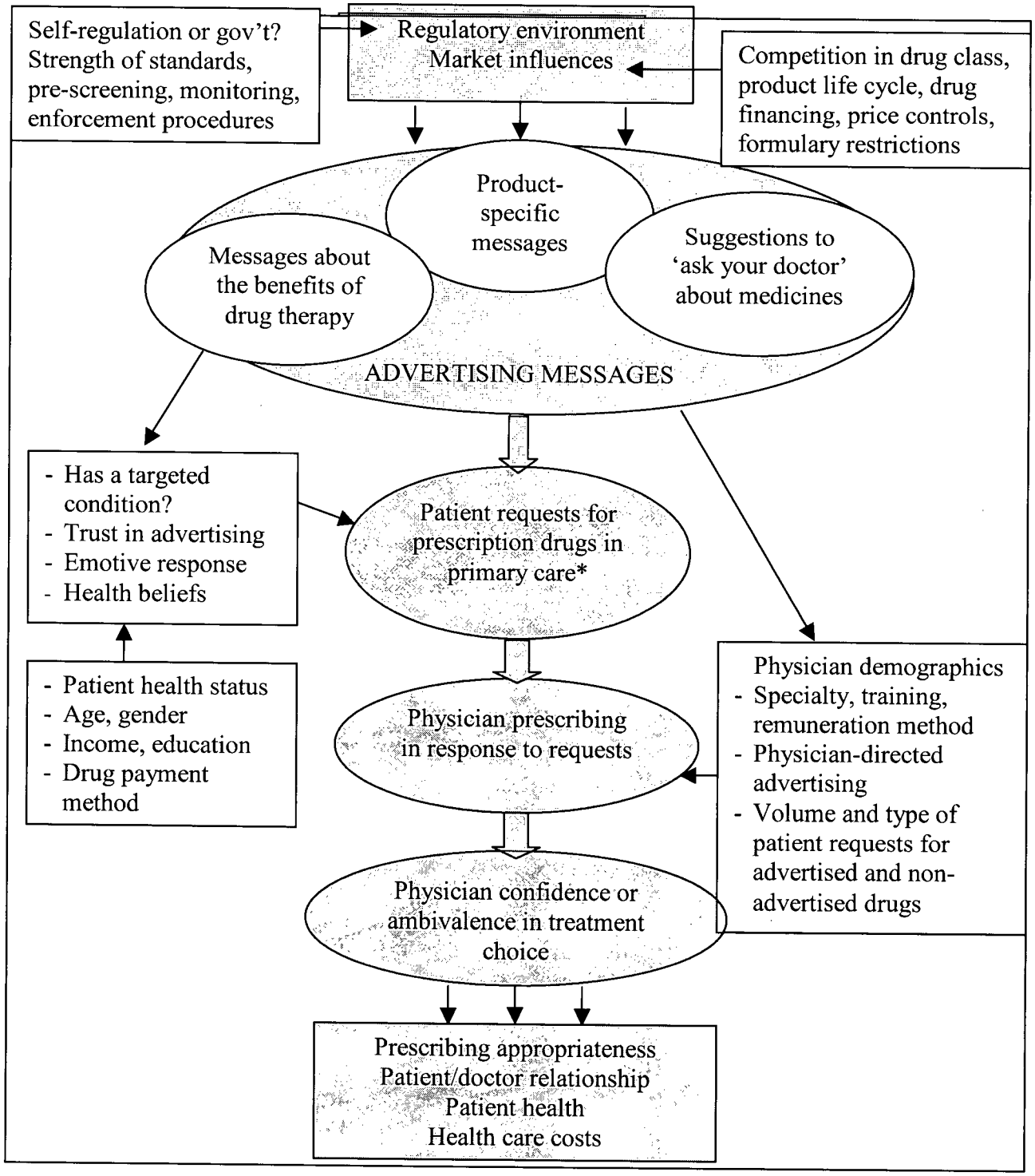
These steps include actions by three key types of players: pharmaceutical firms, patients, and physicians, as well as the influence of the regulatory and market environments, and the organization of health care services. In other words, they result from an interplay between the external environment, patient characteristics, physician characteristics, and the interaction between patients and physicians.

With increased exposure to prescription drug advertising, patients also become increasingly exposed to an environment replete with constant reminders about a range of diseases they might have; the likely benefits of drug treatment; and suggestions that they should ask their

doctor about specific products. The net effect would be expected to be a generally higher volume of prescription drug use, as well as more frequent use of specific advertised products, relative to an environment without the DTCA.

In an environment where DTCA is common, physicians see many of the same mass media messages as patients. Additionally, they are likely to be exposed to promotion for the same products through a range of promotional activities, from medical journal advertisements to pharmaceutical sales representatives and company-sponsored continuing medical education. They may also face patient requests for advertised drugs as an increasingly frequent event. Physicians' responses to individual patients are likely to be influenced not only by specific interactions but also by their own exposures to consumer- and physician-directed advertising, and their experiences with other patients. One question this poses is whether, in an environment where patient requests occur frequently, physicians are also more likely to prescribe advertised drugs.

Figure 4.2 Hypothesized pathway of effect of DTC advertising on prescribing



*includes non-specific requests and requests for disease information stimulated by advertising

4.3 Conclusion

Like the European Union[17] and Australia[18], Canada has been considering legislative change to introduce DTCA.[19] The design of the survey and the main research questions it addresses reflect a specific policy context: discussion of possible legislative change to introduce DTCA in Canada. A two-site survey design was used to allow for comparison of a Canadian and U.S. setting, as the U.S. provides a neighbouring 'living experiment' into the effects of full legal DTCA on prescribing in primary care. Given the exposure to cross-border advertising from the U.S. in Canada, and the increasing prevalence of made-in-Canada prescription drug advertising [20] (see Chapter 6), this survey is better characterized as a dose-response study than a comparison of environments with and without DTCA.

The conceptual model for this study, as described in Figure 4.1 and 4.2, is based on Andersen and Newman's behavioural model of health care utilization,[1] which aims to distinguish between needs-based use of health care services and other factors influencing patterns of use. The study focuses on primary health care services, where most prescribing and patient/physician contacts occur. The design allows for the comparison of patient/physician encounters in which behaviours influenced by DTCA occurred to otherwise similar patient-physician consultation. It also makes it possible to begin to estimate the potential magnitude of effect of DTCA on prescribing decisions. The advantage of this approach over, for example, analysis of administrative data is that the influence of patient-directed advertising can be identified separately, from physician-directed advertising.

The survey was carried out in participating physicians' offices; it is not a random sample of a broader population of the Canadian or U.S. public. Surveys of random samples of the U.S. and Canadian population have the advantage that results can be extrapolated to a broader population. The key disadvantages, however, are in the introduction of recall bias, and the inability to match patient and physician experiences of a single consultation.

DTCA is a controversial health policy area with potentially large financial implications both for manufacturers' profitability and for the financing and sustainability of health care services. As an area of strongly competing interests, DTCA is also fraught with competing claimed effects. Thus there is a need for methodologically sound research to establish what the actual as opposed to postulated effects of DTCA are on health care services and prescription drug use.

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Chapter 5

Patient/Doctor Survey in Vancouver and Sacramento

5.1 Introduction

This Chapter describes the key original research component of this dissertation: a comparative doctor/patient survey on direct-to-consumer advertising (DTCA) in primary care, carried out in family physicians' offices in Vancouver, B.C., and Sacramento, California.

The aim of the survey was to assess the frequency of patient requests for prescription drugs in an environment in which direct-to-consumer advertising is allowed, in the U.S., as compared to an environment in which DTCA is illegal, in Canada, but in which considerable exposure exists to indirect and cross-border advertising.

5.1.1 Background and rationale

As noted in Chapter 2, to date there has been no empirical research on DTCA within primary health care settings, despite the enormous growth in this form of advertising in the U.S.[1] and New Zealand [2] during the late 1990's. Such research is a necessary prerequisite to an assessment of likely health system effects of DTCA. The largest impact of DTCA is expected within primary care because this is where most prescribing occurs, and most advertised products treat common conditions.[3]

A comparison between the U.S. and Canada in 2000 and 2001 contrasts two levels of exposure to prescription drug advertising. It is not a comparison between environments with and without DTCA. Canada prohibits all advertising of prescription drugs to the public with the sole exception of advertisements of name, price and quantity, a regulatory change introduced in 1978.[4] However, the Canadian public is exposed to DTCA in magazines originating in the U.S., and on U.S. cable and cross-border television channels. In the Vancouver area, around 24% of adults' viewing time is of U.S. television channels

which contain U.S. advertising, according to a 16 week survey carried out in the Lower Mainland and on Vancouver Island in late 1998. [5] A U.S. market research company estimated in late 1999 that on average Americans see nine prescription drug ads a day.[6] Canadians would be expected to see on average about two prescription drug ads a day if they are exposed to U.S. programming at the Vancouver area rate.

Cable providers serving a Canadian audience are not required to replace pharmaceutical advertising that is illegal in Canada. U.S. magazines sold in Canada do not contain prescription drug advertising if there is a separate Canadian split run edition, which is the case for major magazines such as *Time* or *Newsweek.* However, magazines without a separate Canadian edition carry both tobacco and pharmaceutical advertising that is legal in the U.S., but not in Canada. Additionally, an increasing number of advertisements for prescription drugs originate in Canada and are aimed at the Canadian public. These advertisements generally state a brand name and hint at the indication or state the indication but not the brand name. Exposure may also be extensive in cases of overt violations of the law, as occurred with a television ad for bupropion (Zyban) that ran for several months.[7]

In sum, although current Canadian law prohibits DTCA, Canadians are exposed to a considerable and growing volume of prescription drug advertising. Because of the proximity to the U.S. and the free movement of print and broadcast media over the border, exposure levels are likely to be higher than in other countries with similar legal restrictions on DTCA.

This survey is therefore best characterized as a "dose-response" study of prescription drug advertising. The primary aim was to examine the differential effect of exposure to DTCA in a U.S. as compared to Canadian city under *status quo* legislative and enforcement conditions. Additionally, the survey provides insights into the current impact of advertising on prescribing decisions in primary health care within a Canadian setting.

This could prove helpful for example for a review of the effectiveness of current enforcement policies.

Outcomes associated with advertising exposure – requests for medicines and prescriptions in response to requests – are examined both as a function of individual advertising exposure and in terms of differences between the two policy environments.

5.1.2 Research questions

The primary research hypothesis is that in a U.S. primary care environment, where DTCA is legal, patients would be exposed to more advertising, would request more medicines from their doctors, and would receive more prescriptions in response to requests than similar Canadian patients. Similarly, I hypothesized that patients in both settings with higher self-reported advertising exposure would request more advertised medicines.

DTCA messages are expected to have both product-specific and 'environmental' effects. Thus I examine whether requests for all medicines, as well as specifically for DTC advertised medicines, occur more frequently in a setting with greater advertising exposure. As noted in Chapter 3, physicians' prescribing decisions are affected by their perceptions of patient expectations of a prescription, whether or not these perceptions are correct,[22] and thus physicians may also prescribe more requested drugs as patient requests become more common.

These are the specific research questions addressed:

Prescription drug requests:

1. In a single consultation with a family physician, is a patient in a U.S. setting with full legal DTCA (Sacramento) more likely to request a prescription for a medicine than in a Canadian setting, where DTCA is illegal but exposure to cross-border DTCA exists (Vancouver)?
2. Are patients in Sacramento more likely to request *advertised* medicines than Vancouver patients?

3. In both settings, are patients with higher self-reported advertising exposure more likely to request advertised medicines, and to receive prescriptions, than patients with less reported advertising exposure?
4. Does the frequency of prescription drug requests within each setting differ by sex, age, self-reported health status, or socio-economic status?

Prescribing decisions:

5. How likely are doctors to prescribe a medicine following a patient's request? Does this differ between Sacramento and Vancouver, or for drugs that are and are not advertised to the public?
6. How likely is a patient to leave a consultation with one or more new prescriptions if they requested a medicine, relative to prescribing rates in the absence of a request?
7. Is there any difference in physicians' confidence in treatment choice if they have prescribed a drug requested by a patient, as compared to other prescriptions?

Patients' opinions about advertising:

8. What is primary care patients' opinion of the accuracy of advertising and its importance as an information source about medicines, in comparison to other information sources?

A comparative cross-sectional questionnaire survey design, with questionnaires filled in by patients in the waiting room and by physicians following patient consultations, made it possible to distinguish between prescriptions provided in response to patient requests and prescriptions initiated solely by the physician.

There are two advantages to surveying patients before a consultation, rather than afterwards. First, the patient is already waiting and may view a questionnaire as a welcome distraction rather than something that takes time away from other activities, improving response rates. Second, following the consultation, a patient's report of their expectations of the consultation may be affected by the doctor-patient interaction.

One concern about surveying patients before a consultation is that the questionnaire could influence the patient's actions during the consultation. However, this was not found to be the case in a survey looking at patient expectations of a consultation, in which some

patients received questionnaires before the consultation and others received questionnaires afterwards.[8] The authors found no difference in numbers of expressed expectations whether the survey was filled in before or after the consultation, indicating little to no activation of expectations by the survey.

The focus of this survey was on primary care because this is where most prescribing occurs, and any changes in prescribing patterns at a primary care level would be expected to have a significant impact on allocation of health care resources and on health care costs. Additionally, as noted in Chapter 2, most of the products heavily advertised to the public in the U.S. are for relatively common and relatively mild conditions. These are most likely to be prescribed in a primary care setting.[9]

It was not possible to measure appropriateness of drug therapy directly, without reviewing patients' medical records. Therefore indirect measures of appropriateness were used: physicians' confidence in treatment choice and a comparison of perceived pressure to prescribe during consultations with and without patient requests for prescriptions.

5.2 Methods

This survey was carried out in primary care physicians' offices in the Vancouver metropolitan area between June and August 2000, and in the Sacramento metropolitan area between March and June 2001. A comparison to a Seattle area primary care setting was originally planned; the delay in U.S. sampling occurred because of the need to secure collaboration with an alternate U.S. research team when planned collaboration in Seattle proved unworkable. A primary care research network affiliated with the University of California at Davis, PC-Aware, worked with the UBC-based project team to carry out the U.S. arm of the survey. Vancouver and Sacramento investigators are listed in Appendix 5.2.

This was a cross-sectional survey, carried out at a single point in time in both jurisdictions; it therefore cannot provide an indication of shifts over time in response to

advertising exposure. I used a cluster sampling technique, with clusters consisting of patients attending the offices of recruited primary care physicians. This technique limits the generalizability of survey results to a broader population because it is not a random population-based sample. However, it allows for direct observation of the impact of patient requests for prescription drugs on prescribing decisions. A cluster sampling technique was also more efficient than alternatives because research assistants could be present in the waiting room to enroll patients and to ensure that physicians had questionnaires to complete following consultations with participating patients.

Patients attending physicians' offices on pre-selected study days were invited to participate while in the waiting room. A research assistant explained the survey to the patients, obtained informed consent, and gave them a questionnaire to fill in. Physicians also filled in a brief checklist following consultations with each participating patient. (Appendix 5.5) The unit of analysis for the study was a matched set of patient/physician questionnaires covering a single consultation.

Ethics approval was obtained from the University of British Columbia's Clinical Research Ethics Board and from the University of California – Davis' Human Subjects Board. Physicians were recruited beforehand and informed consent was obtained from physicians when they agreed to participate. The study description provided to patients (See patient brochure, Appendix 5.5), and the questionnaire, focused on patient information about medicines, rather than on drug advertising directly, in order to avoid biasing study results by focusing patients' attention on prescription drug advertising just before they went in to see their doctors.

Physicians were aware that the study was about direct-to-consumer advertising as well as patient information on medicines, but did not know specific research questions.* Similar study descriptions were provided to patients and physicians in the two settings.

* Whether physicians' opinions affected their decision to participate is unknown, as their opinions of DTCA, or promotion in general, were not measured. However, all information was presented neutrally, and there was little reason to believe that such a bias, in one direction or another, would have led to refusals.

5.2.1 Questionnaire development

The patient and physician questionnaires were developed to reflect the conceptual framework described in Chapter 4, which builds on Andersen and Newman's behavioural model of health care service utilization.[10] Advertising is expected to be one of a range of influences on patients' decisions to seek medical care, and the effects of DTCA are modelled within the context of individual and environmental influences on patterns of use of health care services.

The main focus of the survey was on the interaction between patients and physicians: how often patients request medicines, what these medicines are, and how often physicians comply by prescribing them. Table 5.1 lists the variables on the patient questionnaire that measure individual patient characteristics hypothesized to be determinants of patient behaviours. These are divided into: predisposing factors, enabling factors, and perceived need.

Patient questionnaire

The patient questionnaire included questions about self-reported health status (single item global question), use of health care services (frequency of physician visits and number of OTC and prescription drugs used within the previous two weeks), expectations of the consultation, sources of health information, beliefs about doctor-patient relationships and medicines, age, gender, household income, ethnicity, health insurance and prescription drug coverage (whether patients paid full or partial drug costs or had costs fully covered by a third party payer).

Factors hypothesized to predispose patients to seek care include age, sex, ethnicity, health beliefs, sources of health information and exposure to advertising. Enabling factors include income, education, drug payment method, length of relationship to physician and, in the U.S., health insurance coverage, in other words factors that may enable patients to seek care or limit access to care. Perceived need was measured in terms of patients' self-reported health status, current use of prescription drugs and physician services, and

whether or not patients report that they have a condition that is treated by an advertised drug.

In some cases variables may fit into more than one category. For example, although income is an enabling factor in terms of access to health care services, especially in the U.S., health status also differs by income, with those with lower income on average having poorer health than people of similar age and sex with higher income. Similarly women patients are more likely to seek medical care than men. This is likely to partially reflect biological differences in medical needs, and partially gender differences in help-seeking behaviour.

A single global item was used to ask patients to assess their own health. Bierman et al. examined total health care expenditures and hospitalization rates in comparison to self-assessed health, using the same single item measure.[11] They found it to be a strong predictor of future health care utilization in older adults. Similarly, a review of 27 community studies found a strong relationship between self-perceived health status and subsequent mortality, [12] and follow-up of a Swedish cohort of over 170,000 indicated that the relationship between self-rated health and subsequent mortality holds for adults of both sexes and a range of ages, as well as being consistent across different social classes.[13]

Table 5.1: Variables measuring determinants of patient care-seeking behaviours:

Determinants of Patient Behaviour – Individual Characteristics		
Type	Question	Comments
Predisposing		
Sex	Question 21	Dichotomous; missing values filled in by research assistant
Age	Question 20	By date of birth
Ethnicity	Question 23	Six categories + other
Health beliefs and knowledge	Questions 17&18	Likert scale/ agreement, disagreement w/ range of statements
Health information	Question 11&12	Rates accuracy of information sources; States which are most often used
Information influences	Questions 7,8,10	Asks which information source contributed to specific expectations of the consultation
Exposure to advertising	Questions 13&14	# of products seen advertised; whether or not patient has seen ads for listed products-
Enabling		
Income	Question 25&26	Household income
Education	Question 23	Highest educational degree / achievement
Drug payment	Question 19	Out-of-pocket, partial, or full coverage
Health insurance	U.S. questionnaire	Type and degree of coverage
Relationship to doctor	Question 2	Length of relationship only
Perceived need		
Self-perceived health	Question 1	Single item
Current use of services	Questions 3,4,5	Frequency of physician visits, current use of Rx and OTC drugs
Perceived need for care	Questions 6, 8, 9,10	Reason for visit; belief a test, referral and/or medicine is needed
Diagnosis w/ advertised condition	Question 15	Dichotomous + asks what condition

Advertising exposure was measured by asking patients how many prescription drugs they had seen advertised within the previous year, and whether or not they had seen ads for seven listed brands. One variable measured the external advertising environment: whether the patient resided in Sacramento or Vancouver. The patient questionnaire was designed to focus generally on sources of information about medicines rather than DTCA *per se*, in order to avoid drawing patients' attention to advertising just before they consulted their physicians.

Physician questionnaire

The patient questionnaire measured potential determinants of patient behaviour; the physician questionnaire recorded information on prescribing, whether or not patients had requested medicines, and the physician's judgment about prescribing decisions, patient knowledge about prescribed drugs, and any feelings of pressure to prescribe.

Additionally, information on physician sex, year of graduation, remuneration method (salary, fee-for-service or mixed), specialty (G.P. or Internal Medicine) and practice characteristics was collected.

The physician questionnaire measured requests that patients verbally communicated to the physician by initiating a discussion about whether a medicine would be useful for them or by directly requesting that medicine. These two types of requests aimed to capture all direct patient responses to the suggestion in advertising to 'ask your doctor' about using a specific medicine, and also to allow for individual differences in how directly or indirectly requests were voiced. Doctors were asked to name each newly prescribed drug (≤ 3 per patient) and to say whether or not the patient had 'raised the possibility' of using each drug, and/or directly requested it. Physicians also indicated how likely they would be to prescribe the same drug to other patients with similar problems, and whether patients appeared knowledgeable about each newly prescribed drug. Finally, physicians were asked to list drugs the patient had requested that had not been prescribed, and to state what they had done instead (prescribed another drug, recommended an OTC drug, or a non-drug approach).

The questionnaire did not measure physicians' impressions of patients' unvoiced expectations or desire for a prescription, given the evidence that physicians are frequently wrong.[14] Uhlmann and colleagues stressed the importance of distinguishing between patients' voiced and unvoiced expectations and desires.[15 16] They define expectations as beliefs that something is likely to happen; desires as wishes that something will occur. This survey examines only voiced desires.

Table 5.2: Variables measuring patient behaviours and physician responses

Observed patient and physician behaviours – as recorded on physician questionnaire		
Patient behaviours - drug requests		
Indirect drug request	Question 2b	Did patient raise possibility of taking the drug?
Direct drug request	Question 2c	Did the patient request the drug
Requested not prescribed	Question 3	Dichotomous + name of drug if yes
Physician behaviours		
What happened if requested drug not prescribed	Question 3b	OTC drug, another Rx drug or non-drug approach recommended
Prescribing behaviour	Question 1	New Rx, refill, OTC drug, no drugs
Names of new Rx drugs	Question 2a	New Rx listed (up to 3 per patient);
Physician opinions		
Physician would have chosen same drug 'in the absence of expressed patient desire'	Question 2e	Only relevant to prescribed requested drugs; 3 point scale (very likely, possibly, unlikely).
Physician would treat another similar patient with the same drug	Question 2f	All new prescriptions; 3 point scale (very likely, possibly, unlikely).
Patient knowledgeable about prescribed drug?	Question 2d	All drugs – whether or not requested; dichotomous + 'don't know' option
Physician felt pressured to prescribe	Question 4	All consultations; 3 point scale (No, yes a little, yes moderate to strong);

Classification of prescribed medicines

A drug was classified as having been advertised to the public during the relevant time period if it was among the 50 products with the highest DTCA budgets in the United States in 1999 [9] if it featured on a list of year 2000 and early 2001 television, radio and print ads obtained from a U.S. market research company;[17] or if it was listed in a Canadian marketing magazine article on 1999-2000 DTCA campaigns.[18]

Procedures – questionnaire development

Some questionnaire items were adapted from U.S. consumer questionnaires on direct-to-consumer advertising carried out by the U.S. Food and Drug Administration[19], *Prevention*[20] and *Time*[21] magazines and matched questionnaires used in a U.K. study of physician responses to patient expectations of a prescription[22]; others were designed specifically for this study.

A multi-disciplinary Expert Advisory Panel, which met once in December 1999, assisted with the design of the survey, analytical framework and development of physician and patient questionnaires.† The Expert Advisory Panel provided a broad range of relevant expertise, including economics, marketing, medical anthropology, clinical medicine, pharmacy, and sociology, as well as consumer and regulatory perspectives, and representation from the U.S. and various regions of Canada. See Appendix 5.3 for a list of members and specific expertise.

Draft questionnaires were circulated to members of the Expert Advisory Panel before the December 1999 Panel meeting. The meeting then provided a forum for discussion of the content and approach of questionnaires, as well as broader aims of data collection. A revised draft was circulated back to the panel as well as to other reviewers before being pilot tested in Vancouver. The Panel was especially helpful on specific areas of content of the questionnaire:

- *Measurement of advertising exposure*: Panel members recommended the use of questions focusing on patients' memories of seeing specific product advertisements rather than amounts of television viewing and other media exposure, as the latter is subject to greater response bias. Several panel members had carried out related studies, including research on the impact of tobacco advertising, a U.S. consumer survey on DTCA, and a U.S. survey on DTCA exposure and diagnostic testing.
- *Drug payment:* The Panel pointed out that researchers often encounter difficulties in obtaining reliable information from patients on what their drug plan covers, particularly coverage of new therapies. Therefore they suggested a general question about whether drug costs are covered partially, fully or not at all, rather than more detailed questions;
- *Cultural differences:* Given the potentially confounding effect of differences in culture and in health care systems between the U.S. and Canada, it was

† This advisory panel was set up at the request of the funding agency, Health Canada. The aim was to obtain representation from different regions of Canada and a broad range of disciplines that could help inform the design of the study. Two U.S. panel members also contributed regulatory and clinical expertise.

considered helpful to include questions on attitudes to health and medical care, both to compare baseline characteristics and to control for major differences. This could include, for example, measures of patient assertiveness, as well as whether a patient had requested a medicine from a physician in the past.

- *Length of relationship with physician:* This was highlighted as an important question, given the effect of continuity of care on trust within the doctor-patient relationship.
- *Outcome variables:* A number of outcomes of interest were identified, including whether a person requests a drug, whether they receive a requested drug, whether shifts occur in use of health care services down the line; whether the appointment was made with the doctor as a result of DTCA; and also whether the patient sought care because of DTCA but received a different drug from the one they requested. Given the time frame for the study and lack of access to medical records, long-term effects on health care service use could not be examined.
- *Physicians' opinions on prescribing appropriateness:* The panel discussed approaches to soliciting physicians' opinions of the relative medical need for each newly prescribed drug, given the sensitivity of this question. The final wording reflected suggestions by practicing physicians with research experience.

5.2.2 Pilot survey

The questionnaires were piloted in May 2000 in the Family Practice Unit at UBC. Five medical residents participated in the pilot survey under the direction of Dr Carl Wiebe, and 35 patients were enrolled. The aim was to test content, readability and time required for the patient and physician questionnaires, and practical aspects of study procedures. Several minor changes were made to the wording of the questionnaires and to the study protocol as a result of the pilot survey. For example, patients were encouraged to bring the questionnaire into the examining room if they had not completed it in the waiting room, as many patients were called into the examining rooms fairly quickly, but then had plenty of extra waiting time to complete the questionnaire. Questionnaires took an average of 11 minutes for patients to complete; physician questionnaires took less than

one minute. The questionnaires were not piloted separately in Sacramento, for reasons of timing and the need to retain identical questionnaire wording and survey methods for comparability of results.

Thirty-seven patients agreed to participate in the pilot survey, 35 of whom filled in and returned their questionnaires (95% of those agreeing). These 35 patients represented 73% of the 48 patients attending the Family Practice Unit during the survey days. There were 6 exclusions (13%) and only 3 eligible patients (6%) refused to participate. The remaining 2 patients (4%) were ushered into the doctor's office before they could be invited to participate.

The most common reason for attending the clinic was for ongoing care for a health problem (40%), followed by acute illness or injury (23%). The prescribing rate was lower than expected (5 patients or 14%). This may have reflected the fact that the survey was piloted in a family practice teaching environment. Only one patient (3%) requested a medicine, an advertised diabetes drug, rosiglitazone (Avandia), and the drug was not prescribed. This was broadly consistent with the pre-survey sample size estimations (see below). In conclusion, the pilot survey provided useful feedback on feasibility, allowed for introduction of flexibility into survey procedures, and led to some changes in wording of questions (such as adding 'none of the above' options in questions asking patients about different types of influence on decision-making). The participation rate, questionnaire comprehension, and the proportion of questionnaires that were completed and usable were good, and several patients provided useful comments that were incorporated into the final questionnaire.

5.2.3 Sample size and Methods of Analysis

The primary outcome was patient requests for one or more prescription drugs during observed consultations, as measured by physician responses to their questionnaires. The unit of analysis was a matched set of patient and physician questionnaires covering a single consultation. The required sample size for each study arm was estimated at 636

matched patient and physician questionnaires. This was based on a hypothesized rate of requests for advertised medicines of 6% in the U.S. and 2% in Canada, and a 50% increase in sample size to allow for the extra variance expected due to cluster sampling. The U.S. rate was based on consumer surveys. [20] [21] No data were available for Canada, but a 4% difference in requests was judged to be sufficient to affect prescribing practices. This sample size had 80% power to detect the estimated difference in requests at alpha = 0.05, two-sided.

Differences between the two patient samples in self-reported advertising exposure, rates of drug requests, and prescribing rates were adjusted for potential confounders, including patients' age, gender, self-reported health status, income and education, and whether patients paid for drugs fully, partially or not at all. All questions on prescribing decisions were also adjusted for physicians' sex and number of years since graduation. A Generalized Estimation Equation (G.E.E.) was used to adjust for the correlation between patients of the same physician. This model is similar to a logistic regression analysis. The G.E.E. analysis was performed using the programme S-PLUS 3.0.[23] Chi-square analysis was carried out for unadjusted exploratory bivariate comparisons, using Epi Info 2000.[24]

In order to test for differences in request rates related to self-reported advertising exposure among patients in the entire sample (Vancouver and Sacramento combined), I used dichotomized exposure variables (≤ half versus >half of listed drugs seen advertised).

5.2.4 Physician recruitment

In Vancouver, family physicians were randomly selected from two lists:

- Clinical faculty members with UBC's Department of Family Practice (N=317). These are physicians in the Vancouver metropolitan area who provide clinical teaching sites for medical students.
- The 1999-2000 Medical Directory of the B. C. College of Physicians and Surgeons, Vancouver listings for General Practitioners (N=1084).

200 physicians were randomly selected (SPSS random case selection) and invited to participate, 95 from the Department of Family Practice list and 105 from the College Directory.

The decision to recruit physicians from the Department of Family Practice list had initially been made in order to maximize participation rates. The Department of Family Practice sent out the invitation letter, co-signed by the departmental chair. When recruitment proved difficult despite this strategy, we decided to draw a random sample of all Vancouver family physicians rather than to intensify recruitment within this subgroup.

Of the 200 physicians contacted, 33 were excluded because they were away on holiday during the study period, had moved or retired, were not primary care physicians, or were short-term locums. Twenty-three of the remaining 167 agreed to participate (14%), 17 from the Department of Family Practice sample and 6 from the College Directory. In order to boost participation rates, their partners were also invited. In total, 40 family doctors in 23 practices participated in the study; 17 were recruited from UBC Department of Family Practice's clinical faculty, 6 from the College of Physicians Directory. The remaining 17 were partners of participating physicians.

In Sacramento, 62 primary care physicians who work with University of California-Davis' Primary Care Network were invited to participate in the survey, and 38, in eight practices, agreed. This strategy was used in order to match the Vancouver sample, mainly consisting of primary care physicians affiliated with a university, and to enable the survey to take place within a tight timeframe. Sacramento primary care physicians generally work in practices of 8-10 physicians in order to achieve the necessary economies of scale to hire a practice manager to deal with complex billing procedures.

5.2.5 Patient recruitment

All consecutive adult patients attending participating doctors' offices on two pre-set study days were invited to participate in the survey. Patients were excluded if they were under

18 years of age, not seeing the doctor for their own care, unable to provide informed consent (serious psychiatric disorder, dementia or mental disability), non English-speaking, or were too ill to participate in the study.

Physicians' offices were sampled on two consecutive days whenever possible, in order to minimize disruption of physician schedules and for office staff. In Vancouver, the first of two consecutive study days was randomly selected from a doctor's working schedule during the study period. This was subject to constraints because of the schedules of physicians and research assistants, particularly as the study schedule became more crowded. The schedule in Sacramento faced additional constraints of availability of student research assistants during the term, as well as long distances between the UC-Davis campus and Sacramento practices.

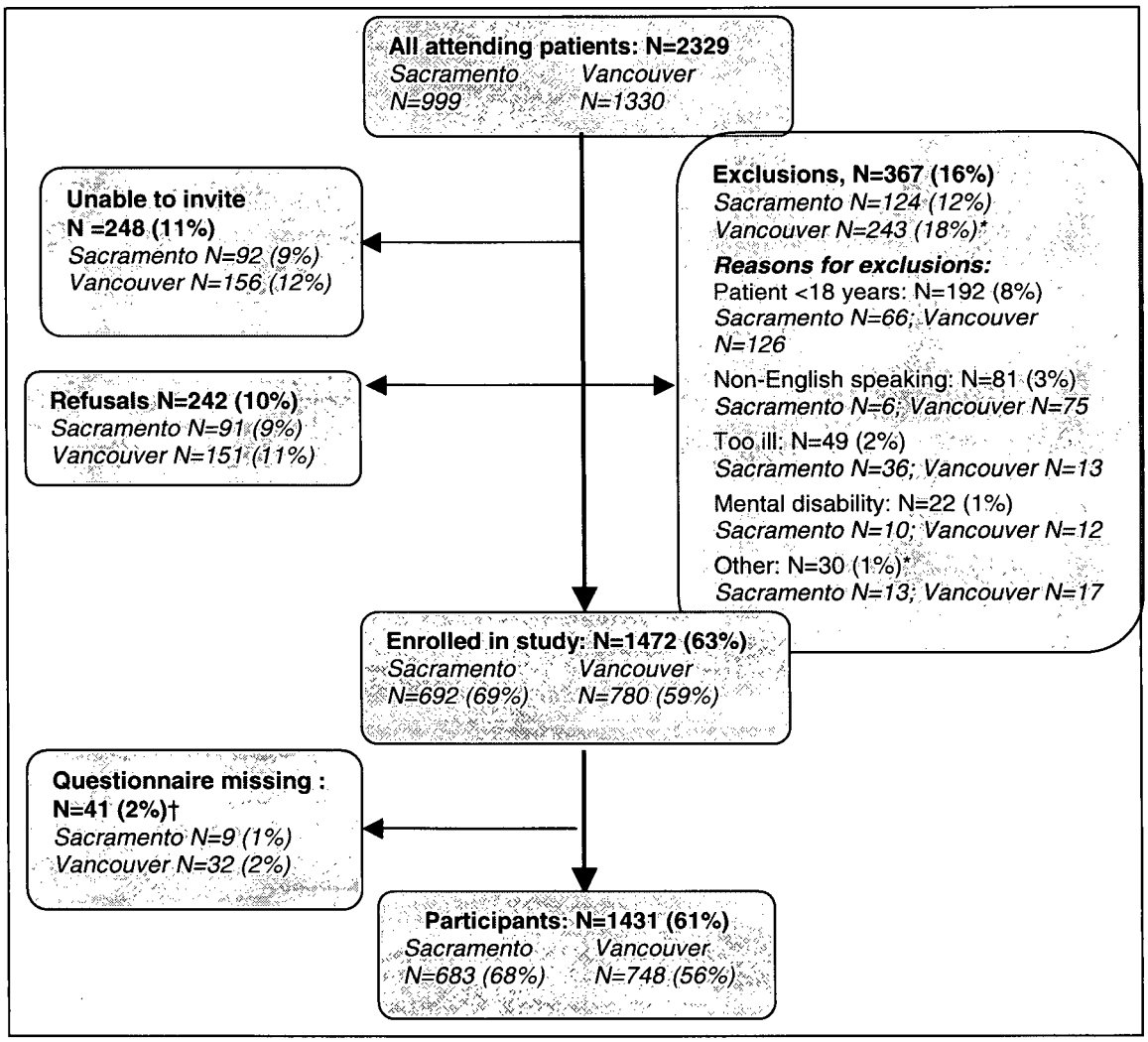
5.3. Results

5.3.1 Sample Characteristics

Patient participation

A total of 2329 patients attended participating physicians' offices on study days, 1330 in Vancouver and 999 in Sacramento (Figure 5.1). Of this potential population, 89% were invited to participate in the study (2081). It was not possible to contact 11% of the patients because they were called into the examination room too quickly. Sixty-three percent of the patients agreed to participate (59% in Vancouver; 69% in Sacramento).

Figure 5.1: Patient participation



*Patients not in for consultations (refills, picking up letters); previous participants; illiteracy; deafness; blindness; 4 unspecified.
†A matched patient and physician questionnaire was needed; in these cases one of the two was missing.

Physician and patient characteristics

In total, 78 physicians participated in the study: 40 from Vancouver and 38 from Sacramento. General Internists were enrolled in Sacramento if they saw mainly primary care patients rather than referral patients from another physician. Table 5.3 briefly describes the physicians' characteristics. Nearly three quarters of the Sacramento physicians were male, and almost all worked full-time. One Vancouver physician with a

very busy full-time practice reported seeing 360 patients per week;‡ patient load was otherwise similar in the two settings, around 100-125 patients per week. The U.S. patient load is consistent with the 1999 National Ambulatory Care Survey indicating that, on average, face-to-face time is 17 minutes in primary care consultations.[25]

A key difference between the two groups of physicians is in remuneration methods: most Vancouver physicians were paid on a fee-for-service basis and most Sacramento physicians were on salary.

The majority of survey participants were women (67% in Vancouver and 64% in Sacramento). More women than men seek primary health care services, both for their own care and care of children. The sex ratio of participants did not differ from non-participants.

A similar proportion of participating patients were Caucasian but there were fewer Asians in Sacramento than in Vancouver, and more African-Americans and Hispanics. This reflects broader population differences in the two cities. The sample had a higher proportion of Caucasian participants than is reflected in the populations of Vancouver or Sacramento (69% in both cities[26 27]). In Vancouver, this is likely to reflect the location of two-thirds of participating physicians' offices on the west side of the city; in Sacramento, the UC-Davis' Primary Care Network mainly serves an employed, insured population. Income and educational levels also tended to be higher than population averages for the two cities. For comparability of samples, similar skewing was not seen as a major problem. Education levels were similar, but a higher proportion of the Sacramento sample were in the highest measured household income bracket of ≥U.S.$80,000, with equivalent purchasing power to ≥$92,000 Canadian per year.[28] Mean household size was similar in Vancouver and Sacramento: 2.6 ± 1.5 versus 2.7 ±1.4.

‡The number of patients seen per week was queried and confirmed by the physician's office.

Table 5.3: Physician and patient characteristics

	Sacramento	Vancouver
Physicians	**N=38 (8 practices)**	**N=40 (23 practices)**
Percent male	74%	55%
***Remuneration**†*		
Fee-for-service	16%	80%
Salaried	68%	15%
Blended payment method	3%	5%
Patients	**N=683**	**N=748**
Percent female	64%	67%
Mean age ± S.D	49.5 ±17.3	47.9 ± 17.5
Caucasian	80%	81%
Good to excellent health	82%	84%
***Household income**†*		
< US$20,000	11%	16%
US$20,000-$59,999	34%	44%
≥ US$60,000	44%	29%
Highest educational level achieved†		
High school graduate or below	21%	30%
Some post-secondary / technical	46%	37%
University graduate or above	30%	33%
Payment for medicines†		
Patient pays full costs	6%	25%
Patient pays partial costs	88%	52%
Full costs covered by 3rd party	6%	23%
Length of relationship with doctor†		
First appointment	16%	9%
Less than one year	21%	19%
≥ One year	63%	72%

*7 (18%) of the Sacramento physicians did not report remuneration method.
**adjusted for purchasing power parity: $1U.S. = $1.17 CDN [OECD, year 2000 rate] http://www.oecd.org/std/ppp1.pdf
† percentages do not equal 100% because of missing data

Similar proportions of patients did not provide income information in the two samples (158 total or 11%). Missing data were imputed using linear regression analysis on sex, age, education, U.S. or Canadian residence, drug payment and health status. For most variables, data were missing less than 5% of the time, with the exception of U.S. patients' insurance coverage (7.6%) and ethnicity (6.6%)

Sacramento patients were more likely than Vancouver patients to report that they have some or all of their prescription drug costs covered (90% versus 74%).§ Almost all Sacramento patients paid partial drug costs, with only 40 (6%) reporting that their drug costs were fully covered, and another 37 (6%) that they paid full drug costs. In Vancouver, patients were more likely to be on one end of the spectrum or the other, with 178 (25%) fully responsible for drug payments and 162 (23%) having their costs fully covered. Ninety-four percent of the Sacramento patients with health care coverage through a health maintenance organization (HMO) said that they paid partial costs, mainly through patient co-payments.

The Sacramento questionnaire included two extra questions about insurance coverage for health care services. Most patients (602 or 88%) reported that they had health insurance coverage all year; 24 reported coverage most months (3.5%) and a further 24 (3.5%) reported that they had little to no coverage. A second question asked whether patients received any health care through listed insurers and health services (health care maintenance organization; other private health insurance, MediCal, MediCare, government health clinic, personal payment or another way). Table 5.4 provides a breakdown of the proportion relying on each type of health insurance coverage at any time during the last 12 months. Patients could check off more than one option. Although only 2.3% reported having no health insurance coverage during the entire year, 7.3% said that they paid for health care services out-of-pocket at some point during the year.

Table 5.4: Type of Health Insurance Coverage, Sacramento Patients

Type of Coverage	Proportion of patients*
Health Maintenance Organization	455 (66.6%)
Other Private Insurance	122 (17.9%)
MediCal (state of California)	38 (5.6%)
Medicare (federal, mainly people >65)	110 (16.1%)
Government health department	9 (1.3%)
Personal out-of-pocket payment	50 (7.3%)
No response	*52 (7.6%)*

*any health care obtained through this type of coverage during the last year.

§ All of the patients would have had catastrophic drug coverage under British Columbia's Pharmacare plan. However, there was no specific reference to catastrophic drug coverage on the questionnaire. Additionally, many patients without high prescription drug costs may have been unaware of the existence of catastrophic coverage.

Patients' attitudes towards health and medicines

As articulated in the conceptual model in Chapter 4, cultural beliefs would be expected to affect decisions to request medicines. Accordingly, the survey included four questions on attitudes towards the doctor/patient relationship and drug prescribing:

- I trust my doctor's judgment if he or she thinks I don't need a medicine
- I would go to another doctor if my doctor refused to prescribe a medicine
- Doctors and patients should have equal say in treatment decisions
- Direct Internet sales of prescription drugs should be allowed.

Attitudes were remarkably similar in the two cities, as shown in Table 5.5. A similar minority, 14% in each sample, said they would go to another doctor if their physician refused a desired prescription. Around 11% of patients in both jurisdictions (76 in Sacramento, 86 in Vancouver) reported both that they trusted their doctor if he or she said that a medicine was not needed, and that they would go to another doctor if a desired prescription was refused, although these are contradictory statements. In most cases (69% in Vancouver; 66% in Sacramento), the patients said that they 'agreed' rather than strongly agreeing with both statements.

Knowledge of therapeutics appeared similar, with just over a third in each sample incorrectly believing that antibiotics are effective against the flu. Appendix 5.1, Patient Attitudes and Beliefs, at the end of this Chapter, provides a more detailed presentation of the results of questions about patients' attitudes, beliefs, and trusts in difference information sources.

Table 5.5: Patient attitudes to the patient/doctor relationship and medicine use*

	Sacramento N=683	Vancouver N=748
Attitudes to the patient/doctor relationship and prescribing		
Believes doctor and patient should have equal say in treatment decisions	74.6%	74.5%
Trusts doctor if he or she says a medicine is not needed	86.3%	92.2%
Would go to another doctor if a desired prescription was refused	14.3%	14.2%
Believes direct Internet prescription drug sales should be allowed	5.0%	3.5%
Beliefs about medicines and diagnostic tests		
Believes new medicines are safer and more effective than medicines developed 10 to 20 years ago	50.2%	49.2%
Believes more expensive medicines are safer and more effective	4.7%	7.5%
Would take antibiotics for a bad case of the flu	37.2%	36.6%
Believes that if a person is depressed, they need to take a medicine to get back to their normal self	34.9%	32.7%
Believes all women over 50 should get their bone density tested	79.1%	71.3%

*Patients who 'agreed' or 'strongly agreed' with each statement. There were no significant differences in opinion at p<.05, unadjusted chi square analysis.

5.3.2 Self-reported health and prescription drug use

Nearly 84% of Vancouver patients and 83% of Sacramento patients reported their health to be good to excellent compared to others their age. Among those aged 65 and over, 79% of Vancouver and 83% of Sacramento patients still judged their health to be good to excellent. In both settings, a predictable trend was seen in declining self-reported health with age. No difference in health status was observed between men and women.

The patient questionnaire included a question about how many prescription medicines a person was currently taking, with 'current' defined as use within the previous two weeks. Sacramento patients reported taking more prescription drugs than Vancouver patients. As Table 5.6 indicates, levels of prescription medicine use were similar among patients with fair to poor health but were greater in Sacramento among healthier patients. Fifty-four percent of the Sacramento patients with good to excellent health were taking two or more prescription medicines, versus 35% of Vancouver patients with good to excellent health. Among the 86 Sacramento patients with excellent health, 44% were taking two or more prescription medicines versus 19% of the 112 Vancouver patients with excellent health (p=.0002, unadjusted chi-square analysis).

Table 5.6: Health status versus volume of current prescription drug use.

How many Rx drugs are you currently taking?	Fair to poor health		Good to Excellent Health	
	Sacramento* N=116 (17%)	Vancouver N=120 (16%)	Sacramento* N=555 (83%)	Vancouver N=627 (84%)
None	17 (15%)	18 (15%)	139 (25%)	225 (36%)
One	12 (10%)	22 (18%)	120 (22%)	185 (30%)
2 to 3	33 (28%)	31 (26%)	191 (34%)	149 (24%)
More than 3	54 (47%)	49 (41%)	103 (19%)	68 (11%)

* 671 patients in Sacramento, and 747 in Vancouver stated both health status and prescription drug use.

One possible explanation for more frequent current prescription drug use among Sacramento patients with good or excellent self-reported health is the difference in prescription-only versus over-the-counter (OTC) status for some drugs frequently used for milder health problems. Examples include non-sedating antihistamines used for allergy. These are OTC in Canada and prescription-only in the U.S. If this were the explanation, however, more OTC drug use would be expected among Vancouverites with better health than Sacramento patients. As Table 5.7 indicates, however, the opposite trend was found, with significantly more Vancouver than Sacramento patients reporting no OTC drug use ($p<.0001$).

Table 5.7:
Over-the-Counter (OTC) Drug Use among those in good to excellent health*

How many OTC drugs are you taking?	Good to Excellent Health	
	Sacramento N=555 (83%)	Vancouver N=625 (84%)
None	189 (34%)	319 (51%)
One	229 (41%)	198 (32%)
2 to 3	122 (22%)	81 (13%)
More than 3	15 (3%)	27 (4%)

* 671 patients in Sacramento and 745 in Vancouver reported both their health status and OTC drug use.

More Sacramento patients had their prescription drug costs at least partially covered and this might lead to a higher volume of use, but no difference was seen in current level of use by drug coverage (NS, $p=0.6$) Another possible explanation is cultural difference, with Americans tending to self-report better health. In this case, Americans would also be expected to visit physicians more frequently at similar self-reported health status, indicating that their health was not quite as good. As shown in Table 5.8, consultation rates were roughly similar and tended to be higher in Vancouver than in Sacramento. In

both settings, those with poorer health attended doctors' offices more frequently, with 71% of those assessing their health as fair to poor in Vancouver and 66% in Sacramento having seen a doctor three or more times within the last six months ($p<.001$ compared to the frequency among patients with better health).

Table 5.8: Health Status vs. Frequency of Visits to the Doctor *

How many times have you gone to the doctor in the last six months?	Fair to poor health		Good to excellent health	
	Sacramento N=117 (17%)	Vancouver N=119 (16.%)	Sacramento N=557 (83%)	Vancouver N=626 (84%)
None	9 (8%)	4 (3%)	114 (21%)	94 (15%)
1 to 2	31 (27%)	30 (25%)	272 (49%)	272 (43%)
3 or more	77 (66%)	85 (71%)	171 (31%)	260 (42%)

*674 patients in Sacramento and 745 in Vancouver reported both health status and frequency of doctor visits.

A final hypothesis is that more discretionary drug use was occurring among healthier Sacramento patients as compared to healthier patients in the Vancouver sample. This seems a plausible explanation, and is further supported by the fact that patients with poorer health reported similar levels of prescription drug use in the two settings. If the less frequent medicine use among patients in Vancouver as compared to Sacramento was primarily due to unmet health needs, a difference should have also been observed among patients with poorer health.

One explanation for this pattern is a difference in the proportion of patients with risk factors for future disease, such as high cholesterol, low bone density or hypertension, receiving drug treatment. This might happen if the threshold for drug treatment differed in the two settings, or if Sacramento patients without symptoms were more likely to seek and obtain diagnoses than Vancouver patients. Drug treatment would be considered discretionary if evidence of better outcomes with drugs than non-drug approaches was lacking among similar patients; or if health benefits of drug treatment, in terms of decreased morbidity or mortality, had not been established, as for example with the use of post-menopausal hormone therapy for disease prevention.

Most patients had an established relationship with the doctor they were seeing. Seventy percent of Vancouver patients and 61% of Sacramento patients had been seeing their doctor for more than a year. In Vancouver, only 9% of patients were attending their first appointment with a participating doctor; in Sacramento the proportion was 16%. This difference is significant ($p<.0001$, unadjusted chi-square analysis).

The difference in length of patient-doctor relationship could be hypothesized to have several effects related to patient requests for advertised medicines. On the one hand, patients might be less comfortable with a new physician and less likely to request a medicine; on the other hand, if patients 'prescription shop' by visiting a new physician after having a request refused, this would be counted as a first consultation.

5.3.3 Patient Expectations of Observed Consultations

As Table 5.9 indicates, patients were consulting physicians for similar reasons in the two settings, with one-third coming in for ongoing care for a chronic health problem. More Sacramento patients had come in because they were unwell or for a regular check-up; more Vancouver patients came in to obtain a prescription refill. This question allowed for multiple responses. However, in both settings few patients said they were coming in specifically to obtain a new prescription, 5% in Vancouver and 4% in Sacramento.

Table 5.9: The ten most common reasons patients went to the doctor

Reason for Appointment	Sacramento (n=683)	Vancouver (n=748)
Long-term health problem –ongoing care	232 (34%)	250 (33%)
Unwell or injured – acute	187 (27%)	140 (19%)*
Regular check-up	166 (24%)	132 (18%)*
Long-term health problem – first consultation	78 (11%)	69 (9%)
To obtain a refill	48 (7%)	122 (16%)*
Anxiety, depression or fatigue	41 (6%)	28 (4%)
To obtain a new prescription	27 (4%)	36 (5%)
Administrative reasons (driver's license, etc)	13 (2%)	17 (2%)
Pregnant	8 (1%)	25 (3%)
Discuss test results	5 (1%)	17(2%)

*p<.05 for difference between settings, chi square analysis, Bonferroni adjustment for 10 comparisons.

A separate set of questions asked patients about their expectations of the consultation: did they think they needed a referral to a specialist, a diagnostic test, and/or a prescription for a medicine they were not already taking?

As shown in Table 5.10, similar proportions of patients in the two samples said they needed a diagnostic test or a referral to a specialist. However, more patients in Sacramento believed they needed a prescription for a medicine they were not already taking: 22.1% vs. 15.1%. Patients in Vancouver were more likely to say they needed a new prescription if they were in poorer health: 24% of those with fair to poor health versus 13% of those with good to excellent health, (p=.003); in Sacramento no difference was seen by health status, 20% in poorer versus 17% in better health.

In Vancouver, no relationship was seen between patients' age and their belief that they needed a new prescription. In Sacramento, nearly one third of people under 35 (30.4%) thought they needed a new prescription, with the proportion gradually declining to 11.2% of patients 65 and over.

Table 5.10: Desired outcomes of consultations *

Desired outcome	Sacramento % of patients (n=683)	Vancouver % of patients (n=748)	Difference (95% Confidence Interval) † Sacramento vs. Vancouver
Referral to a specialist	154 (22.5%)	170 (22.7%)	Odds ratio=0.9 [0.7-1.3], p=0.7, NS
Diagnostic test	194 (28.4%)	187 (25.0%)	Odds ratio=1.2 [1.0-1.5], p=0.06, NS
New prescription	151 (22.1%)	113 (15.1%)	Odds ratio= 1.5 [1.1-2.0],p=0.003 absolute difference =7%

*These were separate questions; patients did not need to choose between different desired outcomes.
†Adjusted odds ratios based on a regression analysis (Generalized Estimation Equation) controlling for age, sex, health status, income, education, drug payment, and cluster sampling.

5.3.4 Advertising exposure

Patients in Sacramento reported greater advertising exposure than those in Vancouver (Table 5.11). Sacramento patients were significantly more likely to have reported seeing more than three specific product ads, and there were dramatic differences in the

recollection of ads for finasteride (Propecia) and raloxifene (Evista).** However, Vancouver patients also reported considerable exposure: 90% had seen at least one DTC ad within the last year and 30% had seen ads for more than 10 products.

Table 5.11: Patient Self-Reported Advertising Exposure†

Advertisements seen in previous year	Sacramento N=683	Vancouver N=748
Number of products		
None	13 (1.9%)	72 (9.6%)
One to Five	171 (25.0%)	295 (39.4%)
Six to 10	178 (26.1%)	135 (18.0%)
More than 10	291 (42.6%)	218 (29.1%)
Not reported	*30 (4.4%)*	*28 (4.7%)*
Six or more products seen advertised Sacramento vs. Vancouver	Odds ratio = 2.7 (95% CI 2.1-3.6)†	
Specific product ads	**Sacramento**	**Vancouver**
Viagra	611 (89.5%)	592 (79.1%)
Claritin	586 (85.8%)	625 (83.6%)
Prozac	487 (71.3%)	426 (57.0%)
Zyban	487 (71.3%)	334 (44.7%)
Propecia	357 (52.3%)	105 (14.0%)
Depo Provera	210 (30.7%)	118 (15.8%)
Evista	83 (12.2%)	27 (3.6%)
Advertising exposure and influence		
Ads seen for over half of listed products (>3) (excludes Claritin, as OTC in Canada) Sacramento vs. Vancouver	321 (47.0%)	118 (15.8%)
	Odds ratio =5.9 (95% CI 4.5-7.7)†	
Advertising influenced patients' decisions and/or was used as an information source Sacramento vs. Vancouver	56 (8.2%)	26 (3.5%)
	Odds ratio =2.6 (95% CI 1.5-4.3)†	
Patients identify themselves as having a condition treated by an advertised drug Sacramento vs. Vancouver	201 (29.4%)	164 (21.9%)
	Odds ratio= 1.4 (95% CI 1.1-1.8) †	

†Adjusted odds ratios based on a regression analysis (Generalized Estimation Equation) controlling for age, sex, health status, income, education, drug payment, and cluster sampling.

A false drug name, 'Rilovan', was included in the question asking patients whether or not they had seen ads for specific products,. The aim was to check reliability of responses. Only 46 patients (6.1%) in Vancouver incorrectly remembered having seen ads for this product. In Sacramento, a much higher proportion of patients, 109 (16%), believed that they had seen ads for Rilovan. Most were not rote responses, in that the patients did not check off that they had seen ads for all listed drugs, but specifically picked this one among others. The number of drug requests in this subgroup did not differ from the

** Brand name only listed on questionnaire.

sample as a whole: 10.9% in Vancouver and 15.6% in Sacramento. This subgroup reported higher than average advertising exposure, with 56% in Vancouver having seen more than 10 drugs advertised and 54% in Sacramento. The finding is intriguing and could reflect confusion with other similar-sounding prescription drug brand names. As the survey findings did not differ if this group was excluded; they were retained in the analysis.

The questionnaire also asked about the contribution of listed information sources to patients' decision to consult the doctor or their belief that they needed a diagnostic test or a prescription. More Sacramento patients, 8.2% vs. 3.5% in Vancouver, mentioned advertising either as having directly contributed to one or more decisions or as an information source they consulted (adjusted odds ratio 2.6 (95% CI 1.5-4.3), $p<.001$ (Table 5.11).

As a measure of both past exposure to prescription drug advertising and potential susceptibility to advertising messages, patients were asked whether they had a health condition that could be treated by a medicine they had seen advertised. A total of 164 (21.9%) Vancouver patients and 201 (29.4%) Sacramento patients said that they did have such a condition: adjusted odds ratio= 1.4 (95% CI 1.1-1.8), $p<.05$. Patients with higher self-reported advertising exposure were also more likely to self-identify as having a condition that could be treated by an advertised drug. This ranged from 11% of those at the lowest exposure level to 30% at the highest levels, as measured by how many products patients remembered having seen advertised within the last year. Table 5.12 lists conditions treatable by an advertised drug identified by at least three patients in either city.

The largest difference was in the proportion of patients identifying themselves as having allergies, 12.9% in Sacramento versus 5.6% in Vancouver. This may be related to seasonal differences in survey administration: from June to August in Vancouver, and from March to June the following year in Sacramento. Sacramento patients may have

been more likely to experience reactions to spring pollen around the time that they were surveyed. The question was not time-limited, but current or recent allergic reactions might have triggered more positive responses.

The direction of the association between self-reported advertising exposure and patient identification with an advertised condition is unknown. Patients with pre-existing conditions may pay more attention to ads, and thus report more exposure, or patients who see more ads may become more aware of advertised health problems and identify their own symptoms as representing these problems.

Table 5.12:
Conditions treated by an advertised drug mentioned by ≥3 people in either city

Conditions mentioned by ≥3 people	Sacramento (% of patients) N=683	Vancouver (% of patients) N=748
Allergies	12.9%	5.6%
Depression	3.5%	3.5%
High cholesterol	2.5%	1.0%
Acid reflux	1.5%	0.4%
Arthritis	1.3%	1.6%
Diabetes	1.3%	0.4%
High blood pressure	1.3%	0.5%
Obesity	0.9%	0.1%
Sinus problems	0.9%	0.4%
Asthma	0.7%	0.9%
Impotence	0.7%	0.5%
Menopause	0.6%	0.3%
Migraine	0.6%	-
Back pain / pain	0.4%	1.1%
Heart Problems	0.4%	0.4%
Smoking	0.3%	1.9%
Birth Control	0.1%	0.4%
Baldness	0.1%	0.4%
Total number of conditions mentioned	**229**	**168**
Number of patients mentioning one or more condition	201 (29.4%)	164 (21.9%)

Ten patients stated both that they thought they needed a prescription for a medicine they were not already taking, and that they had heard about this medicine through advertising. Nine of these 10 patients were from Sacramento: unadjusted odds ratio= 10.0; 95% CI 1.4-438, Fisher's exact test. This is a small subset of patients, but under-reporting of a

direct influence from advertising was expected and is consistent with other studies of the influence of pharmaceutical advertising on health care.[29]

5.3.5 Past patient requests for medicines

Patients were asked whether they had ever requested a medicine from their physician in the past, whether their physician had prescribed the requested drug, and whether they had seen advertising for the drug before requesting it. This question did not measure the frequency of past requests as no time limits were included. However, it did measure patients' willingness to request medicines, as indicated by past actions. The proportion of patients who reported that they had requested a prescription drug from their doctor in the past did not differ in the two samples: 181 or 24.2% in Vancouver and 167 or 24.5% in Sacramento. Those responding affirmatively nearly always reported having received the prescription they requested, 87.3% of the time in Vancouver and 91% in Sacramento. The latter measure is likely to be subject to recall bias, as patients may have preferentially remembered occasions in which physicians acknowledged and complied with their requests. Table 5.13 provides an overview of patient reports of past drug requests.

Table 5.13 Patient reports of past prescription drug requests

Patients who had:	Sacramento	Vancouver	Difference (95% confidence interval) Sacramento vs. Vancouver
Asked for a drug in the past	167/683 (24.2%)	181/748 (24.5%)	OR=1.0 (0.8-1.3) NS
Reported that their doctor prescribed the drug(s)	152/167 (91.0%)	153/181 (87.3%)	OR =1.9 (0.9-3.8) NS
Has seen an ad for a drug before requesting it	75/167 (44.9%) 10.6% of sample	48/181 (26.5%) 6.4% of sample	OR=2.3 (1.4-3.6), p.0003* Absolute difference =4.2%

*unadjusted chi-square analysis

Table 5.14 lists the drugs patients most commonly reported that they had requested in the past (3 or more patients per city). Most of these were advertised drugs and most patients said that they had seen advertising before requesting the drugs. Two patients in Vancouver reported having seen ads for products for which I found no evidence of mass media advertising: citalopram (Celexa) and codeine + acetaminophen (Tylenol 3).

In Vancouver, 14 products, and in Sacramento 13, were mentioned by three or more

patients. There was considerable overlap between the products mentioned most frequently in the two cities (8 products), especially given that the Sacramento list includes two products with OTC status in Canada. In Sacramento, three or more patients reported having requested 9 of the 10 drugs with the highest advertising spending in 2000.[30]

Table 5.14: Drugs three or more patients had requested in the past

Drug name	No. of patients	Therapeutic Category	DTC advertised product? [a]	Did patients report seeing ads before requesting?[b]
SACRAMENTO				
Claritin (loratadine)	15	Antihistamine	Yes	Yes
Allegra (fenoxafenadine)	9	Antihistamine	Yes	Yes
*Viagra (sildenafil)	6	Erectile dysfunction	Yes	Yes
*Zyban /Wellbutrin (buproprion)	5	Antidepressant/ smoking cessation	Yes	Yes
*Paxil (paroxetine)	5	Antidepressant	Yes	Yes
Xanax (alprazolam)	5	Anxiolytic	No	No
*Celebrex (celecoxib)	5	NSAID	Yes	Yes
*Vioxx (rofecoxib)	5	NSAID	Yes	Yes
Meridia (sibutramine)	5	Obesity	Yes	Yes
*Prilosec (omeprazole)	4	Ulcer/reflux	Yes	Yes
*Prozac /Sarafem (fluoxetine)	3	Antidepressant, PMS	Yes	Yes (Prozac)
*Celexa (citralopram)	3	Antidepressant	No	No
Flonase (fluticasone)	3	Nasal steroid	Yes	Yes
VANCOUVER				
*Zyban/Wellbutrin (bupropion)	10	Antidepressant / smoking cessation	Yes	Yes (both)
*Prozac (fluoxetine)	7	Antidepressant	Yes	Yes
*Paxil (paroxetine)	5	Antidepressant	Yes	Yes
Tylenol 3 (codeine/acetaminophen)	5	Combination painkiller	No	Yes
*Losec (omeprazole)	5	Anti-ulcerant	Yes	Yes
Zoloft (sertraline)	4	Antidepressant	Yes	No
*Celebrex (celecoxib)	4	NSAID	Yes	Yes
*Viagra (sildenafil)	4	Sexual dysfunction	Yes	Yes
*Vioxx (rofecoxib)	3	NSAID	Yes	Yes
Propecia/Proscar (finasteride)	3	Balding / prostate	Yes (Propecia)	Yes (Propecia)
Accutane (isotretinoin)	3	Acne	Yes	Yes
Ativan (lorazepam)	3	Anxiolytic/sedative	No	No
*Celexa (citralopram)	3	Antidepressant	No	Yes
Zovirax (acyclovir)	3	Antiviral / herpes	No	No

[a]Findlay S. NIHCM, 2000, 2001.
[b]One or more patients reporting having seen ads for the product before requesting it.
*requested by 3 or more patients in both jurisdictions

5.3.6 Drug requests in surveyed consultations

As discussed in Chapter 4, in order for patient-directed advertising to result in increased sales of prescription drugs, patients must request and receive prescriptions from their physicians. Patient drug requests are a key element along this pathway. In order to focus primarily on observed behaviours rather than intent, patient requests were measured on the physician questionnaire. Additionally, exposure to advertising involves not only product-specific messages, but also messages about the benefits of drug therapy and suggestions to 'ask your doctor'. Thus the survey measured not only requests for advertised drugs but also all drug requests.

The added advantage to measuring all drug requests was the ability to explore different hypotheses about differences or similarities in patterns of requests for advertised versus non-advertised drugs. Given the literature indicating that patients request medicines from their physicians in the absence of DTCA (as discussed in Chapter 3), a different pattern of drug requests might be expected between people requesting advertised and non-advertised drugs. However, if DTCA has a general effect in supporting patients' decisions to 'ask your doctor' about a medicine, as well as product-specific effects, a similar pattern would be expected among people requesting advertised and non-advertised drugs.

Three questions on the physician questionnaire measured whether a patient had requested a drug:

1. Had the patient 'raised the possibility' of taking this drug?
2. Had the patient directly requested the drug?
3. Had the patient requested a drug that was not prescribed?

The first possibility allows for situations in which a patient had initiated a discussion of using a specific drug, but had not directly asked for a prescription. This measure was included to allow for personal and cultural differences in how a patient might broach the subject.

Any prescription drug request (advertised and non-advertised)

In a single consultation with a family physician, is a patient in a US setting with full legal DTCA (Sacramento) more likely to request a prescription for a medicine than in a Canadian setting, where DTCA is illegal but exposure to cross-border DTCA exists (Vancouver)?

Table 5.15 presents an overview of patient requests for prescriptions. There were significantly more consultations involving drug requests in Sacramento than Vancouver, 15.8% versus 9.0% ($p<.0001$, unadjusted chi square analysis). The difference in the proportion of patients requesting drugs in the two cities remained highly significant after adjusting for the cluster sampling technique, the patient's age, sex, income, educational status, drug payment method, health status, and length of relationship with their doctor, using a generalized estimation equation analysis. The adjusted odds ratio was 2.0 ($p=.002$). In other words, Sacramento patients were twice as likely to request a prescription after adjusting for demographic, health and socio-economic factors.

In several cases patients requested drugs that have prescription-only status in one jurisdiction and OTC status in the other. This includes three two low-sedating antihistamines loratadine (Claritin), fexofenadine (Allegra) and cetirizine (Zyrtec), which are prescription-only in the U.S. and OTC in Canada. Additionally, one drug for baldness minoxidil (Rogaine) is available OTC in the U.S. but is prescription-only in Canada, and one Canadian patient requested this drug.

Subtracting consultations in which *only* a product with OTC status in the other city was requested (11 in Sacramento and 1 in Vancouver), the rate of requests either for medicines in general (14.2% vs. 8.8%, $p<.01$; unadjusted chi square analysis) or for advertised drugs (5.6% vs 3.2%, $p<.03$) remained substantially different.

Effects of sex and age on the likelihood a patient would request a medicine

In Sacramento, a larger proportion of women than men requested prescriptions: 79 women (18.2%) versus 29 men (11.8%). This difference was marginally significant

(p=.05, unadjusted chi-square analysis).†† In Vancouver, roughly 9% of women and 9% of men requested prescriptions. More of the men directly asked for a prescription rather than only 'raising the possibility' of using a drug, suggesting gender differences in style or assertiveness in posing the question.

A trend of decreasing frequency of drug requests with age was seen in Vancouver, with only 5.4% of patients aged 65 and over requesting a drug versus 11.7% of those aged under 35. In Sacramento this effect was attenuated but similar in direction (16.4% of those aged under 35 versus 12.8% aged 65 and over). There were no systematic differences associated with education, income or drug payment method and drug requests in general in either jurisdiction.

In Sacramento, 23% of patients in fair to poor health requested medicines versus 14% of those in good to excellent health (p=.03, unadjusted chi square analysis). In Vancouver the proportion did not differ significantly but a similar trend existed: 11% of those in fair to poor health versus 9% in good to excellent health.

Requests for advertised drugs

*Were patients in Sacramento more likely to request **advertised** medicines than Vancouver patients?*

In both settings, were patients with higher self-reported advertising exposure more likely to request advertised medicines than patients with less reported advertising exposure?

Sacramento patients were more likely to request advertised drugs than their Vancouver counterparts: 7.3% vs. 3.3%, odds ratio = 2.2, 95% CI 1.2 –4.1 (Table 5.15). In Vancouver, 67 patients requested 70 drugs, of which 25 (36%) were products known to be advertised to the public in the U.S. or Canada since 1999 [9] [17] In Sacramento, 108 patients requested 119 drugs, of which 55 (46%) had been advertised to the U.S. public.

†† More women than men requested non-advertised drugs in Sacramento: 10.8% vs. 4.9%, p=.01; no difference in request rate was observed for advertised drugs.

Requests for advertised drugs versus advertising exposure

Advertising exposure was measured in three ways: the number of products a person reported having seen advertised, identification with a condition treated by an advertised drug, and use of advertising as an information source (Table 5.15). For each of these measures, differences between settings, and in the effects of level of advertising exposure, were observed in the proportion of patients requesting advertised drugs. For example, nearly 15% of Sacramento patients who identified themselves as having a health condition treated with an advertised drug requested advertised drugs, versus only around 5% of similar Vancouver patients. However, in both settings there were more requests among patients with higher than lower exposure. In Sacramento, all three measures were associated with a higher probability of drug requests (e.g. higher self-reported exposure, identification with a condition treated with an advertised drug, and use of advertising as an information source.). In Vancouver, only patients who used advertising as an information source were significantly more likely to request advertised drugs (adjusted odds ratio = 4.1, 95% CI 1.2 – 13.6), although a similar non-significant trend was seen for the other two measures (Table 5.15).

Table 5.15: Patient requests for medicines

Patient requests for prescriptions during surveyed consultations	Sacramento N=683	Vancouver N=748
≥ 1 new prescription requested (any drug)	108 (15.8%)	67 (9.0%)
Sacramento vs. Vancouver:		
Unadjusted odds ratio*	1.9 (95% CI 1.4 –2.7)	
Adjusted odds ratio†	2.0 (95% CI 1.3-3.1)	
≥ 1 DTC advertised drug requested	49 (7.3%)	25 (3.3%)
Sacramento vs. Vancouver:		
Unadjusted odds ratio*	2.2 (95% CI 1.3 – 3.8)	
Adjusted odds ratio†	2.2 (95% CI 1.2-4.1)	
Proportion of patients who requested DTC drugs vs. self-reported advertising exposure	**Sacramento**	**Vancouver**
Proportion requesting DTC drugs among those who had seen ads for:		
> than 3 of 6 listed drugs	34/321 (10.6%)	7/118 (5.9%)
≤ 3 of 6 listed drugs	15/362 (4.1%)	18/630 (2.9%)
Probability of a DTC drug request at higher versus lower exposure within each setting:		
Unadjusted odds ratio*	2.7 (95% CI 1.4-5.4)	2.1 (95% CI 0.8-5.6)
Adjusted odds ratio†	2.8 (95% CI 1.6-4.9)	1.8 (95% CI 0.6-5.1)
Proportion requesting DTC drugs among those who:		
Identify themselves as having a condition treated by an advertised drug	30/201(14.9%)	8/164(4.9%)
Do not identify themselves as having a condition treated by advertised drug	19/482(3.9%)	17/584(2.9%)
Probability of a DTC drug request among self-identified with advertised condition vs. not in each setting:		
Unadjusted odds ratio*	4.3 (95% CI 2.3 -8.1)	1.7 (95% CI 0.7-4.3)
Adjusted odds ratio †	4.6 (95% CI 2.5-8.5)	1.9 (95% CI 0.9-3.9)
Proportion requesting DTC drugs among those who:		
Used ads as an information source	10/56(17.9%)	3/26(11.5%)
Did not use ads as an info source	39/627(6.2%)	22/722(3.0%)
Probability of a DTC drug request among those using ads as an information source vs. others in each setting		
Unadjusted odds ratio*	3.3 (95% CI 1.4-7.4)	4.2 (95% CI 0.7-15.3)
Adjusted odds ratio†	3.9 (95% CI 2.2-7.0)	4.1 (95% CI 1.2-13.6)

*unadjusted chi square analysis
†Adjusted odds ratios based on a regression analysis (Generalized Estimation Equation) controlling for age, sex, health status, income, education, drug payment, doctor's sex and graduation year, and cluster sampling.

To explore whether there were 'environment' effects other than differential exposure to advertising that might influence the different rates of request for advertised drugs, both city of residence (i.e. Sacramento vs. Vancouver) and measures of advertising exposure were entered into the same multivariate regression analysis (G.E.E.), controlling for age,

sex, health status, income, education, drug payment, doctor's sex and graduation year and cluster sampling. A backward stepwise regression analysis was used, removing potential confounders that were not significantly associated with the outcome ($p>0.1$) but maintaining city of residence and advertising exposure measures in the model. The results are reported below in Table 5.16.

The effect of location of residence on requests for advertised drugs becomes attenuated and non-significant ($p=.06$) when adjusted for measures of advertising exposure. Health status, age, sex, education, income class, drug payment, physician sex and graduation year did not have significant effects on the probability that a patient requested an advertised medicine.

Table 5.16: DTCA drug requests as a function of location of residence and self-reported advertising exposure

DTC drug requests as a function of location and self-reported advertising exposure (combined model)*	Difference	Significance
Patient lives in Sacramento	OR=1.5 (95% CI 0.9-2.6)	P=.057
Has seen ads for > 3 listed drugs	OR=2.1 (95 % CI 1.3-3.3)	P<.002
Has a condition treated by an advertised drug	OR=2.7 (95% CI 1.8-4.2)	P<.0001
Uses advertising as an information source	OR=2.9 (95 % CI 1.7-5.1)	P<.0001

*G.E.E. model with city of residence and three advertising exposure variables entered, as well as potential confounders (age, sex, health status, income, education, drug payment, doctor's sex and graduation year);backward stepwise regression analysis with removal of potential confounders if p >0.1

5.3.7 Patterns of Drug Requests in the Combined Sample

The situations in Sacramento and Vancouver are hypothesized to represent two different environmental dose levels in exposure to advertising, with individual exposure varying within each setting, depending on media exposure, susceptibility to advertising messages and a range of health and demographic factors. This hypothesis is supported by the higher self-reported exposure reported in Sacramento, as well as the range of self-reported exposure levels within each setting (Table 5.11 above).

Within this framework it is interesting not only to compare the different policy environments represented by these two settings, but also the effect of individual

differences across the two settings. A consistent relationship is hypothesized to exist between individual self-reported advertising exposure measures and requests for advertised drugs within both settings. A second strength in examining the combined Sacramento and Vancouver sample is in the larger numbers, which makes it possible to examine differences between subgroups.

Figure 5.2 describes the proportion of patients who requested advertised drugs at different self-reported exposure levels. Exposure levels are based on the number of products listed on the questionnaire, out of a total of six, for which patients reported having seen advertisements. A clear trend is apparent in higher frequency of requests and higher self-reported exposure levels. Few patients reported having seen all six drugs advertised, 41, or 3% of the combined sample. As well as including request rates at individual advertising exposure levels for the combined sample, Figure 5.2 reports the mean exposure levels versus request rate for Vancouver patients, Sacramento patients and the combined sample.

Figure 5.2: Percent of patients requesting advertised drugs vs self-reported exposure

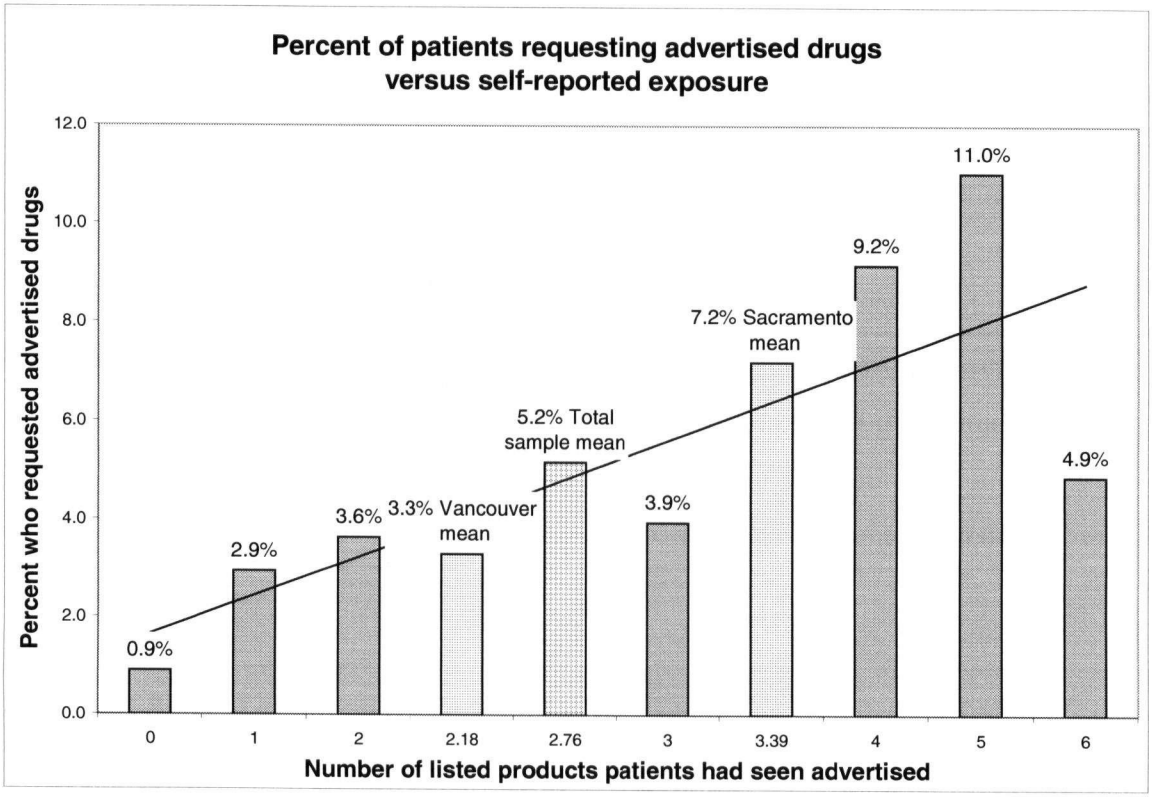


Table 5.17 below examines additional factors associated with patient requests in the combined sample.[31] The patient's belief that a new medicine was needed was highly predictive of a drug request: 75 (28.4%) of the 264 patients who believed that they needed a new medicine requested one. Some patients who did not say on the patient questionnaire that they needed a new prescription nevertheless requested one, but the rate of requests was much lower among these patients (8.1%). The probability of a drug request among those who believed a new medicine was needed was 3.9 times that of other patients (95% CI 2.7 to 5.8; adjusted odds ratio, Table 5.17). This relationship was even stronger for the subset of requests that were for advertised drugs, with patients who reported that they believed a medicine was needed having 5.1 times the likelihood of requesting a DTCA drug as compared to those who did not report this (95% CI 3.0- 8.8, adjusted odds ratio, Table 5.17).

Similarly, patients' reports that they had requested drugs in the past, that they had a condition treated by an advertised drug and that they remembered seeing a higher volume of advertising were all associated with a higher likelihood that they would make a drug request. The magnitude of this difference tended to be larger for advertised drugs than requests in general.

The proportion of patients who received one or more drugs that they requested was similar for requests in general and for requests for advertised drugs.

5.3.8 Are patterns similar for advertised and non-advertised drugs?

Table 5.17 suggests a broad similarity between the pattern of drug requests in general and requests for advertised drugs in terms of patients' belief that a medicines was needed, their history of past drug requests, and measures of advertising exposure and susceptibility. As would be expected, the relationship between factors related to advertising-exposure and requests for advertised drugs is stronger than the relationship between these factors and requests in general.

Another question is how patients who request advertised drugs compare to those requesting non-advertised drugs, in terms of demographics, health status and socio-economic status. If requests for non-advertised drugs were stimulated indirectly by advertising through messages about the benefits of medicine use or the suggestion to 'ask your doctor', patients who requested these drugs would be expected to be broadly similar to patients who requested advertised drugs. If these requests occured for other reasons, then different patterns might be expected to emerge.

Table 5.17: Patient prescription drug requests in the combined sample

Factors associated with requests (N=1431)	Patients who requested ≥ 1 drug (any drug)	Patients who requested ≥ 1 DTC advertised drug
Does the patient believe a new prescription is needed?		
Yes (N=264)	75/ 264 (28.4%)	39/ 264 (14.8%)
No (N=1167)	100/1167 (8.1%)	35/1167 (3.0%)
Unadjusted odds ratio*	4.2 (95% CI 3.0 –6.0)	5.6 (95% CI 3.4-9.3)
Adjusted odds ratio†	3.9 (95% CI 2.7 – 5.8)	5.1 (95% CI 3.0–8.8)
Has the patient requested drugs before?		
Yes (N= 348)	67/ 348 (19.3%)	32/ 348 (9.2%)
No (N=1083)	108/1083 (10.0%)	42/1083 (3.9%)
Unadjusted odds ratio	2.2 (95% CI 1.5-3.0	2.5 (95% CI 1.5-4.2)
Adjusted odds ratio†	2.0 (95% CI 1.5–2.8)	2.5 (95% CI 1.5–4.2)
Does the patient identify themselves as having a condition treatable by an advertised drug?		
Yes (N=365)	67/ 365 (18.4%)	38/ 365 (10.4%)
No (N=1066)	108/1066 (10.1%)	36/1066 (3.4%)
Unadjusted odds ratio*	2.0 (95% CI 1.4-2.8)	3.3 (95% CI 2.0-5.5)
Adjusted odds ratio†	2.0 (95% CI 1.4–2.8)	3.2 (95% CI 2.1– 5.0)
Does the patient use advertising as an information source?		
Yes (N=82)	17/82 (20.1%)	13/82 (15.9%)
No (N=1349)	158/1349 (11.7%)	61/1349 (4.5%)
Unadjusted odds ratio*	2.0 (95% CI 1.1 –3.6)	4.0 (95% CI 2.0-7.9)
Adjusted odds ratio†	1.8 (95% CI 1.1-3.2)	3.9 (95% CI 2.3-6.7)
Does the patient recall having seen ads for at least 4 of 6 listed drugs?		
Yes (N=439)	71/439 (16.2%)	41/439 (9.3%)
No (N=992)	104/992 (10.5%)	33/992 (3.3%)
Unadjusted odds ratio*	1.7 (95% CI 1.2 –2.3)	3.0 (95% CI 1.8 – 4.9)
Adjusted odds ratio†	1.5 (95% CI 1.1 –2.0)	2.6 (95% CI 1.6- 4.4)
Does the patient recall seeing > 5 prescription drugs advertised in the last year?		
Yes (N=822)	111/ 822 (13.5%)	54/ 822 (6.6%)
No (N=609)	64/609 (10.5%)	20/609 (3.3%)
Unadjusted odds ratio	1.3 (95% CI 1.0-1.9)	2.1 (95% CI 1.2- 3.6)
Adjusted odds ratio†	1.2 (95% CI 0.9-1.8)	1.9 (95% CI 1.1–3.2)
Total requests	**175/1431 (12.2%)**	**74/1431 (5.2%)**
Requested drug prescribed	128/1431 (8.9%) 73% of requests	55/1431 (3.8%) 74% of requests

†Odds ratios adjusted for age, sex, health status, income, education, drug payment, doctor's sex and graduation year, and cluster sampling.

Table 5.18 describes demographic, health and socio-economic characteristics of patients requesting non-advertised and advertised drugs, as well as characteristics of their physicians. The main difference between the two groups of patients is in the relationship between drug requests and health status. Patients who requested non-advertised drugs were nearly twice as likely to report fair to poor health status than other patients (OR =1.9; 95% CI 1.2 – 3.2, unadjusted chi square analysis), whereas no association was observed between health status and the likelihood that a patient would request an advertised drug. There were no other statistically significant differences in request rates between patients with different demographic characteristics or socio-economic status.

However, as indicated in Table 5.18, a larger proportion of younger than older patients requested drugs, and the gradient was largest for advertised drugs, (6.7% of patients aged 18-34 versus 3.4% of those aged 65 and above requested advertised drugs, not significant on unadjusted chi square analysis). A trend was also seen towards better-educated and higher income patients requesting advertised drugs more often than those with less income or education. However, the opposite trend was observed in requests for non-advertised drugs, with patients with lower income and less education requesting more of these drugs.

In general, Table 5.18 indicates little association between patient characteristics generally associated with poorer health and requests for advertised medicines. If requests for advertised drugs strongly reflected unmet health needs, such an association would be expected. In contrast, requests for non-advertised drugs did follow a pattern reflecting poorer health status to a greater extent, not only in terms of patients' self-reported health status, but also income and education levels. However, as shown on Table 5.18, there was little difference in request rates for non-advertised drugs with age. If requests had been strongly associated with poorer health, the rate of requests would have been expected to increase with age. This is likely to be confounded, however, by generational differences in the degree of comfort that patients may feel in challenging physicians' authority by requesting a specific treatment.

The three types of non-advertised products most often requested were antibiotics (N=7 in Vancouver; N=11 in Sacramento‡‡), anxiolytics/hypnotics (N=7 in Vancouver; N=7 in Sacramento), and cardiovascular drugs (N=3 in Vancouver; N=9 in Sacramento).

Interestingly, patients of younger physicians (10 years or less post graduation) tended to request more advertised drugs than patients of older physicians.

‡‡ An additional three Sacramento patients requested an advertised antibiotic, azithromycin (Zithromax).

Table 5.18:
Characteristics of patients requesting non-advertised and advertised drugs

Patient Characteristics	Patients who requested only drugs not advertised to the public	Patients who requested ≥1 DTC advertised drug*
Sex		
Female (N=934)	74/934 (7.9%)	50/934 (5.4%)
Male (N=493)	27/493 (5.5%)	24/493 (4.9%)
Age		
18 – 34 (N=344)	23/344 (6.7%)	23/344 (6.7%)
35 – 64 (N=792)	61/792 (7.7%)	41/792 (5.2%)
65 + (N=295)	17/295 (5.8%)	10/295 (3.4%)
Self-reported health status		
Fair to poor (N=238)	27/238 (11.3%)†	13/238 (5.1%)
Good to excellent (N=1193)	74/1193 (6.2%)	61/1193 (5.5%)
Income‡		
High (N=610)	38/610 (6.2%)	40 /610 (6.6%)
Medium (N=643)	45/643 (7.0%)	27 /643 (4.2%)
Low (N=178)	18/178 (10.1%)	7/178 (3.9%)
Education		
University graduate or above (N=448)	28/448 (6.3%)	29/448 (6.5%)
Some post-secondary/technical (N=619)	46/619 (7.4%)	31/619 (5.0%)
High school graduate or below (N=364)	27/364 (7.4%)	14/364 (3.8%)
Drug payment method		
Full 3rd party payment (N=202)	15/215 (7.0%)	9/215 (4.2%)
Partial 3rd party payment (N=936)	73/936 (7.8%)	51/936 (5.4%)
Out-of-pocket (N=215)	10/202 (5.0%)	10/202 (5.0%)
Unknown/ no response (N=78)	3/78 *(3.8%)*	*4/78 (5.1%)*
Physician Characteristics		
Physician's sex		
Female (N=484 patients; 28 physicians)	28/484 (5.8%)	25/484 (5.2%)
Male (N=947 patients; 50 physicians)	73/947 (7.7%)	49/947 (5.2%)
Physician's year of graduation		
≤10 years ago (N=395 patients; 23 MD's)	26/395 (6.6%)	28/395 (7.1%)
10 – 20 years (N=474 patients;23 MD's)	27/474 (5.7%)	21/474 (4.4%)
21 – 30 years (N=431 patients; 25 MD's)	36/431 (8.4%)	19/431 (4.4%)
≥ 31 years (N=131 patients; 7 MD's)	12/131 (9.2%)	6/131 (4.6%)

* patients who requested at least one advertised drug, regardless of whether or not they requested one or more non-advertised drug.
‡ income classes equivalent to <$20,000; $20-$60,000; >$60,000 in each currency; not adjusted for purchasing power parity in order to maintain initial discrete categories as listed on the questionnaire.
†Odds ratio of a requests for a non-advertised drug, poorer to better health = 1.9 (95% CI 1.2-3.2), p=.005; unadjusted chi square analysis

5.3.9 What advertised medicines did patients request?

Table 5.19 lists the advertised drugs requested by two or more patients in the sample as a whole. In total, patients requested 37 different advertised products, 15 of which were requested by only one patient, 22 by two or more. The large number of products requested probably reflects the broad range of conditions encountered in primary care. It also represents a substantial proportion of the prescription drugs that are advertised to the U.S. public at any given time. In 2000, over 95% of U.S. DTCA spending was on only 50 products. [9]

Patient requests include products for generally mild conditions such as allergy (antihistamines and nasal inhaled steroids), as well as products that have been described as "lifestyle drugs", [32] with indications such as baldness, toenail fungus, facial hair, overactive bladder, pre-menstrual-syndrome, social phobia, smoking cessation, obesity and impotence.

Table 5.19:
Advertised drugs requested by two or more patients in surveyed consultations

Requested advertised drugs*	Therapeutic category	Total # requests
Claritin (loratadine)	Antihistamine	10
Allegra (fexofenadine)	Antihistamine	5
Wellbutrin (bupropion)	Antidepressant	4
Viagra (sildenafil)	Erectile dysfunction	4
Zithromax/ Z pack (azithromycin)	Antibiotic	3
Paxil (paroxetine)	Antidepressant	3
Nasonex (mometasone)	Inhaled steroid	3
Celebrex (celecoxib)	Arthritis/ NSAID	2
Alesse (Estradiol/levonorgestrel)	Contraceptive	2
Tricyclen(Estradiol//Norgestimate)	Contraceptive	2
Depo Provera (medroxyprogesterone[MPA])	Contraceptive	2
Vaniqa (eflornithine)	Facial Hair	2
Ambien (zolpidem)	Hypnotic	2
Premarin/Provera (conjugated estrogen/MPA)	Menopausal hormones	2
Meridia (sibutramine)	Obesity	2
Xenical (orlistat)	Obesity	2
Detrol (tolteridone)	Overactive bladder	2
Ditropan (oxybutin)	Overactive bladder	2
Flonase (fluticasone)	Inhaled steroid	2
Zyban (bupropion)	Smoking cessation	2
Diflucan (fluconazole)	Yeast infection	2
Penlac (ciclopirox)	Toenail fungus	2
Prilosec (omeprazole)	Ulcer/reflux	2

Requests from Canadian patients for products advertised in Canada

A list of year 2000 and first half of 2001 prescription drug ads was obtained from a market research company[21] in order to compile a more complete list of advertised medicines than that available through published sources. This list included Canadian as well as U.S. television ads. There were Canadian television ads for three products: a contraceptive, estradiol/levonorgestrel (Alesse), an antidepressant indicated for smoking cessation, bupropion (Zyban), and sildenafil (Viagra), the latter featured in unbranded ads about erectile dysfunction. Additionally, Hoffman LaRoche ran an intensive unbranded billboard and newspaper advertising campaign for an obesity drug, orlistat (Xenical) in 1999-2000. There were three requests in Vancouver for weight loss drugs, two of which specified the product name and one for a "safe weight loss drug". Omitting requests not mentioning a brand name, 7 (29%) of the 24 Vancouver requests for advertised drugs were for products advertised to the public in Canada.

5.3.10 Prescribing – in general and in response to requests

Mirroring differences in reported current prescription drug use, the proportion of Sacramento patients who received a new prescription during observed consultations was considerably higher than the proportion in Vancouver: 41.3% of patients in Sacramento obtained one or more new prescriptions as compared to 24.9% of patients in Vancouver. More Sacramento patients also received several new prescriptions in observed consultations (13% vs. 4% in Vancouver). In Sacramento, 27 patients (3.9%) received at least 3 new prescriptions, as compared to 4 patients (0.05%) in Vancouver ($p<.0001$ for all three comparisons, unadjusted chi square analysis).

A refill (repeat prescription) was provided in 7% more consultations in Vancouver than Sacramento, and in both cities, this rate increased with age, as would be expected: 22% of patients aged 65 and over received refills in Sacramento and 31% in Vancouver, versus 17% of those aged 18 to 34 in Sacramento and 18% in Vancouver. In Vancouver, all patients 65 and over had their drug costs covered through the provincial drug benefit plan, Pharmacare. Theoretically this could lead to higher refill rates versus new prescriptions

because of reimbursement policies such as the existence of a limited formulary. However, the rate of refills was similar among Vancouver patients aged 35 to 64, 27%, although most patients within this age group would not have had their drug costs covered by Pharmacare (only those with specific chronic diseases or very high drug costs).

Overall, 8% more patients received drug therapy of some sort in Sacramento than in Vancouver, as indicated in Table 5.20. However, this difference was not significant after adjusting for potential confounders. Patients who reported their health to be good to excellent, who were seeing a female doctor, or who had no drug insurance coverage were more likely than others to leave the consultation without drug treatment (no new prescriptions, refills, or recommended use of an OTC drug).

Table 5.20: Prescribing during recorded consultations

Proportion of patients receiving prescriptions	Sacramento	Vancouver	Sacramento vs. Vancouver Odds ratio (95% confidence interval)
Patient received ≥ 1 new prescription during consultation (excludes refills)	282 (41.3%)	186 (24.9%)	OR=2.1 (1.6-2.8)† Absolute difference= 16.4%
Patient received ≥ 1 refill	124 (18.2%)	190 (25.4%)	OR=0.6 (0.4-0.9)† Absolute difference =- 7.2%
OTC drug recommended	18 (2.6%)	43 (5.7%)	OR=0.5 (0.3-0.9)† Absolute difference = -3.1%
No drug therapy	269 (39.4%)	355 (47.5%)	OR=0.8 (0.6-1.1)†, NS
Prescribing in response to requests			
Patient received ≥ 1 Rx** for a drug they requested (any drug)	86 (12.6%)	42 (5.6%)	OR=2.5 (1.6-3.9)†
Percent of those requesting drugs	86/108(79.6%)	42/67 (62.6%)	OR=2.3 (1.1-4.9)*
Patient received ≥ 1 Rx for DTC advertised drug they requested	38 (5.6%)	18 (2.4%)	OR=2.3 (1.3 – 4.3)†
Percent of those requesting drugs	38/49 (78%)	18/25 (72%)	NS*
Patients requesting DTC advertised drug who received ≥ 1 new Rx (any drug)	42/49 (86%)	22/25 (88%)	NS*
Odds of ≥ 1 new Rx vs. no request	OR=16.9 (95% CI 7.5-38.2) †		
Patients requesting non DTC advertised drug who received ≥ 1 new Rx (any drug)	47/59 (80%)	28/42 (67%)	NS*
Odds of ≥ 1 new Rx vs. no request	OR= 7.9 (95% CI 4.8-13.2) †		

†Adjusted odds ratios based on a regression analysis (Generalized Estimation Equation) controlling for age, sex, health status, income, education, drug payment, doctor's sex and graduation year, and cluster sampling.

* unadjusted chi square analysis ; **Rx = prescription

More patients were seeing physicians for the first time in Sacramento (16% vs 9% in Vancouver) and these consultations were associated with more new prescriptions. One or more new prescriptions were provided in 58% of first consultations in Sacramento, versus 41% for the Sacramento sample as a whole ($p<.001$). In contrast, among the 65 consultations in which a patient was seeing a doctor for the first time in Vancouver, only 13 patients (20%) received a prescription for one or more new drugs as compared to 24.9% in the sample as a whole (NS). The difference in prescribing rate among this subgroup accounted for a small proportion of the overall difference in prescribing between the two cities: 38.2% of Sacramento patients with an established relationship with their doctor received one or more new prescriptions versus 25.3% of comparable Vancouver patients.

Prescribing in Response to Requests

Are patients in Sacramento more likely to receive prescriptions for medicines they request than Vancouver patients?

If all requests for medicines are examined together, not only were patients more likely to request drugs in Sacramento than Vancouver, doctors in Sacramento were also more likely to prescribe requested drugs. Patients received prescriptions for one or more requested drugs in 79.6% of consultations involving a request in Sacramento vs. 62.6% in Vancouver. However, this difference was largely confined to requests for *non-advertised* drugs; similar numbers of patients requesting *advertised* drugs received them in Vancouver and Sacramento, 72% versus 78% (Table 5.20, above).

In some cases patients requested more than one drug. Physicians prescribed 64% of the 70 individual drugs requested in Vancouver, providing 45 drugs to 42 patients in response to requests. They prescribed 82% of the individual products requested in Sacramento, providing 98 requested drugs to 86 patients.

Physicians occasionally commented on the reasons they had refused a request. For example, one Vancouver patient had heard that tetracycline could be used for rheumatoid arthritis on a radio show. The physician referred her to a rheumatologist instead of

prescribing the drug. Another patient asked for a medicine for anxiety. The physician prescribed zopiclone, a drug that has effects similar to the most frequently prescribed anxiety treatments (benzodiazepines) but is indicated for insomnia. Similarly, a patient who requested acyclovir (Zovirax), an antiviral used to treat herpes, instead received a similar antiviral for herpes, valacyclovir (Valtrex). The physician did not explain the reason for this substitution. One Sacramento physician prescribed fexofenadine (Allegra) rather than loratadine (Claritin), another low-sedating antihistamine, because the patient could obtain fexofenadine on formulary. Although each of these cases was, strictly speaking, a refused request, as the patient did not receive the brand they had requested, the choice of a closely related alternative suggests that the request contributed to the treatment decision. Whether or not the physician would have prescribed similarly in the absence of a patient request is unknown.

As these examples illustrate, the prescribing rates following drug requests in both Vancouver and Sacramento may be underestimates of the influence of a patient request on a physician's decision to prescribe, as they do not count cases in which a specific request was refused but a similar type of product was prescribed instead. In Sacramento, these types of substitutions occurred on five occasions (four for advertised drugs) and in Vancouver on four occasions, in three cases involving anxiolytic/hypnotic drug substitutions, and in one case an advertised drug.

If a patient requested a medicine, he or she was highly likely to leave the physician's office with one or more prescriptions, whether or not this included the requested drug. As shown in Table 5.20, in Sacramento 86% and in Vancouver 88% of patients who requested advertised drugs received at least one new prescription during the observed consultation (adjusted odds ratio = 16.9; 95% CI 7.5-38.2 as compared to patients who had not requested medicines). A similar effect, although not as dramatic, was seen with non-advertised drugs, with 80% of patients in Sacramento and 67% in Vancouver who requested non-advertised drugs receiving one or more new prescriptions (adjusted odds ratio=7.9; 95% CI 4.8-13.2).

Antibiotic prescribing in response to requests

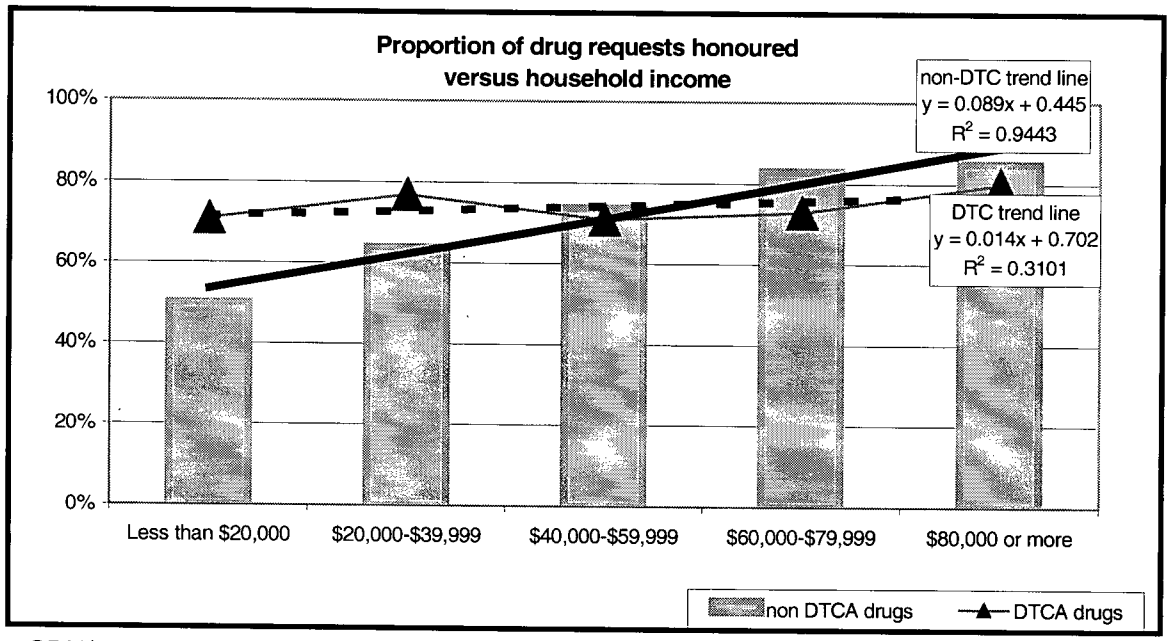
Although it was not the primary focus of this study, the rate at which patients requested and received antibiotics is of interest because physicians often cite patient demand as a reason that antibiotics are overprescribed.[33] Antibiotics were the most commonly requested class of non-advertised drugs (N=11 in Sacramento; N=7 in Vancouver), and an additional three Sacramento patients requested an advertised antibiotic, azithromycin (Zithromax or Z-pack). All of the 14 Sacramento patients who requested antibiotics received them; in Vancouver, only three of the seven patients requesting antibiotics received them (p=.006, unadjusted chi square analysis). Although the total number of antibiotic requests was small, the findings are consistent with other research indicating that patient requests for antibiotics do contribute to the prescribing rate in primary care. The reason for the difference in prescribing rates between Vancouver and Sacramento physicians is unknown. It could reflect differences in intensity of educational initiatives to reduce unnecessary antibiotic prescribing.

Did physicians prescribe more requested drugs for specific patient subgroups?

There were no significant differences in the proportion of requested drugs that were prescribed according to patients' sex, health status or age. The prescribing rate in response to requests also did not differ significantly depending on physicians' sex or number of years since graduation.

However, there was a difference in the proportion of requested *non-advertised* drugs prescribed with patients' income. The proportion increased as patients' income level went up, from 50% of requests among patients who listed their household incomes as being less than CDN $20,000 per year, to 85% of requests for patients with incomes of CDN $80,000 or more (reported U.S. incomes adjusted according to purchasing power parity) As shown in Figure 5.2, no difference was observed in the rate at which physicians prescribed requested advertised drugs by patients' income level. Figure 5.3 presents results for all patients in both cities who requested prescriptions

Figure 5.3: Proportion of honoured requests versus household income



CDN$ equiv; purchasing power parity, OECD, year 2000 rate. <http://www.oecd.org/std/ppp1.pdf>
N=101 patients requested non-DTC advertised drugs, N=74 patients requesting advertised drugs

5.3.11 Physicians' opinions about requested medicines

Physicians were asked to answer several questions about each new drug they prescribed in addition to whether the patient had requested it:

- how likely they were to prescribe the same drug to another similar patient with the same condition.
- whether the patient was knowledgeable about the drug.

The former was a measure of confidence or ambivalence about treatment choice. If physicians stated that a treatment was a 'possible' or 'unlikely' choice, rather than a 'very likely' choice, for another similar patient with the same condition, either response was interpreted as indicating some degree of ambivalence. Patient knowledge was undefined and therefore could not measure the type or extent of knowledge. However, it did provide some insight into physician attitudes.

Table 5.21:
New Prescriptions: physicians' opinions of treatment choice and patient knowledge

New Prescriptions (Rx)*	Sacramento N=420 Rx drugs	Vancouver N=223 Rx drugs	Total N=643 Rx drugs
Patient did not request this medicine	322/420 (76.7%)	178/223 (79.8%)	500/643 (77.8%)
Patient requested this medicine: - Any drug	98/420 (23.3%)	45/223 (20.2%)	143/643 (22.2%)
- DTC advertised drugs only	42/420 (10.0%)	18/223 (8.2%)	60/643 (9.3%)
Physician judged the medicine to be a 'possible' or 'unlikely' choice for another similar patient			
Patient did not request this medicine	39/322 (12.1%)	23/178 (12.9%)	62/500 (12.4%)
Patient requested this medicine: - Any drug	45/98 (45.9%)†	17/45 (37.8%)†	62/143 (43.4%)†
- DTC advertised drugs only	20/42 (47.6%)†	10/18 (55.6%)†	30/60 (50.0%)†
Physician judged the medicine to be an 'unlikely' choice for another similar patient			
Patient did not request this medicine	2/322 (0.6%)	5/178 (2.8%)	7/500 (1.4%)
Patient requested this medicine - Any drug	12/98 (12.2%)†	2/45 (4.4%)	14/143 (9.8%)†
- DTC advertised drugs only	4/42 (9.5%)†	1/18 (5.6%)	5/60 (8.3%)†
Physician judged the patient to be knowledgeable about the medicine			
Patient did not request this medicine	81/322 (25.2%)	37/178 (20.8%)	118/500 (23.6%)
Patient requested this medicine - Any drug	70/98 (71.4%)†	24/45 (53.3%)†	94/143 (65.7%)†
- DTC advertised drugs only	28/42 (66.6%)†	11/18 (61.1%)†	39/60 (65.0%)†

*The unit of analysis is each single newly initiated prescription, not each patient, as physicians recorded their opinion separately for each newly prescribed drug.
† p <.01 compared to drugs not requested by patients.

As indicated in Table 5.21, physicians were much more likely to report ambivalence about treatment choice following prescriptions for drugs requested by patients than for non-requested drugs. The odds ratio for reports of ambivalence for requested drugs (any medicine) vs. non-requested drugs was 5.4 (95% CI 3.5-8.5); the odds ratio was 7.1 (95% CI 3.8-13.0) for requested advertised drugs vs. non-requested drugs; unadjusted chi square analyses. Physicians' ambivalence did not differ significantly for advertised vs. non-advertised drugs.

In most cases in which any degree of ambivalence was expressed, physicians considered a prescription to be a 'possible' versus a 'very likely' choice for another similar patient. Few prescribed drugs were considered to be 'unlikely' choices for other similar patients: 21 (3.3% of prescriptions). Fourteen of these were requested by patients (14/98 or 9.8% of requested drugs) and 7 were not (1.4% of non-requested newly prescribed drugs); odds ratio = 7.6 (95% CI 2.8-21.4), unadjusted chi square analysis.

Patients who had requested a drug were also much more likely to be judged by physicians to be knowledgeable about it than patients who had not requested a drug: odds ratio = 6.2 (95% CI 4.1-9.5), unadjusted chi square analysis. In most cases, when physicians judged patients to be knowledgeable about a drug, they did not also express ambivalence about the choice of treatment. However, physicians expressed some degree of ambivalence about treatment choice, yet judged the patient to be knowledgeable, for 55/643, or 8.6% of new prescriptions. The patient had requested the drug in most of these cases: 33 of 55, or 60%.

Additionally, if a patient had requested the drug they had prescribed, physicians said how likely they were to have prescribed this drug 'in the absence of patient desire', with the options of answering 'very likely', 'possibly' and 'unlikely'.

The responses to this question were broadly similar in the two settings, in terms of any ambivalence being expressed ('possible' or 'unlikely' choice in the absence of expressed patient desire): 21 of 45 requested drugs (47%) in Vancouver, and 49 of 98 requested drugs (50%) in Sacramento. In Vancouver, physicians considered a prescription to be an unlikely choice in the absence of expressed patient desire in 4 cases (8.8%) whereas in Sacramento they considered it to be an unlikely choice in 20 cases (20.4%). The difference between settings was not significant, but the numbers were small (unadjusted chi square analysis, p=.09).

Pressure to Prescribe

Physicians did not report any pressure to prescribe in most consultations in which they provided one or more prescriptions. They also did not report pressure to prescribe in most consultations in which patients had requested prescriptions, although they were more likely to do so in these consultations than in consultations without patient requests for medicines.

Physicians reported some degree of pressure to prescribe, usually 'a little', in 6.3% of

consultations with new or refill prescriptions in Sacramento and 4.8% in Vancouver (n=740 consultations in total in which drugs were provided). Patients had requested medicines in 73% of the consultations in which pressure was reported in Sacramento and 58% in Vancouver.

Physicians reported pressure to prescribe in 15/74 (24.5%) of consultations in which patients requested DTC advertised medicines, and in 16/101 (15.9%) of consultations in which patients requested only non-advertised medicines. The difference was not significant. In both cases, they reported moderate to strong pressure in 4% of consultations. In general physicians were much more likely to report pressure to prescribe in consultations in which a patient requested a medicine, as compared to consultations without patient requests: odds ratio = 9.1 (95% CI 5.3 – 15.9, adjusted for cluster sampling only).

In Vancouver, reports of moderate to strong pressure included consultations in which an antibiotic, an antidepressant, a sedative, and a drug for urinary frequency, were prescribed. Of the four drugs, only the drug for urinary frequency, oxybutin (Ditropan), is advertised to the public. In Sacramento, 12 of the 27 consultations (44%) in which physicians reported pressure to prescribe involved requests for 13 advertised drugs: bupropion (Wellbutrin) (2x), loratadine (Claritin) (2x), fexofenadine (Allegra), zolpidem (Ambien), fluconazole (Diflucan), ciclopirox (Penlac), montelukast (Singulair), mometasone (Nasonex), azithromycine (Z-pack), celecoxib (Celebrex) and sildenafil (Viagra). Physicians reported moderate to strong pressure to prescribe in two of these consultations, one involving a request for a sleeping pill, zolpidem (Ambien), another an allergy drug, loratadine (Claritin).

5.4 Discussion and conclusions

The main question addressed by this patient-doctor survey is whether the rate of prescription drug requests differs in the two settings, reflecting differences in legal status of DTCA and population exposure to advertising. Secondly, if this rate does differ, is the

difference maintained after controlling for factors other than advertising that could influence patient requests and perceptions of a need for a medicine, such as differences in health status, age, sex, socio-economic status and benefit coverage?

The short answer is yes: patients in Sacramento were twice as likely to request a prescription drug from their doctor after controlling for age, gender, income, education, drug payment and self-assessed health status.

Relationship of DTC drug requests to patient characteristics

Age and gender are identified predisposing factors known to affect rates of use of health care services; socio-economic status, as measured through household income and education, would be expected to affect U.S. patients' access to health and drug insurance or ability to pay for services and treatments out-of-pocket, and in both settings patients' sensitivity to the price of heavily advertised drugs would be expected to differ depending on whether they had full, partial or no drug insurance.

More women requested drugs than men, and patients in poorer health requested more drugs than those in better health. These differences are consistent with broader differences in prescription medicine use, with more women and those in poorer health using more medicines. However, these differences were limited to patient requests for *non-advertised* drugs: the rate of requests for advertised drugs did not differ by gender or self-reported health status.

Additionally, younger patients requested more medicines than older patients. This is in contrast to population patterns of prescription drug use. Several factors may have contributed. First, this may reflect age-related differences in the relationship patients have with their physicians. For example, in a U.K. questionnaire study on primary care patients' wishes, only 14% of patients over 60 expressed desires for more patient centred care, versus 35-39% of younger adults.[34] Older patients with serious illnesses may also prefer to defer to physicians' expertise rather than taking on partial responsibility for

treatment decisions.[35] Younger people may also respond more positively to DTCA messages. A U.S. consumer survey on DTCA, by the American Association of Retired Persons, found that younger people (aged 18-39) were more likely to have positive views about the information content of advertising than older respondents (aged 60+).[36] An analysis of images in TV ads for prescription and OTC drugs also found that negative stereotyping occurred more often in representations of older than younger adults.[37]

No difference in the rate of drug requests in general was seen by income or educational status, or the extent of 3rd party drug coverage (none, partial or full). However, a non-significant trend was observed in higher income patients requesting more advertised drugs than lower income patients; the opposite trend occurred for requests for non-advertised drugs, with more requests occurring among lower income patients.

In general, requests for advertised drugs diverged from established patterns of health care service use: they were not concentrated primarily among the elderly, women and those in poorer health. This suggests that factors other than health care needs are at least partially responsible for the observed pattern of requests.

The pattern of physician responses to drug requests also appeared to differ for advertised and non-advertised drugs. Patients who requested non-advertised drugs were more likely to receive prescriptions if they were higher income; no such difference occurred in prescribing in response to requests for advertised drugs. Whether or not this difference in prescribing rate for requested drugs by income is indicative of a broader trend is unknown. For example, physicians may be more conscious of not wanting to displease patients who are of a similar social class to themselves. There may also be differences in the appropriateness of patient requests for medicines between different income groups, reflecting differences in education and in knowledge about medical treatments.

Differences between the two settings

In Vancouver, over one third (37%) and in Sacramento nearly half (46%) of requested drugs had been advertised to the public. Sacramento patients were approximately twice as likely as Vancouver patients to request either an advertised drug or a non-advertised drug from their doctor. This difference in request rate is partially but not totally attributable to differences in request rates for advertised drugs, as the request rates for non-advertised drugs also differed significantly between the two settings.

Some of the non-advertised drugs requested by patients came from heavily advertised drug classes and were therefore likely to be influenced by advertising; others did not. Such an effect is consistent with both a specific effect from advertising and a more general aggregate advertising message promoting a positive view of drug treatment and suggesting patients 'ask your doctor' about treatment options. Such messages may increase the rate of drug requests, but there is no question that they also build on an existing phenomenon. Patient demand for medicines is well documented in settings without DTCA.[38] Additionally, a relationship was seen between poorer health status and requests for non-advertised medicines, and in Sacramento significantly more women than men requested non-advertised medicines. Thus the pattern of requests for non-advertised medicines appeared to be more closely tied to predisposing factors already identified within the literature as being associated with patients' health needs and use of health care services than the pattern of requests for advertised medicines.

Were the American patients simply more assertive than their Canadian counterparts for reasons unrelated to DTCA? In a comparison of patients from two countries, there is a risk of 'confounding by culture', mistakenly attributing cultural differences in behaviour to differences in the advertising environment. Similarly, the results could reflect differences between the U.S. and Canadian health care systems. However, these arguments cannot explain the relationship found in both settings between individuals with greater reliance on advertising, and greater self-reported advertising exposure, and higher request rates for advertised drugs. The most plausible explanation for this consistent

'dose-response' relationship in the two settings is an effect from advertising. The effect of location of residence on the rate of requests for advertised drugs also became smaller in magnitude and non-significant after adjusting for individual advertising exposure and susceptibility.

If the causes were mainly a difference in medical culture and patient/doctor relationships between the U.S. and Canada, opinions about patient/doctor roles would have been expected to differ in the two cities. In fact, responses were remarkably similar, suggesting a similarity in beliefs about the roles of doctors, patients and sources of health care information, among patients in the two samples (see Appendix 5.1 for details).

About one fourth of patients in each city also reported that they had requested drugs from their doctors in the past. This question did not measure how often or how recently patients had requested drugs in the past, and therefore was not a sensitive measure of frequency. It did, however, provide some insight into patients' attitudes towards the act of requesting a drug from their doctor: a similar proportion of patients in Vancouver and Sacramento had evidently been willing to do so. This again suggests cultural similarities in relations between doctors and patients. Although more Sacramento than Vancouver patients reported having seen ads for a drug before requesting it in the past, the drugs they reported having requested in the past in both settings were most commonly those with large advertising budgets. As the question was not time-limited, it did not include a measure of frequency over time of past requests or allow for measurement of comparative frequency.

Health conditions treatable by advertised drugs

One of the key preconditions for successful DTCA is patient identification with the condition a product is intended to treat. Otherwise, patients are unlikely to be motivated to discuss a product with their doctor. Many patients in both cities identified themselves as having a condition that could be treated by an advertised drug. The rate was higher in Sacramento than Vancouver: 29% in Sacramento and 20% in Vancouver, but 7% of this difference was due to a higher proportion of patients identifying themselves as having

allergies in Sacramento. This may reflect differences in timing of administration of the surveys, as the Sacramento survey began in March, and thus spanned the spring pollen season, whereas in Vancouver the survey was administered between June and August.

However, advertising for allergy drugs is also intensive during the spring allergy season. Schering-Plough spent far more advertising loratadine (Claritin), a low-sedating antihistamine, to the U.S. public in 1998 and 1999 than has been spent on any other drug: U.S. $322 million.[39] It is only one of a number of allergy treatments heavily advertised to the public. Oral antihistamines are available over-the-counter in Canada, and they are advertised to the public. However, advertising for specific products such as loratadine (Claritin) is much less intensive in Canada than in the U.S.

There are two main ways that exposure to intensive advertising for allergy drugs could affect the number of people defining themselves as having a condition treatable by an advertised medicine. The first assumes that a fixed number of people have allergies within each setting and that the proportion of people with allergy who have seen the ads, and therefore define allergy as a condition treatable by an advertised product, differs. The second would be through a difference in the threshold symptom level at which people define themselves as having allergies. At what point do the occasional runny nose or itchy eyes become a symptom of a condition suitable for drug treatment? It was not possible to examine the extent to which one or both of these reasons could account for the differences in reported rates of allergy, or whether these different recorded rates reflected differences in underlying disease status or exposure to environmental allergens. The latter is likely to have differed, due to differences in the timing of the survey, and no doubt accounts for some of the difference in frequency in report of allergy. Whether it accounts for the entire difference, or whether advertising exposure is also partially responsible, is unknown.

Patient requests for advertised medicines could lead to considerable health benefits if patients seek and obtain appropriate care at an earlier stage and thus avoid disease

complications and hospitalizations, and these are claimed benefits of DTCA. [40] However, many requests for advertised products were for treatments for symptoms of allergy or for 'lifestyle drugs' for impotence, facial hair, insomnia, menopausal symptoms, and toenail fungus. Drug treatment of such conditions may have positive effects, in that it may relieve distress or discomfort, but it is unlikely to prevent hospitalization or serious morbidity.

More Vancouver than Sacramento patients mentioned smoking as a personal health condition that could be treated by an advertised drug. During the first half of 2000, in the months before the survey, both a television and a billboard ad campaign for bupropion (Zyban) promoted this product for smoking cessation in Canada. Although Health Canada judged the TV ad to be illegal, it ran for several months.[7] Nearly half of Vancouver patients reported that they had seen ads for bupropion (Zyban).

This response is also revealing in that patients were asked whether they had a *health condition* that might be treated by an advertised drug. Smoking, like several of the conditions mentioned above – baldness, facial hair, pre-menstrual syndrome, and menopause— is not, strictly speaking, a health condition (although it has certainly been established as a precursor to many). Smoking has been variously described as an addiction or a lifestyle choice.[§§] It is associated with an increased risk of serious health problems such as heart and lung disease, but the recasting of smoking, rather than the problems it causes, as a health condition treatable by pharmaceuticals is new. A similar situation characterizes obesity, which has become more prevalent with modern sedentary lifestyles. Although all forms of obesity treatment can be problematic, there is no evidence that obesity drugs lead to long-term weight loss or prevent complications of obesity to a greater extent than diet and exercise.[41] The recasting of obesity as a health problem to be treated with prescription drugs is not backed by convincing evidence. Pre-menstrual syndrome and menopause are normal parts of women's reproductive cycles; facial hair and baldness are accidents of genetics that may or may not be seen as attractive in a particular society.

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§§ It may be the latter for a very short period; thereafter it is the former, as anyone with a serious wish to

David Gilbert offers two definitions for the term 'lifestyle drug': first, pharmaceutical treatments for problems considered to be social or aesthetic rather than medical, such as facial hair or male pattern baldness; second, pharmaceutical treatments for problems resulting from so-called lifestyle choices, such as drugs for smoking cessation. [42] The distinction between these products and other medical treatments is often made within the context of discussions about what public or private health insurers should and should not cover.[32] Many DTCA drugs with top advertising budgets fit into these two categories, particularly the products for which spending on advertising aimed at the public has exceeded spending on promotion aimed at physicians.[43]

Another related trend is advertising for conditions such as social phobia or premenstrual dysphoric dysfunction. These ad campaigns have been criticized as blurring the distinction between normal differences in human personality, such as shyness, as well as normal events such as pre-menstrual hormonal changes, and psychiatric disorders that require drug treatment.[44]

With a trend towards treatment of milder conditions, or conditions for which drug treatment is only one of a number of available treatment options, a shift might also be expected in the balance between likely benefit and harm from prescription medicine use. This type of shift was highlighted recently in the results of the Women's Health Initiative, a trial of long-term post-menopausal hormone therapy for disease prevention in healthy women.[45] The trial was stopped prematurely because the overall serious health risks of treatment, as measured by a global index including heart disease, stroke, cancer, pulmonary embolism, fractures and deaths from all causes, exceeded benefits by approximately 1% over a 5-year period. This was a large publicly funded trial, carried out after combined estrogen/progestin treatments had been a commonly prescribed preventive treatment for over 20 years. It highlights the need for caution in assuming that effects on physiological measures such as lipid levels or bone density necessarily translate to health

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quit will attest.

benefits, in other words to lower rates of morbidity, disability, hospitalizations and mortality over specified time periods. In this case effects on bone density did translate into a clinical benefit: there were 5 fewer hip fractures per 10,000 women/years of hormone use. However, this benefit (as well as a reduction in colorectal cancer) was more than offset by the excess in strokes, heart attacks, pulmonary embolisms and breast cancer.

Fewer or more hospitalizations?

The design of this survey does not allow predictions of effects on hospitalization or serious morbidity as a result of medicine use stimulated by DTCA, as it included no examination of medical records or longer-term follow-up. However, as the experience with use of hormones for disease prevention suggests, increased population use of pharmaceuticals has two different potential effects: the potential to prevent hospitalization and serious morbidity; and the potential to increase serious morbidity. A general concern is that DTCA may stimulate widespread use of medicines before their potential benefits or risks are fully known, since the bulk of DTCA investment is on new products for which populations do not yet have the benefit of any long-term follow-up, either through longer-running trials, or through adverse event reporting or systematic post-marketing surveillance. For example, information on the efficacy of bupropion (Zyban) as an aid to sustained smoking cessation is limited [46] and the product was associated with over 680 reported serious adverse events and 19 deaths in the first two and a half years since its introduction in Canada.[47] This is likely to be an underestimate of adverse events experienced by Canadian bupropion users, as Canada devotes limited resources to post-market surveillance, and the reported death rate per thousand prescriptions in the first two years of marketing in the U.K. was 11 times that of Canada.[48]

Some medicines advertised to the public may prevent serious morbidity, hospitalizations and premature deaths. Whether they provide the most cost-effective alternative available to treat a condition is another question. And whether advertising provides the best means

to ensure that a patient receives the most appropriate available treatment for a health problem is also highly questionable. One Sacramento patient commented that: "On my first appointment with Dr.... I tried to get a prescription for pain medicine and he said no because he wanted to solve the problem, not mask the pain. I am still having pain but am trusting that his long-term plan may work." One of the advantages of consulting a physician is the possibility that he or she will try to 'solve the problem, not mask the pain' where this type of strategy is appropriate. With an increasing volume of prescription drug requests, will physicians find it an increasingly difficult choice to make?

More medicine use among the healthier in Sacramento

One of the most striking findings of this survey was the greater volume of current prescription drug use among people with good to excellent self-reported health in Sacramento as compared to Vancouver. Forty-four percent of patients in Sacramento who judged themselves to have excellent health were, nevertheless, taking two or more prescription medicines, as compared to 19% of similar patients in Vancouver. Patients in good to excellent health in Sacramento were also more likely than their Vancouver counterparts to believe that they needed a medicine they were not already taking. This is consistent with the expected direction of effect from DTCA, as most heavily advertised drugs are for milder conditions experienced by large target audiences, i.e. generally healthier people. The number of prescription drugs currently used was similar among patients with poorer health in the two settings, which is consistent as well with less variability in the frequency of use of medicines that are tied more closely to health needs. Additionally, patients in good to excellent health in both settings were equally likely to believe that they needed a diagnostic test or referral to a specialist, suggesting that the difference was indeed related to the belief that a medicine was needed rather than broader beliefs about needs for health care services.

Overall differences in prescribing rate

Patients in Sacramento were much more likely than Vancouver patients to receive one or more new prescriptions during observed consultations. The rate of multiple newly

initiated prescriptions was also higher than in Vancouver. One concern this raises at a population level is the increased risk of adverse effects and especially of drug interactions from polypharmacy with increased per capita pharmaceutical use.

The 1999 U.S. National Ambulatory Care Survey, administered to a large national random sample of the U.S. public and physicians, found that the proportion of visits in which medicines were prescribed and the average number of drugs provided per visit had increased by over one-third since 1985.[25] The year 1985 represents a useful baseline for DTCA in the U.S., as there was very limited mass media prescription drug advertising in the early 1980's, and the FDA two-year moratorium on DTCA ended in 1985. The increase in prescription drug use since then has been consistent across all age groups. On average, patients received 1.5 prescriptions per visit in 1999, up from 1.1 in 1985. At least one medication was provided, either a new prescription or a refill, at 66% of visits in 1999. In the present survey, Sacramento residents received either a new prescription or a refill in 61% of visits, which suggests that the experience in this survey is likely to be reflective of broader U.S. trends.

The trend of increasing numbers of prescriptions per consultation is unlikely to be wholly or even largely attributable to DTCA. It also reflects broader international trends pre-dating the rapid growth of DTCA, including increased prescribing rates in Canada.[49]

DTCA is likely to play a part in this trend, however. The National Ambulatory Care Survey found that 11 drugs accounted for over 80% of prescriptions for newer medicines. They defined 'newer medicines' as all medicines approved since 1997. These 11 products were all drugs that were heavily advertised to the U.S. public.[25]

In both Sacramento and Vancouver many of the drugs requested, both during surveyed consultations and in the past, were heavily advertised drugs. On average, patients who requested medicines had higher advertising exposure and were more likely to judge

commercial information sources to be accurate than patients who did not request prescription drugs.

These findings are consistent with the strong likelihood of a connection between advertising and patients' decisions to request a medicine from their physician. Relatively few patients directly reported that their decision to come to the doctor or to request a drug or diagnostic test was influenced by advertising, although the rate was higher in Sacramento than Vancouver: 7.5% vs. 5.3%. This was more likely to be under- than over-reported, given the limited social desirability of admitting to being influenced by advertising. The finding that patients in both cities tended to rate advertising as an inaccurate information source also supports this view.

In U.S. market research surveys, DTCA has been associated with an increase in physician visits for advertised conditions.[50] Whether a similar effect has occurred in Canada is not known, but U.S. patients face more barriers to accessing physician services than Canadians, both because health insurance is not universal and because many insurance plans involve a co-payment for physician visits, whereas Canadian patients do not pay to see a physician.

Similar prescribing rates in the two settings for requested advertised drugs

I had hypothesized that prescribing rates in response to requests for advertised drugs would be higher in a U.S. environment with full DTCA than in Canada. This did not turn out to be the case. The key difference between the two settings was in the rate of patient requests, not in the proportion of requested advertised drugs that were prescribed. In both settings, patients who asked for a prescription for an advertised drug were highly likely to receive one.

This suggests that the degree of population exposure to DTCA is a key factor in its ability to shift population drug use patterns. In other words, external factors, including the market and the regulatory environment, mediated by patient characteristics such as health

beliefs, susceptibility to advertising messages, and advertising exposure, are key determinants of a subset of prescribing decisions, with individual physician characteristics playing a more limited role. The stable rate of prescribing in response to patient requests for advertised drugs in the two settings also suggest that population exposure to DTCA plays a stronger role in determining the extent to which DTCA can shift prescribing than for example the organization of physician services or other features of the patient-doctor interaction and health care system that differ between primary care settings in Vancouver and Sacramento.

Sacramento physicians did prescribe a higher proportion of *non-advertised* requested drugs than Vancouver physicians. Why was the difference in prescribing rates limited to non-advertised drugs? Any discussion of causes will necessarily be speculative, and this finding remains to be confirmed in additional studies. Vancouver physicians did not prescribe most antibiotics that patients requested; Sacramento physicians did. There may have been more recent exposure in Vancouver to educational messages highlighting the need to limit unnecessary antibiotic prescribing. When a company advertises a product to the public, it is part of a general marketing campaign that also includes promotion aimed at physicians. Prescribing rates following DTCA drug requests may have been affected by a similar pattern of promotional activities aimed at physicians in the two settings, for example sales visits and the availability of free samples, leading to greater uniformity in prescribing rates. Additionally, physicians are exposed to the same mass media advertising campaigns as their patients. These potential reasons must be considered speculative, however, as the present survey was designed to focus solely on patient responses to advertising, not physician exposure or reliance on commercial information sources.

A key argument made in favour of DTCA is that ultimately the physician decides whether to prescribe, and therefore patients are protected against inappropriate self-diagnosis and treatment choice.[51] It was not possible to judge treatment appropriateness directly without access to patients' medical records. However, if physicians prescribe products that they

would not have chosen otherwise, the protection offered by prescription-only status is questionable. Physicians expressed ambivalence about treatment choice for 50% of prescriptions for requested DTC advertised drugs. In some cases patients may have been right and physicians wrong, but this is unlikely to be the case for half of all prescriptions. A 10-year review of U.S. print advertisements for drugs found that most contained no information on the likelihood of treatment success, mechanism of action, or other treatments that are available.[52] Another recent review found that most ads contained only vague emotive claims, or relied on personal endorsements or information on how frequently a product was used to claim a benefit.[53] Regulatory reviews indicate that inaccurate information is common and that patients seldom receive corrections.[54] Patients are unlikely to have sufficient information from advertising to accurately self-diagnose and to make treatment decisions, yet physicians appear to be highly likely to prescribe a drug if a patient asks for it.

Physician ambivalence was nearly as high for non-advertised as for advertised drugs. This is consistent with studies of prescribing that examine the influence of physicians' perceptions of patient expectations of a prescription, [16] [55] which have found that physicians often prescribe medicines they believe their patients want, even when they are uncertain about the medical need for these prescriptions. These studies highlight the social dimensions of patient-doctor interactions and the prescribing decision. The results are also consistent with studies of antibiotic prescribing, in which patient demand is cited as a non-clinical factor contributing to physicians' decisions to prescribe antibiotics even when they believe that the prescription is not indicated. [56]

The pattern prescribing in response to requests recorded in this survey, as well as physician responses such as ambivalence and reports of pressure to prescribe, suggest that some of the effects of DTCA on prescribing and patient-doctor interactions, are *moderating* rather than *mediating* effects. As described in Chapter 3, Schommer and Hansen define a mediating effect as a *necessary* intervening variable: x cannot lead to z unless y is present as a mediator. A moderating variable, on the other hand, causes a shift

in effect, but is not a necessary intervening factor; the effect can also occur without it. [57] Patients clearly do request medicines from their family physicians in the absence of DTCA. In this survey although there were differences in the characteristics of patients who requested non-advertised and advertised medicines, there appeared to be similarities in physicians' experience of these requests, in that similar levels of ambivalence and pressure to prescribe were reported. Thus it is probably incorrect to see DTCA as the cause of a dramatic shift in patient-doctor relationships in terms of introducing pressure on physicians to prescribe advertised drugs; it is more likely to lead to a shift in the frequency of consultations in which physicians experience pressure to provide prescriptions.

In most cases that physicians prescribed requested medicines, they did not also report pressure to prescribe. However, they reported pressure more often in consultations involving a patient request than in other consultations. In general, physicians rarely reported pressure from their patients to prescribe. In Sacramento, 12 of 27 (44%) of the consultations in which physicians reported pressure to prescribe involved advertised drugs, including two of the four consultations in which physicians reported moderately strong pressure. Lipsky and Taylor found that 71% of a random sample of U.S. family practitioners believed that DTCA would lead to pressure to prescribe,[58] and this has been raised as a concern in editorial commentary on the influence of DTCA on the practice of medicine.[59] One Sacramento patient commented on her questionnaire: "Advertising has limited function to educate about medicines...It encourages people to run too quickly for a prescription without regard to the long term and unknown effects. Even doctors are trapped by pressure from patients to prescribe."

The U.S. FDA has also published preliminary results of a survey of a nationally representative sample of U.S. physicians, asking about experiences with their most recent consultation with a patient who initiated a discussion about a drug they had seen advertised. The FDA found much higher rates of pressure to prescribe than in this survey: in total, 47% of the physicians reported some degree of pressure to prescribe. If a patient

had asked for a specific brand, 61% felt some degree of pressure, and 28% felt 'somewhat' or 'very' pressured. In contrast, in this survey, among consultations in which patients had requested a specific advertised brand, physicians expressed some degree of pressure to prescribe 20.3%, and 4.1% said they felt moderate to severe pressure. Rates for U.S. physicians were similar to the sample as a whole: they expressed some degree of pressure 24.5% of the time and moderate to severe pressure 4.4% of the time.

There may be several reasons for this disparity. The first is that when FDA interviewers asked physicians to remember their most recent consultation affected by DTCA, physicians may have been more likely to remember a striking recent consultation than a run-of-the-mill consultation in which a patient mentioned an advertised drug in an offhand way. Thus the reported experience of pressure might be exaggerated. Alternately, during this survey physicians were answering a general question about the experience of pressure during each consultation, rather than a question focused on the patient's request for an advertised medicine. Additionally, this is a survey of a non-random sample of family physicians willing to participate in a study for two days, in two western North American cities; the FDA survey is of a random sample of U.S. physicians, half of whom were family physicians and half specialists. Thus, for several reasons the results of this survey and the FDA survey may not be directly comparable. The FDA's sample is more likely to be broadly representative of U.S. physicians. However, one criticism leveled at the FDA survey is the lack of comparison group, making it impossible to know whether the experience of physicians in DTCA consultations is similar or different from other consultations.[60]

Although the generalizability of this survey is limited because it is based on samples of patients attending primary care physicians' offices rather than random population samples, this design also provides two key strengths. First, it allows for direct identification of individual patient-doctor consultations and prescribing decisions affected by DTCA. Secondly, these consultations and prescribing decisions could be compared to otherwise similar consultations not directly affected by DTCA. The inclusion of a

comparison group allows for assessment of the direction of effect of DTCA. Additionally because the survey was carried out within primary care settings, it allows for estimation of the proportion of patient-doctor interactions affected by DTCA, in other words of the magnitude of the effect of DTCA on prescribing within these primary care settings.

The results of this survey are consistent both with the literature on physician's prescribing decisions in response to patient expectations of a prescription,[22] as discussed in Chapter 3, and with consumer surveys of random samples of the U.S. public on the effects of DTCA, as discussed in Chapter 2. The results are also consistent with research on physician responses to drug promotion, both in terms of the likely direction of effect on treatment appropriateness, and the divergence between behaviours stimulated by advertising and self-reported reliance on advertising as an information source. In this survey, similarly to physician surveys, patients were more likely to exhibit behaviour stimulated by advertising, i.e. requests for advertised drugs, than to report reliance on advertising as an information source (see Appendix A5.1 for details). The results are consistent both with increased pharmaceutical industry spending on patient-directed advertising and with industry-wide support for legalization of DTCA in Canada and other jurisdictions in which it is not currently allowed. In other words, they are consistent with a positive effect on product sales, over and above sales stimulated through promotion aimed solely at physicians.

Implications for Canadian regulatory policies

As mentioned above, this study is best characterized as a comparison of two levels of exposure to advertising, rather than a comparison of environments with and without advertising. One key finding is that DTCA appears to be having a considerable effect on prescribing in primary care in a Canadian setting, despite the illegality of the practice. Nine percent of patients in total asked their doctor for one or more prescriptions in Vancouver, and at least 3.3% asked for DTC advertised drugs. This is likely to be an underestimate, as it omits unbranded requests for drugs from heavily advertised drug classes, such as weight loss drugs or menopausal hormone therapy.

Canada's *Food & Drugs Act* prohibits DTCA as part of the protection offered by prescription-only status. The *Act* specifies that prescription drug advertising aimed at the public is illegal, prohibiting 'any representation other than' name, price and quantity in messages targeting the public. Nevertheless, exposure to DTCA appears to be widespread. Only 10% of patients in Vancouver reported not having seen any prescription drug ads during the last year, and nearly one-third had seen more than 10 products advertised. This is likely to reflect both unimpeded cross-border DTCA from the U.S. and advertising originating in Canada. Twenty-four of the Vancouver patients requested products known to have been the subjects of advertising aimed at the public; in seven cases (29%) they requested products that have been advertised in Canada. One of these brands has only been advertised to the public in Canada, not the U.S.: an estradiol and levonorgestrel birth control pill (Alesse). Only Vancouver patients requested this drug.

One of the claims frequently made for legalization of DTCA is that it leads to educated, informed consumers, empowered to participate in discussions with their doctors about treatment choices.[61] If patients are to take part in shared informed decision-making in health care, they need access to accurate, balanced, comprehensive and up-to-date information about health and medicines. Patients who participated in this study were asked to rate the accuracy of 10 information sources and to say which sources they found the most useful. Print and television advertising received by far the lowest marks, with over 40% of patients in both settings judging them to be inaccurate or fairly inaccurate, and less than 1% in either the U.S. or Canada listing them as their most useful information source on health and medicines.

This suggests that, while there may be pressure in Canada for legislative change, it is not originating from a strong desire on the part of patients and the public for greater access to prescription drug advertising as a preferred information source.

The survey also suggests that DTCA currently has cost impacts in Canada, and that these would be likely to increase if full DTCA is allowed. Vancouver physicians in this survey saw on average 120 patients per week. Under current conditions, Vancouver family physicians might expect on average around 4 patients to request advertised drugs per week. If three quarters of requests end in prescriptions, about 144 prescriptions per G.P. per year (assuming 48 working weeks) could theoretically be attributed to DTCA, half of which would be for products that the physicians might not have chosen otherwise.

There were approximately 29,000 family physicians practicing nationally in 2000.[62] If the results of this survey are representative of broader trends (a speculation, as participating physicians were not a random sample of Canadian primary care physicians) over 4 million prescriptions would be stimulated by DTCA nationally, 2 million for products the physician might not have prescribed otherwise. If advertising exposure increased in Vancouver to a level similar to that experienced in Sacramento, and patient requests similarly increased, each family doctor would have around 8.6 patients per week requesting advertised drugs, of which three fourths would be prescribed. At this rate, 311 prescriptions per G.P. per year would be initiated by DTCA, or on average 167 more prescriptions per G.P. than under current conditions. Among Canada's family physicians, 9 million prescriptions per year would be stimulated by DTCA, 4.5 million of which would be for products the physician would not necessarily have chosen otherwise.

It is important to emphasize again that these calculations are highly speculative, given that physicians agreeing to participate were not a random sample of all G.P.'s in Vancouver or Sacramento, let alone in Canada or the U.S. DTCA is also not a static phenomenon: spending on this form of advertising has increased exponentially since the mid 1990's and shows no sign of decline. Thus any estimated future effect, based on year 2000 advertising levels, is likely to be conservative. These estimates also do not take into account other effects of advertising that could not be measured in this survey, such as the influence on patients' decision to seek care or changes in hospitalization rates as a result

of prescription drug use stimulated by DTCA. They also do not include influences on specialists' prescribing.

Conclusion

The results of this survey suggest that DTCA is affecting prescribing in primary care both in a U.S. setting, where such advertising is legal, and in a Canadian setting, where it is illegal. The main difference between the two settings was in the **magnitude** of the effect on prescribing decisions, which was much larger in Sacramento than Vancouver. Mirroring these differences between the two settings, in both cities individuals with higher advertising exposure, who used advertising as an information source, and who identified themselves as having a condition treated by an advertised drug requested more advertised drugs. Thus this study confirms a hypothesized dose-response between patient exposure to advertising and requests for prescriptions for advertised drugs, mediated by individual differences in susceptibility to advertising messages.

If patients raised the possibility of taking an advertised medicine or directly requested it, they usually received it, whether or not the physician would have chosen the same drug for other similar patients. This did not differ by setting, suggesting that if exposure to DTCA increases in Canada, the proportion of prescriptions affected by advertising will also increase. Thus pharmaceutical industry support for liberalized advertising laws – in Canada, Europe, Australia and elsewhere – appears rational in terms of profitability. The survey results do raise questions, however, about the influence of DTCA on prescribing appropriateness: if DTCA opens a conversation between patients and physicians, that conversation is highly likely to end with a prescription, despite frequent physician ambivalence about treatment choice.

Appendix 5.1

Patient attitudes and beliefs

Although the primary aim of this survey was to examine the relationship between advertising exposure, patient requests for medicines and prescribing decisions in the two sites, the survey also included questions about patients' attitudes to different sources of health information and beliefs about the doctor-patient relationship, health and medicine use. These questions are to a large extent exploratory and descriptive, but they allow comparison of beliefs and attitudes between the two sites. An additional reason for including them in the questionnaire was for face validity, as the survey was presented to patients as being neutrally on 'patient information on medicines' rather than pharmaceutical advertising. As sampling was non-random, these cannot be assumed to represent broader public opinions in either site. Patients attending family physicians differ from the public at large, in that for the most part they are seeking care for a current health problem. For instance, women are over-represented, in comparison to the general population. Additionally, at both sites the income and education of patients participating in the survey was higher than average.

Patient information sources on health and medicines

The questionnaire included a list of common sources of information on health and medicines, including the general media, commercial sources, and health professionals. Patients were asked to judge the accuracy of each information source. These questions were intended:

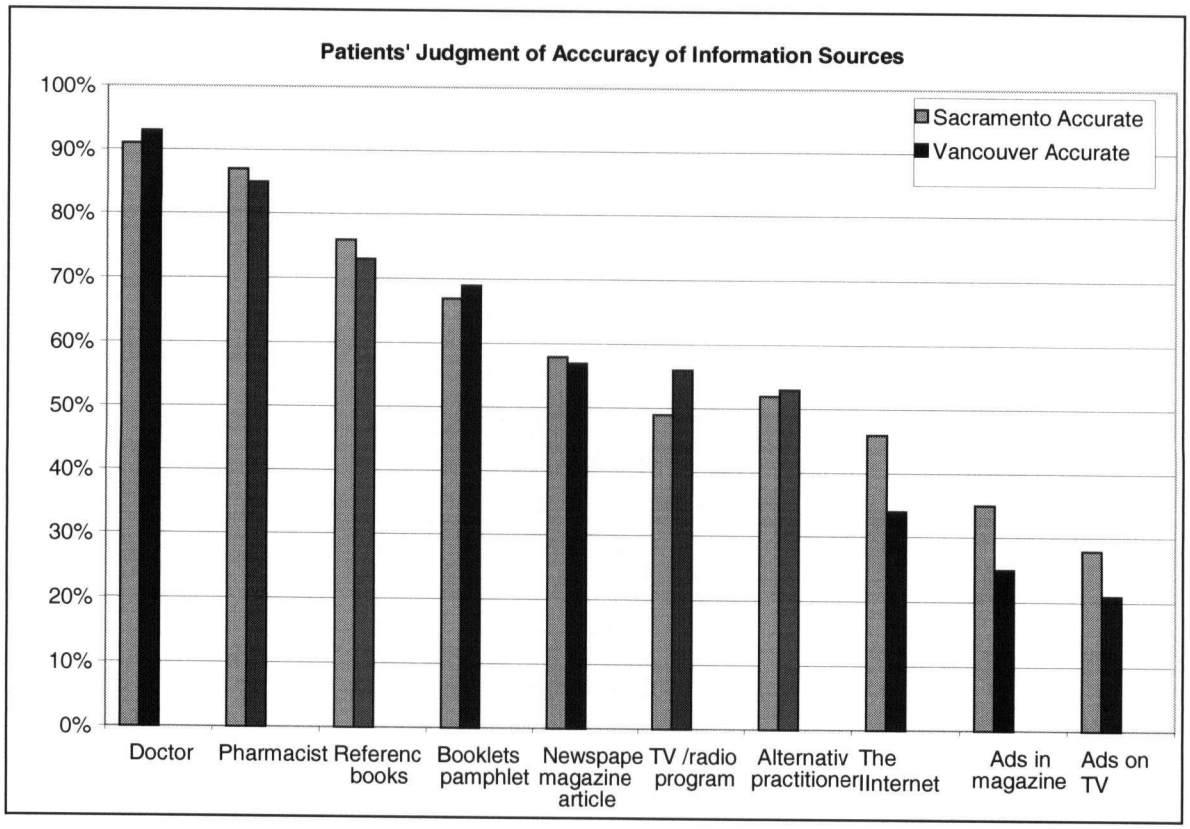
- to determine patients' opinion of the reliability of pharmaceutical advertising as an information source, in comparison to other information sources;
- to explore whether an association exists between trust in commercial information and prescription drug requests; and
- to learn which information sources on health and medicines patients are using.

Patients' opinions of the reliability of information sources

Figure A5.1 summarizes patients' opinions of information accuracy, combining replies on the one hand that an information source was 'accurate' or 'fairly accurate', and on the other hand that it was 'inaccurate' or 'fairly inaccurate'. Patients tended to view doctors, pharmacists and reference books as more accurate than other information sources, and judged TV and print advertising to be inaccurate compared to other sources. Patients' opinions were generally similar in Vancouver and Sacramento. Only 2.2% unreservedly judged TV ads to be an accurate source of information on health and medicines in either city (as opposed to 'fairly accurate' or inaccurate), whereas 64.4% in Vancouver and 62.5% in Sacramento unreservedly judged doctors to provide accurate information. Pharmacists similarly had high ratings for information accuracy: 58% in Vancouver and 57.1% in Sacramento.

The degree of similarity in opinions amongst the two patient populations, regarding information accuracy, is striking. As well, the high proportion who judged television or print ads to be an inaccurate source of information as compared to other information sources is noteworthy. A fair bit of skepticism was also expressed about the accuracy of general media reporting, with only 4.5% in Vancouver and 4% in Sacramento believing that newspaper and magazine reporting is accurate (versus 'fairly accurate', 'fairly inaccurate' or 'inaccurate') and 5.1% in Vancouver and 3.7% in Sacramento unreservedly believing that TV or radio programming is accurate.

Figure A5.1: Percent of patients who judged an information source to be 'accurate' or 'fairly accurate'



Patients who judged DTCA (television and/or magazine ads) to be accurate were more likely to request advertised medicines from their doctors during observed consultations (odds ratio = 1.5; 95% CI 1.0-2.3, p=.01, adjusted for city of residence, health status, sex, age, income, education, drug payment and cluster sampling).

Table A5.1 presents the proportion of patients who answered 'don't know' or 'no response' when asked to judge the accuracy of an information source. There is a remarkable range in these data, with over half of patients in Vancouver and nearly 40% in Sacramento offering no opinion on the accuracy of information from the Internet. On the other hand, more than 90% of patients expressed opinions, mainly positive, about the accuracy of information from physicians. In some cases patients may have had little access to certain listed information sources, such as the Internet or alternative healthcare providers, and may have therefore found their accuracy difficult to judge.

Interestingly, around one third of patients in both jurisdictions did not express an opinion about the accuracy of television or print advertising. Most of these patients had stated elsewhere on their questionnaire that they had seen DTC ads.

Table A5.1: No opinion expressed on accuracy of an information source

Information sources on health and medicines	Vancouver No opinion	Sacramento No opinion
Internet	50.8%	39.1%
Print ads	34.2%	31.7%
Alternative health care providers	34.2%	36.2%
TV ads	33.6%	30.1%
Booklets or pamphlets	24.1%	25.5%
Reference books	23.5%	20.2%
TV or radio programs	23.1%	24.5%
Newspaper or magazine articles	23.0%	24.5%
Pharmacists	12.8%	11.5%
Doctors	5.6%	7.6%

Table A5.2 lists the information sources on health and medicines patients said they had found to be most useful among the ten listed sources. Most patients in both cities listed doctors as the information source they found most useful. Very few considered print or television ads to be a first choice information source on health and medicines. Patients were also asked which of the listed information choices they had found to be the second most useful. Again, few people listed advertising: 1.6% in Sacramento and 1.3% in Vancouver listed television ads as a second choice information source, and 0.7% in Sacramento and 0.5% in Vancouver listed print ads.

Table A5.2. Preferred information sources: first choice.

Preferred information source	Sacramento (N=598)	Vancouver (N=675)
Doctors	68.1%	72.6%
Reference books	7.5%	7.1%
Pharmacists	7.4%	4.6%
Radio or TV programs	3.5%	3.7%
The Internet	6.2%	3.7%
Newspaper or magazines articles	3.5%	3.0%
Booklets or pamphlets	2.8%	2.8%
Alternative health care providers	1.2%	2.4%
Ads in magazines	0.3%	0.4%
Ads on TV	0.7%	0.3%

*85 (12.4%) of Sacramento patients and 73 (10%) of Vancouver patients left this question blank

The patients had the option of writing in other information sources they found more useful than those listed, and many added extra information sources, 11% in Sacramento and 14% in Vancouver. Around 5% in each setting listed informal information sources such as friends, family, colleagues or others with the same condition.

In summary, to a large extent in both jurisdictions, patients expressed greater trust in physicians than in other information sources, with pharmacists running a close second. This is consistent with the results of recent focus groups across Canada on patients' medication information needs, which also found a preference for information from physicians and pharmacists.[63]

Advertising was rarely listed as a preferred information source in either jurisdiction. These findings cannot be generalized to broader population groups, but they do suggest a strong focus on health professionals as trusted and preferred information sources within this group of primary care patients. The similarity of opinions between the two settings is also striking.

Patients' Opinions about Health and Medicines

The questionnaire included thirteen statements about medicines, health and health care policy. They were included for several reasons:

- to control for possible cultural differences in attitudes to the doctor/patient relationship between U.S. and Canadian patients;
- to solicit patients' opinions on relevant health care policies and their understanding of the regulatory context surrounding prescription drug advertising;
- to test for patients' knowledge of principles of rational drug therapy, such as for example lack of efficacy of antibiotics for viral infections, and
- to test for beliefs in commercial myths.

The latter follows the work of Avorn and colleagues[27] who found that self-reported reliance on promotion was a less reliable indicator of its influence than belief in 'commercial myths', ideas frequently found in promotional materials but not supported by the scientific literature.

Table A5.3 summarizes patients' opinions on 13 questions about patient-doctor relations, health and medicines. Most patients in both jurisdictions agreed with two statements: that they trusted their physician if he or she did not believe a medicine was needed, and that doctors and patients should have equal say in decision-making.

Fourteen percent of patients in both cities said they would go to another doctor if their doctor did not give them a prescription they wanted. Patients who had requested a drug in the past were nearly twice as likely as other patients to report that they would go to another doctor if a request was refused; OR = 1.8 (95% CI 1.4 – 2.4), $p<.0001$, unadjusted chi square analysis. Most of the patients who said that they would go to another physician if their doctor did not give them a medicine they wanted also said that they trusted their doctor's judgment if he or she thought a medicine was not needed, 162/264 or 79%. This apparent contradiction occurred mainly among those who 'agreed' rather than 'strongly agreed' with both statements. A possible explanation is a bias towards social desirability in answering a statement beginning, "I trust my doctor's judgment if...", particularly among patients in a physician's waiting room.

In comparison to respondents to U.S. consumer surveys, in which 28% [19] to 43%[64] believed that only the safest drugs are advertised to the public, only 7.6% of the Sacramento sample and 5.0% of the Vancouver sample mistakenly believed this. Unsurprisingly, many Canadians (31.6%) either answered 'no opinion' or left this question blank, most likely because of lack of knowledge about the basis for regulation of U.S. advertising. In Sacramento, the proportion believing that only the safest medicines are advertised on TV, 7.6%, remained much lower than has been previously reported in U.S. surveys. Even if the results are expressed as a proportion of those expressing an opinion, only 9.8% in Sacramento and 7.4% in Vancouver believed this. The difference, in comparison to other U.S. surveys, may reflect the specific characteristics of this sample: a generally affluent, well-educated and insured patient population.

Table A5.3:
Opinion statements, ranked in order of the proportion agreeing in Vancouver*

		Agree*	Disagree	No opinion
I trust my doctor's judgment if he or she thinks I don't need a medicine	Vancouver	92.2%	5.0%	2.0%
	Sacramento	86.3%	6.6%	2.9%
Doctors and patients should have equal say in treatment decisions	Vancouver	74.5%	19.7%	5.1%
	Sacramento	74.6%	16.1%	5.1%
All women over 50 should get their bone density tested	Vancouver	71.3%	9.1%	19.1%
	Sacramento	79.1%	2.6%	15.1%
New medicines are generally safer and more effective than medicines developed 10 or 20 years ago	Vancouver	49.2%	33.4%	16.7%
	Sacramento	50.2%	26.9%	19.6%
If I had a bad case of the flu, I would take antibiotics	Vancouver	36.6%	55.6%	7.0%
	Sacramento	37.2%	50.7%	7.9%
Canada's (or federal US) laws should forbid advertising of prescription drugs to the public	Vancouver	33.0%	49.6%	16.7%
	Sacramento	25.1%	53.6%	18.2%
If someone is depressed, they need to take a medicine to get back to their normal self	Vancouver	32.7%	51.7%	15.0%
	Sacramento	34.9%	46.1%	18.9%
I have a hard time getting the information I want about the side effects and risks of medicines	Vancouver	19.8%	71.0%	8.4%
	Sacramento	13.9%	72.7%	9.1%
I have a hard time getting the information I want about the benefits of medicines	Vancouver	18.5%	67.2%	13.5%
	Sacramento	14.9%	68.8%	12.0%
If my doctor would not give me a medicine I wanted, I would go to another doctor	Vancouver	14.2%	75.5%	9.5%
	Sacramento	14.3%	71.2%	10.2%
If you pay more for a medicine, it's likely to be safer and more effective than a less expensive medicine	Vancouver	7.5%	85.3%	6.6%
	Sacramento	4.7%	85.6%	9.6%
Only the safest medicines are advertised on US TV	Vancouver	5.0%	62.8%	31.6%
	Sacramento	7.6%	69.9%	19.3%
People should be allowed to buy prescription medicines on the Internet without first seeing a doctor	Vancouver	3.5%	93.9%	2.0%
	Sacramento	5.0%	86.1%	6.4%

** Agreement was defined as a response of 'agree or strongly agree'; disagreement was defined similarly. The percentages per city do not equal 100% because some patients left the question blank.*

Patients in both jurisdictions were generally aware that price is a poor indicator of pharmaceutical quality, with only 7.5% in Vancouver and 4.7% in Sacramento believing that if you pay more for a medicine, it is likely to be safer and more effective. However, about half of the sample believed that newer drugs are better, i.e. safer and more effective, than drugs that were developed ten or twenty years ago, despite the fact that new drugs are not required to provide any therapeutic advantage over existing alternatives

in order to be allowed onto the market. As has been amply documented elsewhere, most new products are 'me-too' drugs that do not, in fact, offer any such advantage.[65]

Relatively few people felt that they had difficulties obtaining information they needed on the risks or benefits of medicines. This differs from other research findings indicating that most patients want full information on adverse effects, 'no matter how rare', and that physicians rarely provide such information.[66] One possibility for this difference is that some patients interpreted these questions as implying lack of trust in the information their physician might provide. This is suggested by the correlation found between the statements that patients had a hard time getting information they wanted on benefits and risks of medicines, and the statement that if a doctor did not provide a desired medicine, the patient would go to another doctor. In both cases the degree of correlation is modest. The correlation coefficient between 'prescription shopping' and 'difficulty getting desired information on drug benefits' is 0.274 and between 'prescription shopping' and difficulty obtaining information on risks, the correlation coefficient is 0.328 (Spearman's rho). Both are significant at p=.01, two-tailed.

One question was included to solicit patients' opinion about whether DTCA should be allowed. The wording differed slightly in the two settings, for clarity: in Canada, "Canada's laws should forbid advertising of prescription medicines to the public", and in the US "federal laws should forbid...". What did the patients who had requested advertised drugs think? As might be expected, more of these patients than those who did not request advertised drugs favoured legal DTCA. For example, in Sacramento, 73% of those who had requested advertised drugs believed that it should be legal, versus 52% of those who had not; conversely 14% of those who had requested advertised drugs thought DTCA should be illegal, versus 26% of those who had not. A similar pattern occurred in Canada, with 64% of those who requested advertised drugs believing DTCA should be legal, versus 49% of those who had not requested advertised drugs, and 24% thinking DTCA should be illegal versus 33% of those who did not request advertised drugs. These opinions between those who did and did not request advertised drugs differed

significantly in the U.S. (p=.03, unadjusted chi-square) and for the sample as a whole (p=.03) but not differ significantly in Canada, where fewer patients had requested advertised drugs.

Many Canadians are unaware that DTCA is illegal. A survey of a nationally representative sample conducted by Ipsos-Reid in 2002 on behalf of a coalition of advertising and media companies found that 53% of respondents believed that prescription drug advertising was allowed in Canada.[67] The current survey did not include a question about patients' awareness of Canadian law. Thus it is not possible to know the effect of knowledge of DTCA's legal status in Canada on patients' opinions or the likelihood that they requested advertised drugs.

If Likert scale responses were dichotomized to group those who did and did not agree with each statement, they were generally remarkably similar between the two settings. For example, the same proportion in each setting believe doctors and patients should have equal say in treatment decisions (75%), the same proportion would go to another doctor if they could not get a medicine they wanted (14%) and a similar proportion (92% in Vancouver and 86% in Sacramento) would trust their doctor's decision if he or she thought a medicine was not needed. These similarities may mask other cultural differences affecting the doctor/patient relationship; however, on the surface they reflect a remarkable similarity in attitudes towards the doctor-patient relationship. Interestingly, the same proportion was also unaware that antibiotics are ineffective against the flu, 37% in each city.

If full Likert scale responses are used instead, however, some differences emerge. As 13 statements were being compared, a Bonferroni adjustment was used (p=.0039 would be equivalent to p=.05 in a single comparison, i.e. a 1 in 20 chance of a type 1 error). Patients in Sacramento were significantly more likely to say that all women at age 50 should get their bone density tested, were less likely to oppose the idea that people should be allowed to buy prescription drugs directly over the Internet without first seeing a

doctor, and were less likely to trust their doctor's judgment if he or she believes that a medicine is not needed than patients in Vancouver. (Table A5.4)

Table A5.4: Opinions that differed significantly if full Likert Scale responses are used

Statement	Strongly agree	Agree	No opinion*	Disagree	Strongly disagree
I trust my doctor's judgment if he or she thinks I don't need a medicine	US 27% CA 36%	59% 57%	7% 3%	7% 4%	- 1%
All women over 50 should get their bone density tested	US 45% CA 33%	34% 39%	18% 20%	3% 8%	0.1% 1%
People should be allowed to buy prescription medicines on the Internet without first seeing a doctor	US 2% CA 2%	3% 2%	9% 3%	34% 25%	52% 69%

*missing values were coded as 'no opinion'

Belief in Commercial/Medical Myths

Two statements were included to test patients' beliefs in commercial/medical myths: the idea that all women need to get their bone density tested at age 50 and that if a person is depressed, he or she needs a medicine to get back to their normal self.

Bone density testing is a poor predictor of future fractures and women are at low risk for fragility fractures at age 50.[68] The idea that all post-menopausal women are at risk for fractures as a result of age and gender has been promoted both by manufacturers of osteoporosis drugs,[69] and by many physicians, in spite of the lack of evidence of benefit for population screening.[68] Most patients agreed with this statement in both settings, but the proportion was highest in Sacramento, where nearly 80% agreed. As noted above in Table A5.4, a larger proportion of patients in Sacramento than in Vancouver strongly agreed with this statement, and fewer expressed disagreement.

Patients in both settings were much more divided on the question of whether an antidepressant is needed to get back to one's normal self if depressed. One Vancouver patient commented that it depended on whether a person simply felt sad or had clinical depression. However, even when psychiatrists diagnose a patient with clinical depression, non-drug approaches such as psychotherapy have been found to be equally effective to antidepressants in mild to moderate clinical depression. [70] Additionally, in 6-8 week

randomized controlled trials of antidepressants, depression resolves in between 25 and 40% of placebo users.[71] These trials, which are usually carried out as part of an application for market approval, have strict inclusion criteria, and only patients with clinical depression are invited to participate.

A 2002 meta-analysis of trials of antidepressants and other interventions in mild to moderate depression found for example that the absolute risk reduction (percentage difference in treatment response rate between placebo and treatment) was 10% in mild depression and 18% in moderate depression, in other words a modest advantage.[70] In head-to-head comparisons between antidepressants and cognitive behaviour therapy, a slight advantage was seen for cognitive behaviour therapy, a 2.3% absolute risk reduction versus antidepressants. Thus for a variety of reasons the statement that a person who is depressed needs a medicine to get back to normal is misleading. However, it is a common theme in advertisements for antidepressants. For example, Eli Lilly used the slogan "Welcome Back" to promote fluoxetine (Prozac) and Wyeth-Ayerst promoted venlafaxine (Effexor) with promises such as "I got my mommy back" and "I got my marriage back".[72] These advertisements do not specify the severity of depression or the availability of non-drug treatment options for depression.

Sacramento and Vancouver patients' responses to this question did not differ significantly after adjusting for multiple comparisons (unadjusted $p=.009$; requirement for significance with Bonferroni adjustment, $p\leq.0039$). However, half as many Sacramento as Vancouver patients strongly disagreed that a medicine was needed to get back to normal if someone is depressed: 6% versus 12% in Vancouver.

Although these statements reflect situations in which commercial interests have contributed to an expanded definition of ill health or requirements for medicine use, both are statements that many physicians would endorse. Thus they more broadly measure adherence to health beliefs likely to have been influenced by commercial interests,

including indirect influences, than necessarily a direct influence from pharmaceutical advertising.

Conclusion

In conclusion, patients' opinions about the accuracy of various information sources, and their beliefs about medicines, health and the doctor-patient relationship were broadly similar in the two settings. In both settings, patients expressed skepticism about the accuracy of information in advertising, in comparison to their opinions on all other information sources. However, those who had requested advertised medicines during observed consultations were less skeptical than others. They were also more likely than other patients to believe that DTCA should be allowed, and U.S. patients were more likely than Canadians to agree with direct Internet sales of prescription medicines without a consultation with a physician, and somewhat less likely to agree that they trusted their physician's opinion if he or she believed a medicine was not needed.

Appendix 5.2: Research Teams

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Ms Wendy Armstrong, Consumers' Association of Canada (CAC)

Mr Alan Cassels, Coordinator, Canada Drug Guide Project

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**affiliations in 1999-2000*

Appendix 5.4: Lists of Advertised Drugs

1. 1999 - TOP 50 PRODUCTS BY DTCA SPENDING

spending rank	*brand*	*Indication*
1	Claritin	Antihistamine
2	Prilosec	Ulcer/reflux
3	Xenical	Obesity
4	Propecia	Baldness
5	Zyrtec	Antihistamine
6	Lipitor	Lipid lowering
7	Zyban	Smoking cessation
8	Flonase	Inhaled steroid
9	Viagra	Sexual dysfunction
10	Nasonex	Inhaled steroid
11	Ortho tri-cyclen	Contraceptive
12	Meridia	Obesity
13	Glucophage	Diabetes
14	Allegra	Antihistamine
15	Valtrex	Antiviral, herpes
16	Detrol	Bladder control
17	Zocor	Lipid lowering
18	Prempro	Menopause
19	Zomig	Migraine
20	Flovent	Inhaled steroid
21	Paxil	Depression
22	Celebrex	Arthritis
23	Singulair	Asthma
24	Aricept	Alzheimer's
25	Accolate	Asthma
26	Nolvadex	Breast cancer
27	Patanol	Allergic conjunctivitis
28	Nicotrol inhaler	Smoking cessation
29	Relenza	Flu
30	Lymerix	Lyme disease vaccine
31	Imitrex	Migraine
32	CombiPatch	Menopause
33	Vioxx	Arthritis
34	Ditropan	Bladder control
35	Denavir	Antiviral
36	Procrit	Anemia
37	Renova	Wrinkles
38	Diflucan	Antifungal
39	Enbrel	Arthritis
40	Flomax	Prostate disease
41	Nasacort	Inhaled steroid
42	Synvisc	Arthritis
43	Differin Gel	Acne
44	Lamisil	Antifungal
45	Rezulin	Diabetes
46	Premarin	Menopause
47	Cenestin	Menopause
48	Humulin	Diabetes
49	Depo-Provera	Contraceptive
50	Avandia	Diabetes

Source: Findlay S. Prescription Drugs and Mass Media Advertising. 2000 [www.nihcm.org]

1. **Prescription Drug Advertisements: Jan 1,2000- Aug 1, 2001**

Brand	***Indication***
Accutane	Acne
Actonel	Osteoporosis
Actos	Diabetes
Agenerase	HIV
Alesse	Birth control
Ambien	Hypnotic
Astelin	Allergy
Buspar	Anxiety
Cepalin	Botanical extract
Combivir	HIV
Crixivan	HIV
Evista	Osteoporosis
Glucovance	Diabetes
Lotronex	Irritable bowel
Lunelle	HRT
Nexium	Ulcer/reflux
Ocuflox	Antibiotic/eye infections
OrthoPrefest	HRT
Penlac	Allergy
Periostat	Gum disease
Plavix	Cardiac
Pravachol	Cholesterol lowering
Prevacid	Ulcer/reflux
Prevnar	Vaccine
Prozac	Depression
Regranex	Diabetic foot ulcer
Remicade	Rheumatoid arthritis
Renova	Wrinkles
Retin-A Micro	Acne
Rhinocort	Allergy
Rocephin	Antibiotic/ ear infections
Sarafem	Premenstrual syndrome
Serevent	chronic bronchitis
Sonata	Sleep
Sustiva	HIV
Tamiflu	Flu
Trinovin	HIV
Vaniqa	Facial hair
Visudyne	Macular degeneration
Wellbutrin	Depression
Ziagen	HIV
Zithromax	Antibiotic
Zoloft	Depression

Source: Video Monitoring Service. Commercial Reports Rx 2000, Rx2001.

Appendix 5.5: Survey Materials

1. Physician invitation letter
2. Physician questionnaire
3. Patient information brochure
4. Patient questionnaire

Physician invitation letter
[Faxed to physicians on UBC Department of Family Practice Letterhead]

Dear Dr ____,

An invitation to participate in a study

We are writing to invite you on behalf of the Department of Family Practice and the Centre for Health Services and Policy Research at the University of British Columbia to participate in a study on *Patient Information on Prescribed Medicines.* This is a comparative study in around 90 doctors' offices in Vancouver and Seattle, funded by Health Canada.

The aim of the study

The aim of this study is to contribute to a better understanding of the effects of direct-to-consumer prescription drug advertising on the patient/doctor relationship and the use of health services in primary care.

Although the patient/doctor interaction is increasingly seen as one of shared decision-making, little research has been carried out on where patients get information on health and medicines, and how this affects their decisions to seek care or their expectations of a consultation with their family doctor. In the U.S., prescription drug advertising has grown enormously over the last few years, with substantial spillover effects in Canada. There has been no direct empirical research to date on the effects of advertising on primary care.

Your participation

We are inviting you to participate in this study during two consecutive pre-set working days in June or July. Adult patients who come in for appointments on these two days will be invited to participate in the study by filling in a questionnaire in the waiting room. We will ask you to fill in a brief checklist following the consultation with each participating patient. This checklist will take less than one minute to fill in.

A research assistant will be present in the waiting room on both days to inform patients of the study, obtain informed consent, and distribute and collect questionnaires.

The names of all participating physicians and patients will be kept strictly confidential, with all identifiers removed from questionnaires as soon as patient and doctor questionnaires have been matched. Patients will be assured that their participation is purely voluntary and that their choice will in no way affect their medical care.

Your reward

While we recognize that your major reward will be an enhancement of understanding of clinical decision-making, we also understand that participation in a study involves a commitment from yourself and your office staff. As a token of our appreciation, we would like to offer a $100 honorarium. We will also send you a report of the study results. We hope that they prove useful to your practice and to the clinical training you provide to medical students.

Consent to participate

We require both your consent and your patients' consent for participation in the study. As mentioned above, a research assistant will invite patients to participate in the study and obtain consent in the waiting room, when they come in for their doctor's appointments on the two study days.

Please read through the enclosed informed consent form, which provides additional information about the study. If you are interested in participating, please fill in the cover sheet and fax it back to us at **822-5690** together with the signed consent form. A research assistant will get back to you to make practical arrangements for the study.

If you have any additional questions, please call the study coordinator, Barbara Mintzes at 822-0565 or send me an e-mail at <bmintzes@chspr.ubc.ca>.

We are looking forward very much to working with you on this study.

With best regards,

Robert F. Woollard, M.D., F.C.F.P
Royal Canadian Legion Professor and Head, Dept of Family Practice

Barbara Mintzes
Centre for Health Services and Policy Research
University of British Columbia
bmintzes@chspr.ubc.ca

PARTICIPANT CODE:_____

PHYSICIAN QUESTIONNAIRE

1. Did you prescribe any medication for this patient? (Please mark all that apply)

❑[1] Yes, new prescription(s)

❑[2] Yes, refill(s) →
❑[3] No, suggested an OTC drug →
❑[4] No drug therapy provided →

⟩ If you ONLY marked these, go directly to QUESTION 3

2. Please write the name of each NEWLY PRESCRIBED DRUG and answer the questions below.

	Drug 1: _____	***Drug 2:*** _____	***Drug 3:*** _____
2a. Name of prescribed drug:			
2b. Did the patient raise the possibility of taking this drug?	❑[1] Yes ❑[2] No	❑[1] Yes ❑[2] No	❑[1] Yes ❑[2] No
2c. Did the patient directly REQUEST this drug?	❑[1] Yes ❑[2] No	❑[1] Yes ❑[2] No	❑[1] Yes ❑[2] No
2d. Was the patient knowledgeable about this drug?	❑[1] Yes ❑[2] No ❑[3] *don't know*	❑[1] Yes ❑[2] No ❑[3] *don't know*	❑[1] Yes ❑[2] No ❑[3] *don't know*
2e. Would you have chosen this therapeutic option in the absence of expressed patient desire?	❑[1] Very likely ❑[2] Possibly ❑[3] Unlikely ❑[4] *No desire expressed*	❑[1] Very likely ❑[2] Possibly ❑[3] Unlikely ❑[4] *No desire expressed*	❑[1] Very likely ❑[2] Possibly ❑[3] Unlikely ❑[4] *No desire expressed*
2f. If you were treating another similar patient with the same condition, would you prescribe this drug?	❑[1] Very likely ❑[2] Possibly ❑[3] Unlikely	❑[1] Very likely ❑[2] Possibly ❑[3] Unlikely	❑[1] Very likely ❑[2] Possibly ❑[3] Unlikely

3. Did the patient REQUEST any prescription drug(s) you did not prescribe?

❑[1] No

❑[2] Yes → a) What drug or drugs?_____

→ b) What did you recommend instead?

- ❑[3] OTC drug
- ❑[4] Another prescription drug
- ❑[5] Non-drug approach

4. Did you feel pressured to prescribe during this consultation?

❑[1] No

❑[2] Yes, a little

❑[3] Yes, moderate to strong

Comments:_____

(please use back of page if necessary)

Thank-you!

PATIENT INFORMATION ON MEDICINES

A COMPARATIVE PATIENT/DOCTOR SURVEY IN SEATTLE AND VANCOUVER

If you have any questions at any time, please feel free to contact the Research Coordinator:

Barbara Mintzes, PhD Candidate
Centre for Health Services and Policy Research
#429 - 2194 Health Sciences Mall University of British Columbia
Vancouver, British Columbia
Canada, V6T 1Z3
Tel: (604) 822 0565; Fax: (604) 822 5690

WHAT IS THE PURPOSE OF THE STUDY?

This study is being carried out in 90 doctors' offices in Vancouver and Seattle. The aim is to learn more about where patients get information on health and medicines, and how this might affect a visit to their family doctor.

Canada and the U.S. have different laws regulating health information. We would like to see how these differences affect people's sources of health information, and what they expect from a visit to the doctor.

We hope that this research contributes to better communication between doctors and patients, and to the development of health information policies that reflect people's needs. This survey is funded by Health Canada.

This study has been approved by the University of British Columbia's Clinical Research Ethics Board.

IF I AGREE TO PARTICIPATE, WHAT IS INVOLVED?

- You will be asked to read and sign a consent form, and to fill in a questionnaire while you are in the waiting room. The questionnaire should take 10 to 15 minutes to complete.
- Your doctor will fill in a short questionnaire about the visit and any treatments he or she recommended.
- If you would like a report of the results of the study, you can leave us your name and address. We will also ask whether you agree to be contacted again if we have any further questions.

HOW IS CONFIDENTIALITY MAINTAINED?

- Your doctor will not see your questionnaire or any other information you provide.
- Your questionnaire will not have your name on it; only a code, and will be kept apart from any information that might identify you or your doctor.
- No names of patients or doctors participating in the study will be included in any study reports.

PATIENT INFORMATION ON MEDICINES

A COMPARATIVE PATIENT/DOCTOR SURVEY IN SEATTLE AND VANCOUVER

Please return your completed questionnaire to the research assistant or leave at the front desk.
If you were unable to complete it in the waiting room,
please ask the research assistant for a pre-stamped envelope and mail to:

Barbara Mintzes
Centre for Health Services and Policy Research
#429 - 2194 Health Sciences Mall • University of British Columbia
Vancouver, British Columbia V6T 1Z3
Tel: (604) 822 0565 • Fax: (604) 822 5690

PARTICIPANT CODE:_____

SECTION I: These are a few general questions about your health and your upcoming doctor's appointment.

1. **In general, compared to others your age, would you say your health is?**
   - ☐[1] Excellent
   - ☐[2] Very Good
   - ☐[3] Good
   - ☐[4] Fair
   - ☐[5] Poor

2. **When was your first appointment with the doctor you will see today?**
   - ☐[1] This is my first appointment
   - ☐[2] Less than 1 year ago
   - ☐[3] 1- 2 years ago
   - ☐[4] More than 2 years ago
   - ☐[5] *don't know*

3. **In the past six months, how many times have you gone to a doctor *for your own health*?**
   - ☐[1] Not at all
   - ☐[2] One to two times
   - ☐[3] Three or more times

4. **In the past two weeks, how many different prescription medicines have you taken? (medicines a doctor prescribed for you)**
   - ☐[1] None
   - ☐[2] One
   - ☐[3] Two or three
   - ☐[4] More than three

5. **In the past two weeks, how many different over-the-counter medicines have you taken? (medicines you can buy without a prescription)**
   - ☐[1] None
   - ☐[2] One
   - ☐[3] Two or three
   - ☐[4] More than three

6. **Did you decide to make an appointment with your doctor because :**
(Please mark as many as apply)
☐[1] you suddenly started to feel unwell or were injured
☐[2] you're seeing the doctor for the first time for a problem you've had for a while
☐[3] you came for ongoing care for a health problem
☐[4] it was time for a regular checkup
☐[5] you need to get a prescription refilled
☐[6] you need a new prescription
☐[7] you are pregnant
☐[8] you are anxious, having trouble sleeping, or unusually tired
☐[9] Another reason? *please explain*_____

7. **Did someone you talked to, or something you saw or heard, contribute to your decision to go to the doctor? (Please mark as many as apply.)**
☐[1] A friend or family member
☐[2] A doctor, pharmacist, nurse or other health professional
☐[3] An article in a magazine or newspaper
☐[4] A TV or radio program
☐[5] An advertisement
☐[6] A 1-800 telephone line
☐[7] Information on the Internet
☐[8] A book, booklet or pamphlet
☐[9] Anything or anyone else? *please explain*_____
☐[10] *None of the above*

8. **At your appointment, do you think you'll ask about getting a medical test, such as a blood or urine test, mammography, ultrasound or other similar test?**
☐[1] No ➔ *go to question 9*
☐[2] Yes ➔ What test or tests? _____

Where did you hear this test might be helpful to you?
(Please mark as many as apply)
☐[3] Friends or family
☐[4] A doctor, pharmacist, nurse or other health professional
☐[5] An article in a magazine or newspaper
☐[6] A TV or radio program
☐[7] An advertisement
☐[8] A 1-800 phone line
☐[9] The Internet
☐[10] A book, booklet or pamphlet
☐[11] Somewhere else? *please explain*_____

9. **Do you think you need a referral to a specialist?**
☐[1] No
☐[2] Yes

10. Do you think you need a prescription for a medicine you're not already taking?

☐[1] No ➔ *go to question 11*

☐[2] Yes

a) What medicine(s)? _____

b) What health problem does it treat? _____

c) Where did you hear this medicine might be helpful to you?

☐[1] Friends or family
☐[2] A doctor, pharmacist, nurse or other health professional
☐[3] An article in a magazine or newspaper
☐[4] A TV or radio program
☐[5] An advertisement
☐[6] A 1-800 phone line
☐[7] The Internet
☐[8] A book, booklet or pamphlet
☐[9] Somewhere else? *please explain*_____

SECTION II: These are a few questions about your opinion of different sources of health information and where you go for information.

11. Listed below are some sources of information on health and medicines. Please indicate how accurate you think each of these is by circling the appropriate number.

		accurate	**fairly accurate**	**fairly inaccurate**	**inaccurate**	***don't know***
A	Newspaper or magazine articles	1	2	3	4	5
B	Programs on TV or radio	1	2	3	4	5
C	Advertisements on TV	1	2	3	4	5
D	Advertisements in magazines	1	2	3	4	5
E	Doctors	1	2	3	4	5
F	Pharmacists	1	2	3	4	5
G	Alternative health care providers	1	2	3	4	5
H	Reference books	1	2	3	4	5
I	Booklets or pamphlets	1	2	3	4	5
J	The Internet	1	2	3	4	5

12. a) Which of the above information sources have you found most useful?
(PLEASE WRITE ITS LETTER IN THE BOX.)

	Most useful
	Second most useful

b) If you find another information source more useful than those listed above, what is it?_____

13. In the last year, how many different prescription medicines have you seen advertised? (Include ads on TV, on radio or in print.)

☐[1] None
☐[2] 1 to 5
☐[3] 6 to 10
☐[4] More than 10

14. Have you seen any ADVERTISEMENTS for the following medicines?

	Yes	No	*don't know*
Zyban	1	2	3
Viagra	1	2	3
Rilovan	1	2	3
Prozac	1	2	3
Propecia	1	2	3
Evista	1	2	3
Depo Provera	1	2	3
Claritin	1	2	3

15. Do you have a health condition that can be treated by a medicine you have seen advertised?

☐[1] No
☐[2] Yes ➔ a) What condition? _____
b) Do you plan to discuss this condition with your doctor today?
☐[1] No
☐[2] Yes

16. Have you ever asked your doctor to give you a new prescription for a medicine? (Note: only NEW PRESCRIPTIONS, not REFILLS for a medicine you're already taking.)

☐[1] No ➔ *go to question 17*
☐[2] Yes ➔ a) What medicine? _____
b) Did your doctor prescribe it?
☐[1] No
☐[2] Yes
c) Before requesting this medicine, had you seen any advertisements for it?
☐[1] No
☐[2] Yes

SECTION III: We would like to ask you a few questions about your opinion of health care services and the use of medical tests and treatments.

17. Please let us know whether you agree or disagree with the following statements.

	strongly agree	agree	disagree	strongly disagree	*no opinion*
A. All women over 50 should get their bone density tested	1	2	3	4	5
B. New medicines are generally safer and more effective than medicines that were developed ten or twenty years ago	1	2	3	4	5
C. If someone is depressed, they need to take a medicine to get back to their normal self	1	2	3	4	5
D. People should be allowed to buy prescription medicines over the Internet without first seeing a doctor	1	2	3	4	5
E. Canada's laws should forbid advertising of prescription medicines to the public	1	2	3	4	5
F. Only the safest prescription medicines are advertised on US TV	1	2	3	4	5
G. If you pay more for a medicine, it's likely to be safer and more effective than a less expensive medicine	1	2	3	4	5

18. Do you agree or disagree with the following statements about your own health care?

		strongly agree	agree	disagree	strongly disagree	*no opinion*
A.	If I had a bad case of the flu, I would take antibiotics.	1	2	3	4	5
B.	I trust my doctor's judgment if he or she thinks ***I don't need*** a medicine	1	2	3	4	5
C.	I have a hard time getting the information I want about the ***benefits*** of medicines	1	2	3	4	5
D.	If my doctor would not give me a prescription for a medicine I wanted, I would go to another doctor	1	2	3	4	5
E.	I think doctors and patients should have an equal say in treatment decisions	1	2	3	4	5
F.	I have a hard time getting the information I want about the ***side effects and risks*** of medicines	1	2	3	4	5

SECTION IV: Finally, we would like to ask you some questions about yourself.

Like the rest of your answers on this survey, these will be kept confidential, and will only be used to analyze survey results.

19. When you get a prescription, how do you pay for the medicine?
(Please mark all that apply)

- ☐[1] I don't pay for any prescription medicines - all costs reimbursed
- ☐[2] I pay the ***full*** cost of all prescriptions - no costs reimbursed
- ☐[3] I pay only ***part*** of the costs of each prescription
- ☐[4] I pay for ***some*** prescriptions, not others
- ☐[5] *Don't know*

20. What is your date of birth?

_____/_____
month year

21. Are you?

- ☐[1] Female
- ☐[2] Male

22. Are you?

☐[1] Black or African-American
☐[2] White or European background
☐[5] Hispanic or Latino
☐[4] Aboriginal
☐[5] Middle Eastern or Indian Subcontinent
☐[6] Asian or Pacific Islander
☐[7] Other (please specify)_____

23. What is the highest grade or year of school you have completed?

☐[1] Less than grade 9
☐[2] Some high school
☐[3] High school graduate
☐[4] Some college, university or trade school
☐[5] Trade school or vocational college graduate (diploma/certificate)
☐[6] University graduate (bachelor's degree)
☐[7] Master's, doctoral or professional degree

24. Are you currently employed in a health care profession, company, or organization?

☐[1] No
☐[2] Yes

25. How many people live in your household? ***(Include yourself, other adults, and children)***

_____people

26. Approximately what was the total income of your household last year before taxes?

☐[1] Less than $10,000
☐[2] $10,000 to $19,999
☐[3] $20,000 to $39,999
☐[4] $40,000 to $59,000
☐[5] $60,000 to $79,000
☐[6] $80,000 or more

Do you have any additional comments? Please mark below.

Thank you very much for your help!

Please return your questionnaire to the research assistant or the front desk.
If you were unable to complete it at the doctor's office, please ask the research assistant for a pre-stamped envelope and mail to:

Barbara Mintzes
Centre for Health Services and Policy Research,
#429 - 2194 Health Sciences Mall
University of British Columbia,
Vancouver BC V6T 1Z3

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Chapter 6

The policy debate

Both in jurisdictions where it is allowed, and where it is forbidden, DTCA is highly controversial. This chapter describes the historical background to the current policy debates on DTCA, both in Canada and internationally.

The framing of these discussions depends on three key factors: whether or not DTCA is currently allowed within a country; the extent of commitment to public health care financing, including provision of public pharmaceutical benefits; and the approach currently used to regulate pharmaceutical advertising and other forms of promotion.

The U.S. and New Zealand represent very different types of situations in which DTCA is allowed: the U.S. relies heavily on private funding and provision of healthcare in comparison to most other OECD (Organization for Economic Cooperation and Development) countries, and most prescription drugs are paid for by private insurers. Among OECD countries, the U.S. also devotes the smallest proportion of its public health care budget to pharmaceuticals.[1] The two major public plans are Medicare, a federal programme which covers the elderly, and Medicaid, which is co-administered by state governments and covers those on income assistance. Medicare does not include prescription drug coverage.[2] Medicaid, which covered 36 million recipients in 2001, generally does include some prescription drug coverage, although the amount of coverage varies from state to state.[3]

New Zealand covers the costs of both inpatient and outpatient prescription drugs for the entire population as a component of public coverage for health care services. A crown corporation, PHARMAC (Pharmaceutical Management Agency) manages drug procurement and reimbursement, as well as formulary restrictions and related strategies aiming to improve cost-effectiveness of pharmaceutical use.[4] Patients pay a NZ$15 (CDN $12) co-payment for each prescription or a $3 co-payment for low-income recipients.

Whether drugs are paid for publicly or privately has less effect on the content of DTCA than on policy discussions surrounding it. For example, in New Zealand, PHARMAC has taken a strong stand in opposition to DTCA.[5] In the U.S. state governments are responsible for administration of Medicaid plans, and state legislatures have initiated policies attempting to curb the potential impact of DTCA on drug costs.

On the other hand, there is much greater direct government oversight of advertising content in the U.S. than in New Zealand. The U.S. Food and Drug Administration (FDA) directly regulates the content of DTCA, regularly requires companies to withdraw ads judged to be illegal, and posts all regulatory decisions on the Internet, for all to see. New Zealand, in contrast, relies on industry self-regulation, with rare governmental intervention. These regulatory differences are reflected in the content of advertising in the two countries, although the same companies are advertising many of the same products in both countries. Table 6.1 describes the presence or absence of various regulatory requirements for content in the two countries.

Table 6.1 : Regulatory requirements for DTCA content in the U.S. and New Zealand

	United States	New Zealand
Direct government monitoring of advertising content	Yes	No
Pre-screening of advertising content	No	Yes
Detailed risk information required in print ads	Yes	No
Detailed risk information required in broadcast ads	No	No
Sources of more detailed risk information must be mentioned in broadcast ads	Yes	No
A balance of risk and benefit information required in all ads (print and broadcast)	Yes	No
Financial incentives such as free trial offers prohibited	No	No
Personal testimonials prohibited	No	Yes

In Canada, Australia, South Africa, and the European Union, legislative change to introduce DTCA has been under discussion, with strong support from the international pharmaceutical industry. These discussions have been framed in terms of manufacturers' rights to commercial freedom of expression, public information rights, the need to modernize legislation that predates current medical and commercial norms, and the irrelevance of laws forbidding DTCA when pharmaceutical ads are freely accessible to

all on the Internet via U.S. sites, particularly in English-speaking countries. In Canada, cross-border exposure to U.S. advertising is said to render current laws meaningless.

Opposition has mainly centred on the role of DTCA as a cost driver, and on potential erosion of public health care services, as cost overloads are shifted onto patients and private payers. A second key argument concerns the evidence – or lack thereof - of benefits to health or the quality of health care services from DTCA, as well as questions about how well DTCA meets public needs for information on medicines.

An interesting aspect of the policy debates relating to DTCA is their similarity in different jurisdictions. This is not surprising, given the multinational nature of the industry, and the similar pressures faced by governments, on the one hand to provide health care coverage for their citizens in as effective and efficient a manner as possible, and on the other hand, to support economic development and employment. This latter is of particular importance in countries and regions with a domestically-based brand-name pharmaceutical industry.

This chapter begins with a discussion of national historical developments and policy reviews on DTCA in the U.S., New Zealand, Canada, Australia, the European Union and South Africa. This is followed with a discussion of legal factors that are frequently cited as contributing to this debate, including product liability, privacy and freedom of expression. A central issue raised in national discussions about introduction of DTCA is its role as a source of much-needed information on medicines for the public. The chapter concludes with a brief discussion of consumer drug information standards. A case study, a U.S. radio ad for esomeprazole (Nexium), is used to illustrate the relationship between these standards and DTCA.

6.1 National and international experiences with DTCA

6.1.1 Growth of DTCA in the U.S.

The U.S. has never had any legislation specifically prohibiting advertising of prescription drugs to the public. The 1938 Wheeler-Lea amendment of the Federal Trade Commission Act, introduced following a sulfa drug elixir disaster that killed nearly 100 people, established prescription-only drug status and gave the FDA regulatory authority over pharmaceuticals.[6] This was followed by the 1962 Food, Drug and Cosmetic Act, introduced after the international thalidomide disaster, which required manufacturers for the first time to provide evidence to the FDA to back claims of product effectiveness. This was also the first legislation to include specific requirements for advertising.

The U.S. FDA directly regulates pharmaceutical advertising. False and misleading claims, failure to provide a fair balance of risk and benefit information, or other activities that do not conform to U.S. regulatory standards are considered to be product misbranding, and the FDA has the authority to require the company to undertake corrective actions and ultimately to remove a product's marketing license if a company refuses to comply.

U.S. pharmaceutical companies first began to advertise their products to the public in the early 1980s. U.S. DTCA grew relatively slowly at first, in terms of the number of products being advertised and the amount of spending.[7] In 1981, only one prescription drug was advertised to the public, ibuprofen (Rufen), and this was a price advertising campaign.[8] By 1989, 21 companies had advertised 30 products and the estimated annual spending on promotion aimed at the public had grown to U.S. $80 million dollars. However, most advertising campaigns were disease-oriented and did not mention specific product names. The first full product advertising campaign, including brand name, indication and fine print labelling information (referred to as the 'brief summary' in U.S. FDA regulations) began in 1983.

Pinto et al.[9] list several reasons companies chose to advertise prescription drugs to the public in the late 1980's and 1990's: These are related to the growth of managed care, and the introduction of policies to restrict pharmaceutical spending:

- Some managed care organizations had policies restricting sales representatives' access to doctors;
- Managed care companies had brought in policies to limit pharmaceutical spending, including formularies and bulk purchasing; DTCA allows manufacturers to bypass these limits by going straight to the consumer;
- Patients can help break doctors' static prescribing patterns by asking for new drugs;
- Drug discounting and generics had increased competitive pressures within the industry;
- The growth of the patient rights movement had contributed to a social climate in which patients expected increasingly to play an active role in health care decisions, including prescribing decisions, and patient-directed advertising was expected to have an impact.

FDA Commissioner Arthur Hayes asked the industry to respect a voluntary moratorium on DTCA in 1983 in order to allow for research into the impact of this form of advertising and the development of appropriate legislation, if required. This moratorium followed soon after Lilly's promotional campaign for benoxaprofen (Oraflex), a drug that was withdrawn because of injuries and deaths from liver failure only five months after its U.S. introduction in 1982.[10] A highly successful press and publicity campaign had led to more than 500,000 prescriptions within a few months of the product's introduction. The FDA had judged this campaign to be in violation of federal law because of company claims that the product modified the progress of arthritis, without evidence to back those claims. The FDA did not specify that the benoxaprofen (Oraflex) campaign, which was carried out largely through press releases and public relations, was responsible for the decision to introduce a moratorium on DTCA. However, Sidney Wolfe, of Public Citizen's Health Research Group, was undoubtedly correct when he noted that "[t]his was at least in the minds of people...when the decision to impose a moratorium not many months later was made."[11]

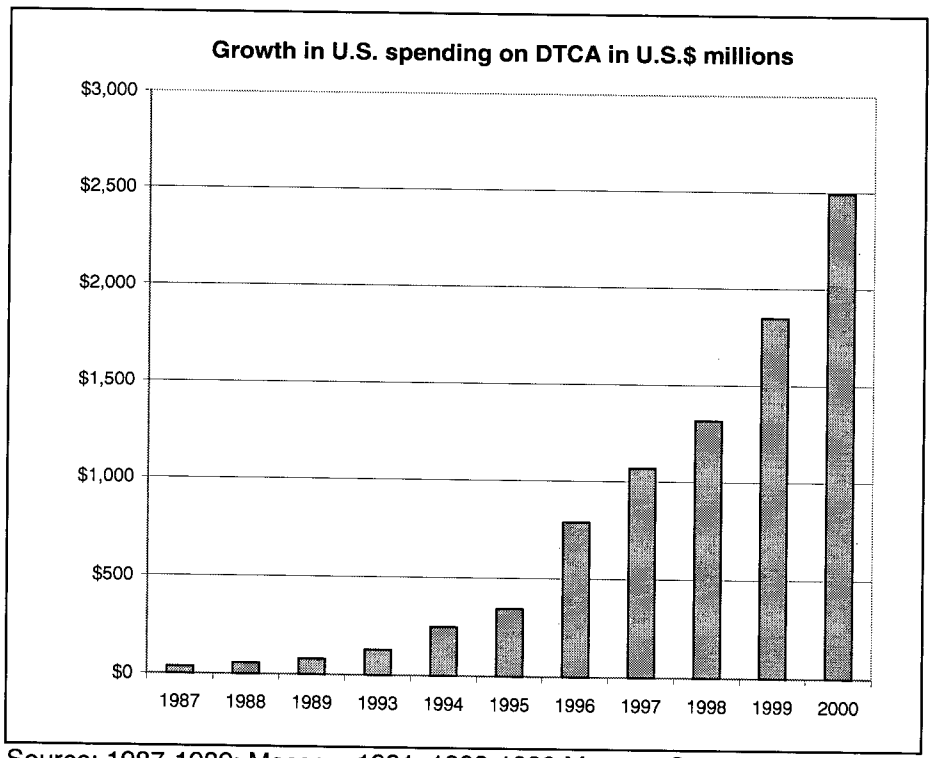
The American Medical Association and most consumer organizations and members of the public attending FDA public consultations during the moratorium were opposed to product-specific DTCA. Pharmaceutical industry views were also mixed. At a conference organized by the industry in 1984, nearly 80% of drug industry executives were opposed to DTCA, citing fear of increased product liability and marketing costs and lower profitability.[12] Kirk R. Schueler, Director of Marketing at Merrell Dow, said that: "It would be a Pandora's box which once opened would unleash demons that would have a lasting effect on our industry. If a manufacturer feels a product is appropriate for OTC-style advertising, they should file for OTC status."[13]

The FDA also expressed reservations. Kenneth Feather, Chief, Drug Advertising Branch, described a 1984 symposium presenting research on DTCA: "The major conclusions of this symposium were that, while virtually no one was really in favour of it, some form of DTC promotion was inevitable; it would not serve an educational purpose; it would be very expensive, and the major driving force was the ad agencies."

On September 9, 1985, the FDA ended the moratorium on DTCA. Feather called this a housekeeping measure.[14] The agency felt the issue had been adequately studied and there was no need to issue new regulations or revise existing ones. DTCA would be regulated in a manner similar to ads targeting health professionals. Feather states that the end of the moratorium, which coincided with two new DTCA campaigns, "... was interpreted as the agency encouraging DTC promotion. Nothing is further from the truth." [14] At first DTCA grew relatively slowly. By 1989, only six products were fully advertised to the public. By 1997, however, the U.S. industry association, PhRMA, estimated that 79 products were being advertised to the public.[15] This is still a small number as compared to the thousands of pharmaceuticals on the market in the U.S. It is a larger proportion, but still a minority, of recently approved products, a category that would include most advertised drugs. The U.S. FDA approved 436 new drugs during the five-year period from 1992 to 1996 inclusive.[16]

Within a single decade, the industry has gone from spending approximately U.S. $100 million on advertising directed at consumers in 1990 to $2.5 billion in 2000. This was estimated to be 16% of promotional spending in the U.S. in 2000, with most spending still directed at health care professionals. However, if the retail value of free samples is subtracted from the total spent on promotion, and the $1.9 billion spent on promotional 'events' in 2000 is included in this total,[17] DTCA would have accounted for 26% of promotional spending (or 32% of the total excluding promotional events).[18] With this level of spending, it is fair to say that the industry's reticence about DTCA as a marketing strategy, as expressed during the 1980's, appears to have disappeared.

Figure 6.1: Growth in U.S. Spending on DTCA 1987-2000



Source: 1987-1989: Masson, 1991; 1993-1998 Mertens G. 1998-2000 Rosenthal et al, 2002

The FDA held a second set of public consultations on DTCA in 1995. Nancy Ostrove, one of the FDA organizers, said that the remarkable thing about the second symposium was how similar the discussions were to those that had taken place ten years earlier.[19] Virtually no new research evidence on the impacts of DTCA was brought forward.

One change, however, was in the proportion of major companies supportive of DTCA and already engaging in this form of promotion. Another was the pressure for relaxation of the regulations governing television and other broadcast advertising. The industry had been pressing the FDA to relax its rules on broadcast advertising because regulatory requirements to accompany ads with the full 'brief summary' of risk information in product labelling made full product advertising on television costly and unwieldy.* Most companies advertising on television chose to run only reminder ads stating the product name, but no health claims, as no risk information was required with reminder ads. This was consistent with regulations for reminder ads directed at health professionals. However, the FDA was aware that reminder ads were problematic because they presented vague positive allusions to a product but often left consumers wondering what health condition it treated.[20]

The FDA announced its draft guidance on broadcast advertising on August 8, 1997, [21] which would allow manufacturers to omit the 'brief summary'. Instead, they would need to state a product's major risks and provide additional sources of information: a toll-free phone number viewers could call to request full labelling by mail, fax or recorded phone message; an Internet site; and simultaneous DTC print ads or brochures in doctors' offices, libraries and stores, that included the brief summary. In essence this is a relaxation of the regulations governing risk information provision in advertisements. Instead of providing the full risk information contained in approved product labelling, as was previously required, manufacturers could provide information just on major risks, with more complete information available elsewhere.

This regulatory change has led to a large increase in the amount of television advertising of prescription drugs, with over 30 drugs advertised in the following year and the majority of new DTCA spending going towards television since 1998. A market research company estimated in late 1999 that, on average, Americans see nine prescription drug ads a day on television.[22]

* The 'brief summary' consists of all of the risk information in approved product labelling.

1997 was also the year of the Food and Drug Modernization Act. This Act allows pharmaceutical companies to disseminate information promoting their products for unapproved uses. Companies are only allowed to disseminate reprints of studies published in peer-reviewed journals. The use of such studies in product promotion, however, has traditionally been considered objectionable, and is forbidden in other industrialized countries. This change represents a radical departure from previous regulations, which restricted companies to claims and information dissemination based on approved product labelling. When the FDA approves an indication for a product, it confirms that the company has provided sufficient evidence of efficacy and safety in pre-marketing trials to justify this use. An unapproved use, by definition, has not gone through this process and may be supported by relatively little evidence. Studies of drugs for unapproved users are common and are an important part of scientific inquiry. However, their distribution by manufacturers is in effect promotion of a product for a use for which it has not been approved.

The 1997 Food and Drug Modernization Act also reauthorized changes to FDA regulations introduced in 1992 through the Prescription Drug User Fee Act, which had led to speedier drug approvals by authorizing the FDA to charge fees for new drug applications. Although more new drug approvals per year translate to more promotional campaigns and more adverse drug reaction reporting, the FDA as a whole has not seen similar budgetary expansion. User fees are collected to facilitate the review process, not for the FDA's general operating budget. Several consumer and women's organizations have raised concerns about the effects of budgetary constraints on the agency's ability to regulate DTCA effectively.[23]

The FDA followed up the 1997 draft guidance on broadcast advertising with a final guidance issued in August 1999.[24] This guidance confirms the key changes introduced in the 1997 draft guidance, and includes only minor adjustments:

- Faxing of product labels to consumers is no longer an option;
- Companies must broadly disseminate print ads during broadcast campaigns, so viewers can get detailed risk information in a way that does not threaten privacy;

- Print brochures may only be used as a source of additional information for broadcast advertising to restricted audiences, as it is difficult to disseminate them broadly;
- Healthcare providers other than doctors and pharmacists can now be listed as sources of additional information;
- The requirements for telephone advertising have been clarified.

In information accompanying the announcement of the final guidance, the agency stated that: "Despite years of print DTC advertising, no rigorous evidence has been presented to demonstrate that DTC advertising has had any of the hypothesized ill effects."[25] The agency failed to state that no rigorous evidence of any sort had been presented, be it on potential harm or benefits. Absence of evidence appears to have been taken as evidence of absence of deleterious effects.

In U.S. news reports during 2001, DTCA was linked to concerns about rising pharmaceutical costs[26] and to unsustainable costs for employee health benefits borne by large employers such as General Motors.[27] According to a report in *Advertising Age* in April 2001, U.S. Senators and House members are reviewing the issue and planning to introduce new legislation on DTCA. The aim would be to improve regulation by increasing FDA staffing to review DTC ads and establishing an advisory panel to develop additional voluntary standards for the ads, which the industry and FDA would be encouraged to follow.[28] However, by early 2003 no such legislation had been introduced.

State legislators in 15 states proposed bills that included provisions on DTCA during 2001 and 2002. Only one has been passed: West Virginia-enacted a law that gives the director of the West Virginia Public Employees Insurance Agency discretion to require prescription drug manufacturers to disclose their advertising spending and its impact on drug costs. [29] Other proposed legislation includes requirements for manufacturers to disclose advertising costs, changes to tax law that would eliminate tax deductions for DTCA expenses, changes to manufacturers' liability in cases in which prescription drugs had been advertised to the public, and proposals for 'counter detailing' to provide public education on cost-effective prescription drug use.

In May 2002, the FDA initiated a consultation on whether its regulatory activities infringed unduly on first amendment rights to freedom of expression, as established in case law.[30] The consultation was a response to recent court cases that had "emphasized the need for not imposing unnecessary restrictions on speech." The initial consultation period ended in September 2002, with an additional period until the end of October 2002 in which comments could be made on consultation submissions. The FDA has not yet published its evaluation and response. However, Former FDA Commissioner David Kessler warned of the potential for this review to jeopardize the FDA's ability to regulate: "It represents a frontal attack on the fundamental responsibilities of the agency under the Food, Drug and Cosmetic Act. I have great concerns that this is simply an attempt to deregulate while doing it in the name of the First Amendment."[31]

John Calfee of the American Enterprise Institute, a U.S. think tank supported by a range of corporations, argues that regulation of DTCA should be moved from the FDA to the Federal Trade Commission (FTC), which currently has jurisdiction over OTC drug ads as well as most other forms of advertising.[32] This in effect would situate regulation of prescription drug advertising with other consumer products, rather than within a health agency. Calfee argues that, "this would permit regulation to focus on advertising and communication, unencumbered by pervasive regulatory linkages such as new drug approvals and manufacturing oversight." He argues additionally that the FTC has more expertise in evaluating advertising than the FDA.

A U.S. congressional office raised concerns in October 2002 that FDA oversight of drug promotion, including DTCA, had been severely weakened through the introduction of new administrative procedures. A new Chief Counsel was appointed to the FDA in August 2001, Daniel Troy.[33] He had previously represented pharmaceutical industry plaintiffs in cases against the FDA. In November 2001, a policy was introduced requiring the FDA's Division of Drug Marketing, Advertising and Communication (DDMAC) to send all regulatory letters to the Office of the Chief Counsel for approval before sending them out to companies. DDMAC is responsible for oversight of drug promotion and had previously sent letters out immediately. California Congressman Henry Waxman noted a

70% drop in the numbers of letters sent out per month in 2002 as compared to the previous few years, in spite of an increase in the number of submissions and similar numbers of complaints. A 2002 report by the U.S. General Accounting Office confirms that delays following the introduction of this new policy had led to a drop in the number of regulatory letters, and an increase in the time between when the FDA noted a violation and the company was required to pull an ad.[34] Particularly with broadcast advertising, such delays can lead to dramatic differences in population exposure to illegal ads. By the time an ad is pulled it may also have already finished its run.

In summary, two recent trends can be identified in U.S. policy debates on DTCA. On the one hand, private employers, state governments, seniors' groups and the media have raised concerns about DTCA's effects on drug costs, and there has been considerable negative press both over the high prices of drugs in the U.S. and the effects of advertising on demand for newer, more expensive drugs.[26] On the other hand, the FDA's capacity to regulate DTCA, as well as other forms of pharmaceutical promotion, is being challenged both in court and through the introduction of new administrative procedures leading to regulatory delays. Given the strong legal precedents for commercial freedom of expression in the U.S., severe restrictions on DTCA are unlikely in the near future. A more likely scenario is further deregulation, for example if regulatory oversight is removed from the FDA.

6.1.2 New Zealand : the 2nd frontier

Why did New Zealand, like the U.S., choose to allow DTCA? According to a report in the March 1999 issue of *New Zealand Doctor*, the reason is a loophole in New Zealand's *Medicines Act*.[35] New Zealand has never explicitly prohibited advertising of prescription drugs to the public. However, the issue had not arisen until recently. DTCA has been much less extensive in New Zealand than the U.S. and was reported in 1999 to be "only about four years old" [35]

DTCA has grown rapidly in New Zealand since then, in many ways mirroring the recent U.S. experience. A 1999 New Zealand press report listed 10 drugs that had been

advertised to the public between 1996 and 1999.[36] An additional DTCA campaign is described in a second 1999 article,[37] and by June 2000, a report by the Researched Medicines Industry Association of New Zealand (RMI), listed six additional products advertised to the public on television.

A November 2000 report by PHARMAC, New Zealand's national pharmaceutical benefit scheme, stated that 46 products had been advertised to the public on television from October 1999 to 2000, and that these included 20 products on the National Pharmaceutical Schedule (43%), 12 of which were fully subsidized and eight partially subsidized.[5]According to PHARMAC, the industry spent approximately $14 million New Zealand dollars (equivalent to U.S. $7.7 million) on television advertising from October 1999 to September 2000, excluding advertising of anti-obesity drugs. PHARMAC excluded obesity drugs from this estimate because it does not fund this class of drugs.

New Zealand's population size is only approximately 1.4% of the U.S. population. At an equivalent rate spending per population, New Zealand spending on DTCA would have been around NZ $64 million, or 4.6 times the rate of spending reported by PHARMAC. One company, Roche, heavily advertised an obesity drug to the New Zealand public during 1999 and 2000, and therefore the NZ $14 million is an underestimate of total DTCA spending. Prices of advertising spots are also likely to differ since New Zealand represents a much smaller market than the U.S. Therefore differences in population exposure to DTCA are unlikely to be as large as differences in advertising spending. However, it is fair to say that the industry currently spends much less per capita on DTCA in New Zealand than in the U.S.

A controversial 1998 ad campaign for the anti-obesity drug orlistat (Xenical) prompted the Minister of Health to call for an inquiry into DTCA.[38] The New Zealand Medical Association and individual health professionals claimed that these advertisements put pressure on doctors to prescribe inappropriately. One doctor was so angry about this campaign that he called for all New Zealand doctors to boycott the manufacturer, Roche.[39] An IMS Health New Zealand fax poll of 400 General Practitioners, with a 30% response rate (121 responses) found that 75% either wanted DTC advertising to stop

altogether or to be decreased; 61% felt it created disharmony in the doctor/patient relationship and 62% believed it to be of no benefit to patients.[40]

Another campaign, for the asthma medication montelukast (Singulair), provided a promotional offer of one month's free medication.[37] The price of the drug is around New Zealand $118 a month (CDN$95). Nearly 20% of New Zealand's GPs prescribed montelukast during its first two weeks on the market. The free promotional offer has come under criticism as creating an unnecessary strain on patients, since the medication is intended for long-term use. The role of montelukast in the management of asthma is unclear and it is less effective for prevention of asthma attacks than steroid inhalers.[41 42] As a new product, its full safety profile is unknown. Therefore such widespread prescribing appears unjustified. Additionally, the U.S. Food and Drug Administration had required montelukast's manufacturer, Merck, to send out a safety alert about the product to U.S. physicians in 1998, the previous year because of post-market reports of serious adverse reactions.[43]

One difference between New Zealand's public health care system and Canada's is in user charges. New Zealanders pay the equivalent of CDN $33-$41 per consultation with a family physician. These charges are subsidized for those on low incomes through a Community Services Card, but uptake of this card is incomplete, with only 60% of those who are eligible obtaining it.[51] Thus if members of the public see ads for prescription drugs and believe that these products may help them, they face a non-discretionary charge for the physician visit before they can obtain a prescription. This would be expected to have an effect both on the initial response rate to advertising and on patients' responses to physicians' refusals to provide prescriptions for requested drugs. These potential effects have not been studied. However, a televised advertising campaign for bupropion (Zyban) in 2002 attempted to overcome this barrier by offering to reimburse patients' charges for the physician visit.[44]

One of the most contentious aspects of DTCA in New Zealand has been its effect on public payment for drugs as part of national health care services. In 1999, PHARMAC

attempted to impose a ban on DTCA of subsidized prescription drugs through a clause in its contracts with pharmaceutical suppliers.[45] Following objections from the industry association, RMI, the clause was changed to only require suppliers to abide by relevant national and industry regulations. This allows PHARMAC to judge any breaches of law or industry advertising codes as a potential breach of contract on the manufacturer's part. No public information is available about this clause being used to consider manufacturers to be in breach of contract, but it may have provided PHARMAC with leverage in private negotiations with companies.

New Zealand's regulatory framework is broadly similar to Canada's, in that it relies on industry self-regulation with a fallback possibility of legislative action in case of non-compliance. All ads must comply with the Medicines Act and Medicines Regulations, enforced by the Health Ministry's Medsafe Division. RMI's Code of Practice covers most forms of promotion. The Advertising Standards Authority, the voluntary self-regulatory body governing the New Zealand advertising industry, has also developed a Code of Therapeutic Advertising, which came into effect in February 1999.

Unlike the U.S., New Zealand has no explicit requirements for fair balance of benefit and risk information in consumer-directed advertising. In television ads, required risk information is generally not included in the audio message, but is flashed onto the screen as text at the end of the ad. Hoek and Gendall note that, "most technical details appear in an end-screen that features for approximately five seconds. Research examining consumers' knowledge of information provided in television end-screens has confirmed that most retained few of the key details." [46] They were presumably referring to unpublished market research, as no published studies had assessed New Zealanders' knowledge following exposure to television DTCA. The authors did not conclude that advertisers should allow enough time for viewers to read the information, but rather that fewer details should be provided.

In July 1999, the Association of New Zealand Advertisers (ANZA) set up the Therapeutic Advertising Advisory Service (TAAS). Most pharmaceutical companies are

members of ANZA. TAAS was a voluntary service for pre-screening of advertisements, financed through user fees. As such, it had a broadly similar mandate to Canada's Pharmaceutical Advertising Advisory Board (PAAB). It provided companies with advice on whether proposed ads comply with legal and code requirements. Complaints could still be lodged against ads that had been pre-screened, but were much less likely to be successful. Since its 1999 inception, Dr Nigel Andrews, an ex Ciba-Geigy manager, was responsible for all TAAS advertising reviews. He consulted with other bodies, including Medsafe, New Zealand's drug regulatory agency, at his own discretion.

In October 2000, at the initial stage of a New Zealand Ministry of Health policy review into DTCA, TAAS became the Therapeutic Advertising Pre-vetting Service (TAPS), moving from a purely advisory role to a pre-clearance procedure, in which ads are issued a number to show they have been pre-cleared. Criteria and procedures remain otherwise similar, although the greater volume of advertisements to be cleared has led to the hiring of additional personnel.

Annette King, the Minister of Health, stated in 2000 that she was considering restrictions or a ban on DTCA.[47] This statement followed negative press coverage on DTCA, and concerns raised by PHARMAC about fiscal pressures and inappropriate use of medicines linked to DTCA campaigns.[48] New Zealand's Ministry of Health initiated a policy review of DTCA between November 2000 and February 2001, outlining a range of options from maintaining the current law to endorsing a total ban.[49] Forty-three submissions were received, 18 of which the Ministry judged to clearly support DTCA and 20 to oppose it.[50] Of the 18 submissions in support of DTCA, 12 were from pharmaceutical companies or advertising agencies.[51] PHARMAC's submission strongly supported a ban on DTCA, based on both financial and clinical concerns. These are outlined in Table 6.2 below.

Table 6.2: Key concerns about DTCA raised by PHARMAC

DTC advertising:
1. Places a fiscal strain on the New Zealand pharmaceutical budget, as it:
a) drives up demand for subsidized pharmaceuticals, which has a significant fiscal impact on New Zealand's pharmaceutical expenditure;
b) distorts demand by moving patients to high cost medicines;
c) increases demand for Pharmac to subsidise pharmaceuticals that are advertised.
2. Increases the medicalisation of the population.
3. Presents an unbalanced picture of the potential risks all medicines carry.
4. Ignores key treatment information
5. Damages the doctor/patient relationship.
6. Targets the vulnerable with emotional rather than rational information.
7. Is not appropriately managed through self-regulation.

Source : PHARMAC submission to NZ Ministry of Health DTCA Review[5]

The New Zealand Medical Association (NZMA) published its position on DTCA in May 2000.[52] The NZMA has not joined PHARMAC in calling for a ban on DTCA, but is opposed to advertising that is emotive and manipulative, interferes with the doctor/patient relationship, or tries to create a market where one does not clinically exist. NZMA provided an example of the latter in the promotion of vaccines, "that are undoubtedly a good idea for some travelers and a few people at particular risk in New Zealand, but quite unnecessary for the vast majority." [52]

In its response to the Ministry's review, the brand-name industry association, Researched Medicines Industry (RMI), referred to a report it had produced earlier that year documenting DTCA's role in enhancing public health.[53] RMI described four case studies of New Zealand advertising campaign showing the beneficial health effects of DTCA: advertising of an influenza vaccine (Fluarix), fluticasone (Flixotide), a steroid inhaler for asthma, orlistat, (Xenical), for obesity, and sildenafil (Viagra), for impotence.

The influenza vaccine campaign was carried out together with the New Zealand Health Funding Authority (HFA). From a public health perspective, influenza vaccines are a useful intervention for those at risk of complications from influenza, particularly the elderly and those with chronic illnesses. RMI reports that 1999 sales were 27.6% above those in 1998. Unfortunately, however, no breakdown is provided in characteristics of users, in terms of whether they were within population groups most likely to benefit.

The fluticasone (Flixotide) campaign generated over 24,000 phone calls, and 10,000 callers completed a telephone questionnaire, over 90% of whom provided evidence of imperfect asthma control.[53] In a smaller sample of 400 respondents, 37% went to their physician about breathlessness as a result of an information pack on fluticasone. Maoris and Pacific Islanders were over-represented in the database of callers in comparison to the New Zealand population, evidence, according to RMI, that difficult to reach patients are being reached through televised advertising campaigns. These data suffer from self-selection of respondents and the lack of comparison group.[54]

Inhaled steroids are an effective therapy for moderate to severe asthma, and their under-use has been highlighted as a concern for asthma management. However, fluticasone is no more effective than a less expensive available alternative steroid inhaler, beclomethasone, and a systematic review raised concerns about increased adverse event rates.[55] PHARMAC's analysis of administrative data indicated that as sales of fluticasone inhalers increased during the advertising campaign, sales of beclomethasone decreased, suggesting a substitution effect.[5]

The orlistat (Xenical) campaign cited by RMI was subject to a complaint that it breached Principle 2 of the Code for Therapeutic Advertising, that ads should "observe a high standard of social responsibility." Coney describes this campaign as an illustration, "...that the primary purpose of DTC advertising is to appeal to emotions such as shame and anxiety about social exclusion, rather than impart good-quality information, particularly evidence-based information about benefits and risks." [51] She also suggests that Roche's slogan, "*Lose Weight. Gain Life*" implies that orlistat is for anyone who would like to lose weight, not a treatment approved in New Zealand only for significant obesity. Nowhere were side effects such as fecal incontinence mentioned.[†]

The New Zealand Ministry of Health concluded its policy review with a recommendation

[†] Another criticism is the cost to patients for relatively little weight loss. Orlistat (Xenical) costs NZ $2040 for a 12 month supply and is not publicly subsidized. At an average of 3.3kg weight loss over a one-year period observed in clinical trials, as compared to placebo, in people weighing on average 100kg, the cost per kilo lost is estimated to be NZ$618 or CDN$500.[56]

to continue to allow DTCA with strengthened self-regulatory procedures.[50] The Ministry argued that there was no empirical evidence of harm to the public, and that a ban on DTCA would unduly restrict the industry's freedom of expression as guaranteed under the New Zealand Bill of Rights Act. Additionally, the Ministry recognized the need to support the advertising industry's economic activities and contribution to employment. The pharmaceutical industry had argued that DTCA brings health benefits, but this was not part of the Ministry's justification for maintaining DTCA. Although the Minister stated that she intended to restrict some activities, nearly two years after the conclusion of this review, in March 2003, no such restrictions had been implemented.

In February 2003, professors of general practice at four New Zealand medical schools submitted a report to the Minister of Health calling for a ban on DTCA, explaining the reasons they believe a ban on DTCA was necessary, together with a review of the evidence on outcomes of DTCA from the U.S. and New Zealand.[56] Chief among the reasons cited was the poor information quality in DTCA, the use of persuasion and emotional appeals, and the minimization of risks, exaggeration of efficacy, and lack of mention of alternative treatments. This initiative also included the recommendation that a centralized consumer drug information service be publicly financed as a means to provide unbiased comparative information on treatment options. This initiative was also backed by university-based public health physicians[57] and clinical pharmacologists,[58] as well as New Zealand's Royal College of General Practitioners.[59]

The authors wrote to New Zealand's 3200 family physicians informing them of this campaign for a ban on DTCA and enclosing a brief questionnaire about their experiences. Over half replied without reminders within 10 days (N=1611), 69% of whom, or 35% of New Zealand's GPs, reported pressure from patients to prescribe advertised medicines. A consumer survey of a random sample of the New Zealand public was commissioned as well: 13% of the 500 respondents said that they had requested a prescription from their physician, 62% of whom reported receiving the prescription they requested.[56] ‡

‡ The results of this New Zealand consumer and physician surveys are not included in Chapter 2 because results were not published until mid February 2003, after the literature review was completed.

The Minister of Health's response to this initiative is expected in 2003. DTCA is controversial both in New Zealand and in the U.S. In the U.S., however, critics of DTCA are pessimistic about the possibility of legislative change to ban DTCA because of the strong legal protection afforded to freedom of commercial expression.[60] In New Zealand, national policy discussions have included the possibility of a legislated ban.[47] This difference may in part reflect the precedent in New Zealand of a ban on tobacco advertising for public health reasons, which has been in place since 1990, and was extended to include sponsorship of events in 1995.[61] New Zealand also represents a much smaller pharmaceutical market than the U.S., and thus the stakes are not as high, in terms of effects on the industry's profitability. However, the pressure for legalization of DTCA in Europe, Canada, Australia and elsewhere would be weakened by a ban in New Zealand, as no longer could DTCA be presented as an inevitable 'wave of the future'. Thus, the industry's interest in maintaining DTCA in New Zealand may be greater than is implied by the country's small size.

6.1.3 Canada: Indirect and Cross-Border DTCA

Regulation of pharmaceutical advertising is covered under section 9(1) of Canada's Food and Drugs Act, which states that: "No person shall label, package, treat, process, sell or advertise any drug in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its composition, merit or safety."

Schedule A of the Act sets out a list of diseases for which treatments or preventatives may not be advertised to the public. This is an extensive list, which includes many conditions treated or prevented by drugs that have been advertised to the public in the U.S. (and in some cases in Canada), such as impotence, baldness, diabetes, asthma, and heart disease. Additionally, the Act states that prescription-only (Schedule F) drugs may not be advertised to the public. The sole exception is an amendment introduced in 1978 to allow pharmacies to advertise price comparisons, section C.01.044: *"Where a person advertises to the general public a Schedule F Drug, the person shall not make any representation other than with respect to the brand name, proper name, common name, price and quantity of the drug."* [62]

The Health Protection Branch's[§] Advertising Coordinator, Valerie Robertson, testified at U.S. FDA hearings on DTCA in 1995, explaining why Canada prohibited advertising of prescription drugs to the public. The Food and Drugs Act, Robertson said, "is a public protection act, and the limitations and prohibitions imposed are intended to minimize the risks to the general public associated with the use of drug products."[63]

The official interpretation both of the aim and content of the prohibition against DTCA in the Food and Drugs Act appears to have shifted since 1995. A November 2000 advertising policy statement posted on Health Canada's website interprets the Act to allow a product's name to be advertised to the public, but not its indications, or the product's indications but not its name.[64]

No explanation is provided for this policy shift, which used the 1978 clause introduced to allow price advertising in order to state that two types of DTCA for prescription drugs were legal in Canada: reminder advertisements and disease-oriented advertisements.

Disease-oriented advertisements do not state a specific brand name, but instead describe a treated condition, usually stating that new treatments are available and suggesting that the viewer or reader asks their doctor about treatment options. This strategy tends to be used for market leaders within a drug class, or for drugs without close competitors, such as sildenafil (Viagra). It is difficult to effectively regulate because companies are only subject to regulation under the Food and Drugs Act if they are advertising a regulated product – a pharmaceutical or a medical device. It can sometimes be difficult to prove a connection between a disease-oriented ad and a specific product. However, the November 2000 Health Canada policy paper stated that a company may advertise a product's indication as long as it does not mention the name. This represents a shift in interpretation of the law because the explicit context is prescription drug advertising.

[§] It is now called the Health Products and Food Branch.

Health Canada's statement that brand names may be mentioned in prescription drug advertisements, as long as the indication is not also mentioned, is even more controversial.[65] Ads that mention a brand name but not an indication are called 'reminder advertisements' in the pharmaceutical marketing literature. They are defined under U.S. advertising regulations: "Reminder advertisements are those which call attention to the name of the drug product but do not include indications or dosage recommendations for use of the drug product." [66] In addition to the brand name, they generally include an advertising image and text that suggests you 'ask your doctor' about the medicine, and often images or text that hints at a product's use without directly stating it. It is impossible to mistake a reminder ad for anything other than product-specific prescription drug advertising.

The rationale for this new interpretation of the law is puzzling if the aim of prohibiting DTCA is to minimize risks associated with use of prescription-only products by forbidding companies from advertising these products to the public in order to stimulate sales. It also contrasts with the wording of the Act and Regulations, as the 1978 amendment allowing comparative price advertising is the only exception to a general prohibition of prescription drug advertising aimed at the public. The Minister's interpretation did not explicitly exclude advertising with emotive images, advertising text, or suggestions to 'ask your doctor', although these are 'representations other than' name, price and quantity, and as such are excluded under the price advertising amendment (Section C.01.044).**

An April 1999 Health Canada discussion document on direct-to-consumer advertising, which contained a detailed explanation of the law, enforcement procedures, and the experience in Canada to date, did not say that reminder ads and disease-oriented ads were legal in Canada.[67] This suggests that the interpretation of the law shifted sometime between April 1999 and September 2000.

** This has not been tested in a legal case.

The Food & Drugs Act sets out the general principles governing regulation of pharmaceutical promotion, but the job of developing standards and enforcement procedures has been largely delegated to the industry. Rx&D (Canada's Research-Based Pharmaceutical Manufacturers), the brand name industry association, regulates most forms of promotion aimed at health professionals through its Code of Marketing Practices. This covers information dissemination, free samples, continuing medical education, advertising displays, drug detailers, post-marketing surveillance, gifts and related promotional items, and market research.[68]

Published advertisements of prescription drugs, in print, audio, or audio-visual form, are subject to voluntary pre-screening by the Pharmaceutical Advertising Advisory Board (PAAB), a semi-autonomous organization with a board that includes members of the pharmaceutical and advertising industries, medical publishers, health professional associations, and consumers. Although the Board represents a range of sectors, those benefiting financially from pharmaceutical advertising (pharmaceutical and advertising industries and media) form the majority of members. Regulation of over-the-counter (OTC) drugs has been delegated to an advertising industry association, Advertising Standards Canada.

A 1997 report of a survey of marketing executives of multinational pharmaceutical firms in Canada indicated that the amount spent on 'patient education initiatives' had increased since 1994, with 9% of firms spending between 21-30% of their promotional budget on activities and materials aimed at patients, 22% spending 11-20% and the remaining 66% spending 1-10%.[69] The main techniques reported were: distribution of printed, audio-visual and other educational materials; educational grants to non-profits; toll-free information lines; disease awareness ads; package inserts; disease management programmes and health promotion programmes.

Many Canadian disease awareness ads are identifiably linked to a specific product. Prominent recent examples include a series of erectile dysfunction ads Pfizer ran in the Globe & Mail in October 1999 to promote sildenafil (Viagra), weight loss ads by Roche

in major newspapers and on bus shelters in Vancouver in late 1999 and early 2000 to promote orlistat (Xenical), and posters by Berlex in Montreal in December 1999 advertising estradiol and cyproterone (Diane-35) as an acne treatment. The latter included the name 'Diane' in an ambiguous reference that could have been to the drug or to the woman featured on the billboard. This was linked to a toll-free telephone number providing product information. The company stopped running the toll-free number after Health Canada stepped in several months later.[70] However, a follow-up billboard campaign included the product name and the suggestion that viewers 'ask your doctor or your dermatologist.' In an interview on the campaign, Carl St-Pierre, Berlex's marketing director, explained: "We saw what's happening south of the border and how it could impact our business." [70]

In December 2002 Health Canada published a safety advisory about estradiol and cyproterone (Diane-35), urging physicians to prescribe it only as a second-line product for severe acne, its approved indication. The advisory warned against use for birth control or mild acne due to higher risks of potentially fatal blood clots than with use of other combined estrogen/progestin products approved for birth control.[71]

Since late 1999, branded advertising has become increasingly common in Canada. In addition to the estradiol and cyproterone(Diane-35) campaign mentioned above, Glaxo Wellcome (now GlaxoSmithKline) has advertised bupropion (Zyban) to the Canadian public and Wyeth-Ayerst has advertised an estradiol and levonorgestrel contraceptive pill (Alesse). Both companies have run both reminder and disease-oriented ads for these products. Glaxo Wellcome aired a testimonial on a national television station, CTV, in which a woman says that she went to her doctor and finally found a solution to quit smoking, 'brought to you by Zyban'[72] and Wyeth-Ayerst ran separate but related disease-oriented and reminder video ads on a youth video channel.[73] The birth control pill (Alesse) campaign was found to violate Canada's Food and Drugs Act, but Wyeth-Ayerst was only asked to consider this decision "when developing future advertisements", and was not subjected to any fines, sanctions, or corrective actions, or required to immediately cease the current advertising campaign.[74] Health Canada asked Glaxo

Wellcome to stop running the bupropion (Zyban) television ad and the company refused, again without discernible negative consequences.[72]

Drugs are also being advertised on the Internet in sites originating in Canada. A U.S. FDA official raised concerns that it is often hard for viewers to distinguish commercial from non-commercial drug information.[75] This appears no less true for some Canadian promotional web sites. For example, a Canadian website promoting oseltamivir (Tamiflu) in January 2000 did not mention the sponsor's name.[76]

Regulatory response to these activities remains limited. Health Canada's Drug Directorate (now the Therapeutic Products Directorate) issued a policy paper in January 1996 on the distinction between advertising and other activities, which attempts to clarify precisely these grey areas.[77] This paper stresses that for a message to be considered advertising, its primary purpose must be to promote drug sales, and the manufacturer or sponsor must pay for it. A recent interpretation of this policy stresses further that "No one factor in itself will determine whether or not a particular message is advertising. Each message must be evaluated on its own merit..." [77] This leaves room for a large degree of leverage and ambiguity. In contrast, the Food and Drugs Act defines advertising as any representation by any means whatever for the purpose of promoting directly or indirectly the sale of any food, drug or cosmetic device.[62] In the Act, the aim of promoting sales is a clearly identified single factor that would allow regulators to determine whether or not a message was advertising.

Health Canada initiated a regulatory review in 1996 to discuss whether DTCA should be allowed, and sponsored a first consultative workshop in June 1996. The provincial governments, which are responsible for administration of health services and public drug plans, were opposed to the introduction of DTCA. Health Canada initiated a further round of consultations on DTCA in late 1998, as part of a broader discussion of renewal of Canada's health protection legislation, and a separate multi-stakeholder consultation on DTCA in April 1999. At this latter consultation, Health Canada proposed compromise solutions including partial introduction of DTCA or introduction for a limited range of

prescription-only products.[78] There was little support for these proposals, either among the advertising and pharmaceutical industries, which preferred full DTCA, or among opponents, who wondered aloud why only deregulation was on the agenda. A White Paper outlining proposed legislative changes, including proposals related to DTCA, was promised for early 2000 but had not appeared by April 2003.

The degree of Canadian exposure to DTCA originating in the U.S. via U.S. magazines, television and radio is not known. However, exposure is likely to have increased considerably since television advertising became common following 1997 U.S. regulatory changes. Canada does not require cable providers to replace advertising that is illegal in Canada if they are providing programming to a Canadian audience. If Americans see on average nine TV ads daily, Canadians would be estimated to see an average of two. [79] According to an Ipsos-Reid poll of a nationally representative sample in 2002, around half of the Canadian population (53%, 95% confidence intervals 50.5%-55.5%) is unaware that prescription drug advertising is illegal in Canada. [80]

Visiting Health Canada's website provides little clarification. A Health Canada fact sheet on pharmaceutical advertising, posted on the web in August 2001, includes no general statement on the illegality of prescription drug advertising to the public in Canada. Instead it says only that "specific requirements exist for advertisements of prescription drugs to consumers."[81]

In November 2002, The Canadian Medical Association (CMA) published a policy position in opposition to DTCA in the *Canadian Medical Association Journal.*[82] The CMA explained its belief that advertising made the public think of prescription drugs as consumer goods rather than medical treatments and "may not provide enough information to allow consumers to make appropriate drug choices". The CMA additionally raised concerns about effects on the cost of care and on the patient-doctor relationship. The CMA's rationale for developing this policy was their understanding that the federal government intended to review DTCA policy again in late 2002, and the lack of opposition to DTCA expressed by the industry minister, Alan Rock. Interestingly, the

CMA placed responsibility for policy development on DTCA with Industry Canada, not Health Canada.

In summary, Canada has seen a large change in exposure to DTCA during the late 1990's and early 2000's, due to two factors: U.S. deregulation of broadcast advertising, which has increased the flow of cross-border advertising, and a shift in interpretation and enforcement of the law in Canada, leading to two forms of advertising becoming widespread: reminder ads and disease-oriented ads. These are likely to have affected both private and public drug costs. The British Columbia provincial government raised concerns in May 2000 about increases in provincial drug costs due to "Aggressive direct-to-patient marketing by pharmaceutical companies..." [83]

If DTCA is not allowed under the Food and Drugs Act as a health protection measure, enforcement is justified. If a precedent now exists for treating the 1978 price amendment as a loophole allowing reminder advertising, a further amendment with clarifying language may be needed. Interestingly, Australia's review of its health protection legislation provided an example of how such an amendment might be worded; a recommendation to introduce price advertising included detailed provisions that would prohibit advertising images or product-specific reminder advertisements.[84]

Introduction of DTCA appears still to be under discussion, although it has not been highlighted as such: a new round of 'legislative renewal' is announced for 2003, highlighting the need to modernize federal health protection legislation. The introduction of DTCA appears to be back on the table as part of this move towards 'modernization'. Health Canada has also begun a review of the list of Schedule A diseases in the Food and Drugs Act. This list of diseases provides a potential barrier to DTCA, although at present there is little enforcement activity focussing on Schedule A diseases.

If the federal government proposes to change the law, proposals to introduce prescription drug advertising should be clearly identified as such and should be subject to full public and parliamentary debate. To date, changes have been introduced by stealth rather than

through legislative change, and it is becoming increasingly clear whose interests Health Canada is intent on protecting.

6.1.4 Australia: DTCA to remain illegal

Australia prohibits the advertising of prescription drugs to the public. Like Canada and most European countries, Australia also relies on industry self-regulation of promotion. The Australian Pharmaceutical Manufacturers' Association (APMA) Code of Conduct Committee is responsible for enforcing promotional regulations. The APMA's code specifies that, "Any activity directed towards the general public which encourages a patient to seek a prescription for a specific prescription-only medicine is unacceptable."[85] However, disease-oriented advertising is allowed as long as a product name is not mentioned. In 1998, Pfizer's launch of sildenafil (Viagra) was accompanied by an advertisement featuring faceless men in boxer shorts and the caption, "52% of men aged 40-70 have one thing in common. Erectile dysfunction. See your family doctor about treatment options that are now available." Some of the ads carried a large red 'V', which Pfizer insisted was for victory, not Viagra, according to a report in *Australian Doctor*.[85]

In 1999 and 2000, Australia undertook a review of its health protection legislation from a trade and competition perspective. Health economist Rhonda Galbally was asked to carry out this review for the Therapeutic Goods Administration, Australia's national drug regulatory agency. It involved broad consultation among interested parties and the public, and addressed restrictions on prescription drug advertising among a range of other limitations imposed by health protection legislation. Her report, published in September 2000, firmly recommends against the introduction of DTCA, with the exception of comparative price advertising.[84] The recommendations on price advertising include strict criteria, such as limited font size, no advertising images, and inclusion of competing products from different manufacturers in postings of product prices, to prevent this provision from being used as a loophole for product-specific DTCA.

6.1.5 The European Union: Intense pressure for legislative change

Advertising of prescription drugs to the public is prohibited in all countries of the European Union. The European Council's 1992 Directive on advertising of medicinal

products for human use explicitly says that, "Member States shall prohibit the advertising to the general public of medicinal products which are available by prescription only. "[86] In April 1999, the European Commission suggested setting up a dedicated working group of its pharmaceutical committee to look into direct-to-consumer advertising. Patrick Deboyser, head of the pharmaceuticals unit in the industry directorate DGIII, said that the current blanket ban was 'out of phase with world developments.' However, legislative change would need approval by the European Parliament and the Council of Ministers and would be unlikely to occur for five to 10 years, according to Mr Deboyser.[87]

As in Canada and Australia, the pharmaceutical industry has increasingly begun to target promotional campaigns at the public in Europe. "As for advertising prescription drugs to European consumers," said Wayne Koberstein, editor of Pharmaceutical Executive, "I've spoken to European [chief executive officers of pharmaceutical companies]. They say there are laws against it, but you'd be surprised how much is going on." [88]

A U.K. campaign in July 1999 accompanying the launch of tolterodine (Detrusitol, brand name Detrol in Canada) featured full-page newspaper ads: "Greater freedom from bladder problems... your doctor, nurse and continence advisor have treatments that can help."[89] The campaign mentions sponsorship by Pharmacia & Upjohn but not the product's name. Novartis had carried out a similar campaign for terbinafide (Lamisil), a product for toenail fungal infections, the year before.

Pharmacia & Upjohn was the first company to take its campaign one step further and follow up print ads with television ads telling viewers that help was available from their doctor for bladder problems.[90] The U.K. Medicines Control Agency reviewed the ads and did not believe they contravened the Medicines Act. However, the U.K. Consumers' Association has called for a government review, questioning the appropriateness of industry-sponsored disease information campaigns tied to a product launch.
In the Netherlands, Roche advertised its anti-obesity drug orlistat (Xenical) to the public with newspaper ads on obesity in November 1999, referring readers to its website. Roche's site is then linked to an obesity site with information on orlistat. Similarly, Glaxo

Wellcome launched bupropion (Zyban) with advertisements in newspapers and cinemas. A news report in late January 2000 stated that the Dutch Health Inspectorate had taken legal action against the companies on the grounds that they violated Dutch laws prohibiting advertising of prescription drugs to the public.[91] The Dutch Health Inspectorate reported large increases in patient visits to family physicians for toenail fungus following an unbranded television campaign.[92] This campaign also prompted a group of Dutch family physicians to call for a boycott of Novartis in 2002. [93]

These are examples not only of companies' attempts to circumvent Dutch laws but also of the Dutch government's willingness to take regulatory action in response to alleged violations. Both bupropion (Zyban) and orlistat (Xenical) have also been advertised to the public in Canada, without any threat of legal action in response. One barrier to regulatory action mentioned by Health Canada personnel in private conversations is that the Food & Drugs Act states that the maximum fine for a violation is $5000. Under Dutch law the maximum fine for a violation is similarly restricted. However, the Dutch Health Inspectorate has interpreted this restriction as applying to the maximum fine for each showing of an illegal advertisement, which can quickly add up to fines of tens to hundreds of thousands of Euros.[94]

The Dutch government set up a special unit to enforce pharmaceutical advertising laws in April 1999, the Health Care Inspectorate Advertising Monitoring Department.[95] The Dutch Health Inspectorate has taken GlaxoSmithKline to court over an advertising campaign for bupropion (Zyban) that linked a television and cinema smoking cessation ad with a the company's website and information materials. The court ruled that that, "The Internet site and brochures contained inadmissible promotional text that was, in fact, advertising." [96] Another court case against Roche judged that advertorials (paid editorial text) promoting use of the obesity drug orlistat (Xenical) were illegal. In this case, only one of a number of charges brought against the company was upheld. Although a newspaper account reports that the prosecution requested a prison sentence for Roche's director, Mr. Bieri, this was refused and he was fined for 35 infractions instead.[97]

For European countries with national medicines reimbursement, a key concern is the effect of DTCA on costs. Philip Brown, publisher of the pharmaceutical industry bulletin *Scrip*, predicts dire consequences for the public provision of health services: "What will happen, I suspect, is that health service authorities in Europe and elsewhere will have to start thinking the unthinkable, namely that more and more patients will have to pay fully for their prescription medicines. So much so that only the needy and destitute will get their pharmaceutical treatment at no cost."[98] The U.K. Consumers' Association similarly raises concerns that DTCA will lead to unsustainable cost increases and an erosion of public commitment to health care coverage.[99]

In July 2001, the European Commission released a proposal to allow pharmaceutical companies to promote products for three types of illnesses – HIV/AIDS, diabetes, and asthma – directly to consumers.[100] The rationale presented for their introduction was "to respond to expectations expressed by patient groups," and Commissioner Erik Liikanen emphasized in public statements that, "this is not direct to consumer advertising."[101]

The proposals under discussion, however, were for changes to Articles 86-88 of Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use, including deletion of a clause listing specified serious diseases that could not be advertised to the public, and replacement of a general clause stating that prescription drugs could not be advertised to the public with a proposal allowing companies to disseminate information on drugs for AIDS, asthma and diabetes.[102] These proposals included no restrictions on dissemination media or on target audience. Thus, although the Commission stated that its proposal was not for introduction of DTCA, the proposed changes to advertising regulations did not exclude product-specific DTCA campaigns. The proposal included a provision for pre-screening of materials by the European Medicines Evaluation Agency (EMEA), Europe's centralized drug regulatory agency. Leon Wever, Director of Pharmaceutical Affairs and Medical Technology at the Dutch Ministry of Health, commented that: "If access to information is the purpose, then new E.U. legislation is not necessary. If, on the other hand, permitting direct-to-consumer

advertising is the purpose, then E.U. legislation is needed."[96]

In spite of claims that the proposed changes to European legislation were a response to requests by patient groups, European networks of AIDS, diabetes and asthma patient groups failed to support this proposal.[103]

Following two negative European Parliament committee reports, by the Environment and Health Committee and the Committee on Industry, External Trade, Energy and Research, the Parliament voted against this proposal 494 to 42 on October 23, 2002.

The European experience is of interest because of the confusion created by an unclear distinction between 'advertising' and 'information' in the discussion of a proposal for partial deregulation of pharmaceutical advertising. This proposal was embedded within broader recommendations for change to pharmaceutical regulation, similar to 1998 and 2003 discussions of legislative change in Canada. Originally, DTCA was barely mentioned in Health Canada documents discussing these legislative proposals.[104] As with the European proposal, when this part of the legislative renewal process became publicly known, it was highly controversial and received considerable press attention.

The proposal to introduce DTCA in Europe came from DG Enterprise (the European Commission directorate concerned with industry and industrial development), as pharmaceutical regulation falls under its mandate, rather than within health. This has led to suggestions that the proposal's aim is to support the European pharmaceutical industry, rather than giving central priority to public health aims.[101] During the discussion of the Commission's proposal, one fourth of the members of the expert committee responsible for overseeing pharmaceutical regulation, the Committee on Proprietary Medicinal Products (CPMP) wrote an open letter to the European Parliament not only recommending against introduction of DTCA, but also suggesting that pharmaceutical regulation be moved from industry to health.[††] [105]

[††] The recent Canadian experience would suggest that even if the regulatory responsibility resides within a health agency, it can be affected by industrial interests.

Concerns about sustainability of publicly funded health care services featured prominently in parliamentary comments on the proposal, as did the lack of evidence linking DTCA to beneficial health outcomes. Several non-governmental organizations, including the European Public Health Alliance, Health Action International, BEUC (European network of consumer organizations), U.K. Consumers'Association, La Revue Prescrire (a French independent drug bulletin), and BUKO Pharma-Kampagne in Germany, played a key role in raising awareness about the proposal and coalescing opposition. It was probably helpful that the major pharmaceutical producers in Europe – the U.K., Germany and France – were represented by nationally based consumer groups, as these countries were likely to have had the greatest initial influence on the Commission's proposal. National governments in Finland, Germany the Netherlands and the U.K. expressed their opposition to the proposal before the parliamentary vote. Additionally, a broad coalition of health professionals, consumer and patient groups, and insurers (mainly French), called *Medicines in Europe Forum,* was formed while the legislation was under discussion with the aim of opposing the Commission's proposals and recommending other changes seen as necessary from a public health perspective. See Appendix 6.1 for a list of member organizations.

A *Financial Times* article published on the eve of the parliamentary vote commented that: "The way medicines are sold has become one of the touchstone issues of modern capitalism. Companies in the U.S. believe they have a right to publicise their products, while Europeans fear that spurious science will be used to push unnecessary cures on people for diseases they did not really have."[106]

Given the nearly 12 to 1 European Parliament vote against the introduction of DTCA, is the policy debate over? Writing in the *British Medical Journal* in 1999, Annabel Ferriman suggested that, with large potential profits at stake, the DTCA debate in Europe, "...is not likely to end until the drugs industry gets its way."[107] An article in the pharmaceutical industry trade bulletin *Scrip* published one week after the parliamentary vote quoted E.U. officials as saying that the Commission intended to keep its proposal

alive, although "there would be flexibility on certain aspects."[108]

Following the Parliamentary vote, the next step for the Commission's proposed changes to pharmaceuticals regulation was discussion by the Council of Ministers. In March 2003, the Council's Working Party on Pharmaceuticals and Medical Devices released the proposal to be passed on to the European Council.[109] Although the preamble to this document states that the Working Party "accepted a number of the European Parliament's amendments", the Commission's initial provision to introduce DTCA for AIDS, asthma and diabetes drugs remained unchanged. This was highly unusual: overwhelming parliamentary opposition would normally lead to abandonment or fundamental changes to a proposal for legislative change. However, in June 2003 the Health Council also rejected the Commission's proposal.[110] Thus, the introduction of DTCA in Europe appears unlikely anytime in the near future. However, Ferriman may still be correct in her prediction: with large profits at stake, such proposals are likely to resurface.

6.1.6 South Africa: DTCA regulation in the context of globalisation

Currently, South Africa allows advertising of OTC drugs to the public, but not prescription-only medicines. For regulation of advertising aimed at health professionals, South Africa relies on the PMA Code of Practice for Marketing of Medicines, a national industry self-regulatory code.

A South African policy review was carried out in 2000 to examine whether DTCA should be introduced in that country within the context of globalisation and access to U.S. advertising on the Internet. [111] This is the only analysis of national DTCA policy to date that aims to look at policy development within an international context and specifically takes as a starting point the accessibility of prescription drug advertising on the Internet.

Like Australia, South Africa is unusual among industrialized countries in having an explicit national drug policy, which incorporates principles of rational drug use as well as regulatory standards and management of supply and distribution of essential medicines. The aim of the DTCA review was to consider, "...to what extent local and international

policies have taken into account new technologies available to drug advertisers, and what mechanisms might be employed in South Africa to reach the objectives set by the National Drug Policy" for a "...consistent, coherent, comprehensive and sustainable model for regulating drug advertising in South Africa."

The authors of the policy review began with a review of guidelines governing the regulation of drug promotion developed by the World Health Organization, U.S. FDA, South African Medicines Control Council, South African Pharmaceutical Manufacturers' Association (PMA), and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA). On the basis of these guidelines, they developed a set of policy questions posted via electronic list serves to individuals and organizations with expertise in essential drugs and pharmaceutical policy. The responses were used to supplement the review of regulatory guidelines and to develop a model of regulation of drug advertising meeting criteria for coherence, policy consistency, comprehensiveness and sustainability.

The authors received 10 responses to their e-mail survey of pharmaceutical policy experts: four from South Africa (2 hospital pharmacists; an industrial pharmacist and a community pharmacist); two from the U.S. (one molecular biologist; one advertising executive); a European pharmacy journal editor; a U.K. academic; and an Indian community pharmacist. Only the two U.S. respondents and one South African supported legalization of DTCA, and all but one believed that national laws should take precedence over industry self-regulatory mechanisms. Based on their own analysis of existing regulatory mechanisms and these responses, in combination with the stated objectives of South Africa's drug policy, the authors offered a number of recommendations:

- A preference for a co-regulatory system rather than sole reliance on industry self-regulatory codes because of the need for effective enforcement mechanisms. This should be funded through a dedicated levy on manufacturers;
- A national rather than international focus on regulating promotion, including websites that are locally based;
- Pre-vetting of websites prior to publication is unmanageable, due to the volume of information; but there should be a registration system for types of sites plus

organization of content, combined with an active monitoring system;

- All information providers, not just manufacturers, should be similarly subject to advertising regulations;
- DTCA should be prohibited;
- Substantiated, independent, contextualized treatment information is needed; a nationally funded information centre is needed in South Africa, and existing providers should be built upon, and "weaned, where necessary, from direct company support."

This review concludes with a recommendation against introduction of DTCA in spite of ready access to Internet advertising in South Africa and internationally. Instead, the authors suggest that South Africa undertake the regulation of Internet advertising originating within its borders. This is proposed as a practical solution, given the limited resources available and the pressing health needs of the South African population. The authors recommend making the industry responsible for the costs of regulation in order to avoid placing an undue financial burden on already overstretched national health services. They stress the need to provide independent information on medicines for the public as an activity that is separate from the regulation of drug advertising.

One of the interesting aspects of this and other policy discussions on the use of the Internet for DTCA is the suggestion by national pharmaceutical industry associations that national laws prohibiting DTCA are unenforceable because of the population's ready access to Internet advertising. For example, Canada's industry association, Rx&D, suggests that one of the key reasons Canada's law needs to change is that: "Today, Canadian consumers see pharmaceutical advertising and information daily on American television, the Internet, and in foreign magazines."[112] Given the international nature of the pharmaceutical industry, Rx&D is referring to advertising campaigns carried out by its own member companies in media originating in the U.S. Another option might have been for these companies to plan their U.S. advertising campaigns differently, in order to minimize population exposure to DTCA where it is illegal.

6.1.7 World Health Organization: ethical promotion excludes DTCA

The World Health Organization developed a set of criteria to guide the regulation of pharmaceutical promotion in 1988, the *Ethical Criteria for Medicinal Drug Promotion.*[113] This is the only international standard governing promotion of prescription drugs apart from an industry marketing code.[114] The W.H.O. *Ethical Criteria* recommend against DTCA, stating that: "Advertisements for the general public ... should not generally be permitted for prescription drugs or to promote drugs for certain serious conditions that can be treated only by qualified health practitioners, for which certain countries have established lists."

Several additional points are relevant, for example that advertisements "should not take undue advantage of people's concern for their health" and that, "scientific and educational activities should not be deliberately used for promotional purposes. These criteria are not legally binding; they are standards that can be used to develop regulation.

Kees de Jonchere, Regional Advisor for Pharmaceuticals and Technology for W.H.O.-Europe, stressed W.H.O.'s commitment to the *Ethical Criteria* in a 2002 discussion of the European Commission proposal to introduce partial DTCA: "Based on the *Ethical Criteria*, W.H.O. believes the E.U. and any country should be cautious in changing legislation when there is considerable potential for harm and little if any documented evidence of benefit."[115] However, he recognized that there are problems with current approaches to regulation of drug promotion in Europe. Existing E.U. legislation is being interpreted differently in different countries, particularly in terms of the dividing line between manufacturers' activities that are judged to be 'information' and those judged to be 'advertising' to the public. In some countries, manufacturers may freely post package inserts and approved labelling information on their websites, as this is non-promotional information; in others, manufacturers assert that they are prevented by law from doing so.

There are also widespread difficulties in dealing with hidden advertising, such as disease-oriented advertising and television news programming with advertising content. De Jonchere recommended closer collaboration between national Ministries of Health in

order to share strategies and resources, and also stressed the need to look at medicine use more holistically: "...a medication is actually the product plus the information plus the culture in which it is being used." As in the South African review described above, he stressed the need for high quality independent medicines information for the public in order to promote better medicine use, with improved health outcomes.

6.1.8 Conclusion – national and international policy reviews

A recurrent theme in DTCA reviews is the need to differentiate between the public's need for *information* on medicines as a basis for shared informed health care decisions, and manufacturers' interests in *advertising* marketed products. This theme appears in two key ways: in the blurring of this distinction in proposals to introduce DTCA (for example in the European Union); and in the recognition by promoters and critics of DTCA alike that provision of medicines information for the public is currently inadequate. Reviews in South Africa and Australia that have recommended against introduction of DTCA have also recommended that public authorities incorporate medicines information into health care provision.

Where DTCA is not allowed, governments have thus far decided to continue to prohibit it. Where DTCA is illegal, the burden of proof is on the industry to provide evidence of benefit and of safety. Where DTCA is currently allowed, governments have stated that they require clear evidence of harm before introducing more restrictive legislation. Thus, in the latter environments, the burden of proof appears to be put not on industry but on the government to ensure that newly introduced legislative restrictions would be justified.

In the U.S., for example, the federal government's right to regulate is being challenged as an undue restriction on companies' freedom of expression. Whether this challenge will be upheld is as yet unknown. In New Zealand, although a policy review ended with a recommendation for stricter standards for industry self-regulation, to be imposed by government, no new standards or procedures have been proposed nearly two years later, and a new policy review appears imminent.

Thus, in spite of similar goals for health protection and effective use of limited health care resources, different jurisdictions have come to opposing conclusions. In part, this may be explained by pressure from outside government, such as the court cases in the U.S. that restrict a federal agency's ability to regulate DTCA. However, these different conclusions have also been based on a single body of evidence – as well as gaps in evidence – on outcomes of DTCA.

Evidence and policy

As was discussed in Chapter 1, research evidence is only one of many influences on policy development, and barriers often exist to research uptake in policy decisions. Innvaer and colleagues carried out a systematic review of studies of health policy makers' perceptions of their use of evidence. They identified 24 interview studies and questionnaires surveys addressing policy-makers' use of evidence. These were mainly qualitative studies that attempted to explore determinants of the uptake of evidence; only three used random sampling techniques and an explicit sampling frame, allowing for generalizability. Table 6.3 highlights the importance of social relationships: over twice as many studies identified good communication as a facilitator as good quality research, and the main barriers identified were social rather than scientific. Two-way communication predominates as a facilitating factor or barrier to research uptake. This is sensible in terms of trust and ensuring that researchers address questions of importance to policy decisions. The authors point out that the key difficulty with close two-way communication, however, is in the potential for bias; the results may meet policy-makers' needs but may not necessarily be objective and reliable.

Table 6.3: What determines whether policy-makers use research evidence?

Factors facilitating use of research	Percent of studies (N=24)
Personal contact between researchers and policy-makers	54%
Timelines and relevance of research	54%
Summary report with clear recommendations	46%
Good quality research	25%
Research that confirms current policy	25%
Community pressure or client demand for research	25%
Inclusion of effectiveness data	13%
Additional barriers to use of research evidence*	
Mutual mistrust, including perceived political naivety of scientists and scientific naivety of policy-makers	33%
Power and budget struggles	29%
Political instability; high turnover of policy-making staff	21%

*excludes statements directly contrary to facilitating factors, such as 'absence of personal contact between researchers and policy-makersk.'

What is meant by use of evidence? The authors identify three types of use: direct, selective and enlightening. Direct use involves the incorporation of specific research results into policy decisions, simply put, if a policy-maker wants to build a bridge, he or she should use a design of proven strength and flexibility. A funding agency's decision not to pay more for a drug without evidence of therapeutic advantages over less expensive treatment alternatives would be an example of direct use of evidence. In the case of selective use, evidence that concurs with existing policy decisions would be used, other research results would be ignored.[116] This can also be called self-serving evidence use. If the evidence that is ignored is of marginal importance to health or society, fine; if it proves to be a key determinant of outcomes of policy decisions, then such an approach can prove disastrous. 'Enlightening use' helps to foster deeper understanding, and may extend beyond the immediate problem at hand. This is particularly difficult to assess, as it may underlie longer-term approaches to policy-making rather than specific decisions.

A related factor is the strength, quality and admissibility of evidence, as discussed by Hadorn (see Chapter 1).[117] This is especially relevant to the evidence that has been raised in policy discussions of DTCA. For example, the U.S. FDA's survey of physicians'

experiences of consultations affected by DTCA could not examine the direction of effect as it included no comparison to consultations not affected by DTCA.[118] In spite of this shortcoming, which makes interpretation difficult if not impossible, survey results were presented as convincing evidence that DTCA benefits the patient-doctor relationship and should be introduced in Canada.[119] Similarly, the Research Medicines Industry in New Zealand provides evidence that DTCA has provided health benefits to obese patients through reports of patients who enrolled in the 'Xenical Weight Management programme', 70% of whom rated the drug positively, and only 1% of whom reported severe gastro-intestinal adverse effects.[53] This ignores any self-selection on the part of patients who decided to contact the company or not, or a connection between the decision to enroll or remain in the company's programme and positive or negative experiences on the drug. In contrast, a randomized controlled trial with adequate follow-up of all initially randomized patients could have provided reliable information about the proportion of patients benefiting from the drug and/or experiencing negative effects.

Following the New Zealand policy review, the Ministry of Health published a discussion paper summarizing the 43 submissions received on DTCA.[120] This discussion paper simply summarizes the claims made in different submissions. It fails to transcend an approach of: "some people said this; others said that"; there is no analysis of the validity of claims or the quality and strength of evidence used to back them.

Diverging policy aims and interests

Underlying the different responses among policy-makers to a single body of evidence (and considerable gaps in evidence) on the outcomes of DTCA is a contradiction between diverging policy goals: public health, equity and industrial development.

DTCA increases product sales and thus may be expected to have a positive effect on the profitability of companies and on industrial development within the pharmaceutical sector. The rapid growth in spending on DTCA in the U.S. and New Zealand also suggests a boon for the advertising industry and media. Its effects on equity in health care provision are likely to be negative, given the importance of the growth in drug costs in

primary care to unsustainable increases in overall public health care costs.[121] From a public health perspective, there is little to no evidence of benefit, and a precautionary approach does not support the introduction of DTCA, given the evidence that it stimulates widespread use of new pharmaceuticals before their less common and longer-term risks are known.

Given the similarity of discussions on legalization of DTCA in different jurisdictions, it is no surprise that initiatives advocating introduction sometimes transcend national boundaries. A forum organized by health sciences editors in 2003 to discuss pros and cons of introducing DTCA in Canada included only one organization claiming to represent consumer interests.[122] The organization, Advocare, was formed recently and has as its primary aim the legalization of DTCA in Canada. It is financed entirely by the pharmaceutical industry and includes pharmaceutical and biotech companies among its affiliates (arguably producers, not consumers).[119] At a seminar in Italy in May 2002 on potential introduction of DTCA in Europe, a speaker from Farmindustria, the Italian brand-name industry association, included a quote in her presentation from the president of a 'Canadian patient organization', to show that patients wanted DTCA as a means of obtaining information on medicines.[123] The quote was from the president of Advocare.

Policy decisions are strongly influenced by who has a voice at the table, and the values they bring to decisions.[124] In an editorial in the *British Medical Journal,* Hoffman and Wilkes caution against the assumption behind pluralistic approaches that define health professionals and pharmaceutical companies as equivalent stakeholders in terms of their role in health policy discussions. Their relationship to patients and public health is not the same: "Doctors have a fiduciary responsibility to act in the best interests of their patients, and secondary goals including increased income or professional stature, must be held subordinate to that primary commitment. For-profit companies, on the other hand, have a primary goal of maximizing profits; indeed the responsibility of company executives is first and foremost to owners and shareholders."[125] One critique of the New Zealand Ministry of Health's review of DTCA is that when the results were transmitted to the

Minister, the Ministry failed to mention that nearly all submissions in favour of maintaining DTCA came from advertising and pharmaceutical industry interests.[51]

This review of national experiences with DTCA policy also raises questions about the relationship between democracy and commercial imperatives. In Europe a democratically elected parliament has voted against the introduction of DTCA by a nearly12-1 majority. Nevertheless, the initial proposal to introduce DTCA has been passed on to the Council of Ministers, as would usually have occurred only if the parliament had voted in favour of the proposal. In Canada, consultations have been held since 1996 on the possibility of legislative change to introduce DTCA, but no new legislation has been tabled thus far. However, far-reaching changes have been introduced without being subject to parliamentary debate. Although such a change could be subject to legal challenge, thus far no such challenge has occurred.

6.2 Legal Issues: Liability, privacy and freedom of expression

6.2.1 DTCA and product liability

Pharmaceutical executives expressed hesitation about embarking on DTCA in the U.S. in the mid 1980s because of fears that it would increase their liability by weakening the 'learned intermediary' defence. This legal defence is based on the physician's responsibility for prescribing decisions. Because the patient's physician is acting as a 'learned intermediary' when he or she prescribes a medicine, the company is protected against lawsuits from patients who claim that they were not adequately warned of potential risks. The manufacturer must adequately inform the doctor about the product's potential risks and conditions for appropriate use. It is the doctor's responsibility to take this information into account in prescribing decisions and to pass it on to the patient. If companies directly advertise their products to the public, does their liability change? In a commentary in the *Journal of the American Medical Association*, Mello and colleagues argue that DTCA has already resulted in changes to the learned intermediary defence, but the jury is still out: the extent to which DTCA will lead to heightened liability remains

unknown.[126] How it will change in coming years depends on the empirical evidence that becomes available on the effects of DTCA on doctor-patient relationships, as well as on the content of advertising, and the aggressiveness and truthfulness of individual marketing campaigns.

Throughout most of the 1990s, U.S. courts upheld the learned intermediary doctrine in product liability cases, whether or not the product was advertised to the public. A 1999 New Jersey Supreme Court decision on a product liability case involving levonorgestrel implants (Norplant) is the first case to call the learned intermediary defence into question in the case of a product that is advertised to the public.[127] ‡‡ In a 5-2 ruling, Justice Daniel O'Hern found that Wyeth Ayerst had not adequately warned users about side effects such as painful removal with permanent scarring. He ruled that because mass marketing of prescription drugs seeks to influence the patient's choice of drug, the physician's role is altered and the manufacturer has a duty to provide proper warnings of the dangers or side effects of a product.[128]

This ruling is only binding in New Jersey courts, but many pharmaceutical companies are based in New Jersey. Levonorgestrel implants (Norplant) must be surgically implanted, and therefore the doctor was centrally involved in administering the product. The ruling is expected to have even greater implications in product liability cases involving self-administered prescription drugs.

This type of ruling was anticipated in a case study of a multi-page 1993 DTC advertisement for another contraceptive, medroxyprogesterone injections (Depo Provera).[129] The author uses this ad to pose questions about the manufacturer's potential liability. Following review of related cases, he concludes that the ad could expose Upjohn to state product liability suits because it does not disclose a serious short-term side effect: heavy and prolonged menstrual bleeding. Although the company would probably raise the learned intermediary defense in a court case, it might fail. He argues that in the

‡‡ Levornestrel implants (Norplant) have since been withdrawn from the U.S. market.

absence of evidence that the FDA-required fine print labelling information (the 'brief summary') is read and understood by the public, warnings are insufficient.

A related question was raised during the FDA's 1995 consultations on DTCA. A U.S. consumer organization, Public Citizen Health Research Group, raised the spectre of FDA liability for harm associated with inadequate regulation of DTCA: "If DTCA leads to less appropriate, perhaps more dangerous or more expensive therapy, the FDA has a legal responsibility to halt DTCA until regulations specific to this form of promotion are finalized that will ensure the public safety."[130]

Regulation of print DTCA is governed by the same rules in the U.S. as physician-directed advertising. Thus the required 'brief summary' of risk information is frequently presented in very small print and in medical language that even well-educated members of the public find incomprehensible. An analysis of 10 ads in the May 2002 issue of *Reader's Digest* applied a standardized readability scores to assess language difficulty. [131] Six were scored as 'very difficult' requiring on average 17 years of education (one year beyond a bachelor's degree); the remaining four on average required a high school education. Only 9% of U.S. adults have more than a bachelor's degree, and the proportion is between 4% and 7% for age groups over 65, according to March 2000 census data.

Under existing U.S. law, although companies must provide specific risk information in print advertisements, they are free to do so within a variety of formats, including more 'consumer-friendly' question and answer formats in a normal size front, using language that is easily understood. Companies that provide risk information in DTCA in a form that has been shown not to communicate the information adequately to the public could find themselves more vulnerable in future product liability suits, particularly under conditions of a weakened learned intermediary defense.

6.2.2 Privacy – state legal cases

One potential effect of DTCA is invasion of privacy, because marketers are interested in tracking sales and following up customers. This is of particular concern if members of the

public are directed to contact the company for additional information, either through a 1-800 number or a web site. In either case, availability of detailed risk information is linked to an opportunity for the company to obtain personal information about consumers.

As suggested by the description of a session at a 1999 New York marketing workshop on DTCA, reproduced below, companies are tracking individual patients who contact them through 1-800 numbers and web sites. In this case, it is not a person's professional activities that are subject to scrutiny but personal medical records.

Table 6.4: A DTC Marketer's Perspective on Patient Privacy

"What Really Happens After a Consumer Responds to a DTC Ad by Dialing an "800 number" for More Product Information
In this session, an examination of consumer behavior after a consumer has called in response to an ad will be examined [sic] so as to develop a strategy to mine prospects and measure downstream response. ➢ Developing and structuring a highly-segmented database of those who call in from the various media vehicles i.e. TV, print, etc. ➢ Measuring conversion rates: patients who see their physicians, request a drug, are prescribed it, and purchase it. ➢ Understanding the interaction at the doctor's office ➢ Contrast conversion rates between patients referred to physicians and those who seek out their own primary care physicians. ➢ Follow up at periodic intervals to determine who's still on the drug. *Lorri Sidotti, Vice President, The Marketing Workshop, Inc*

Source: Brochure for DTCA conference, Strategic Marketing Service[132]

David Woodward, Assistant Attorney General for Minnesota, reviewed the consumer protection implications of new trends in pharmaceutical marketing in 1996.[133] He described state legal cases that have set a precedent for protection of privacy and called for measures to safeguard the confidentiality of patient medical records. He states that, "A central aspect of privacy is the right to control personal information about oneself, including medical information." These comments were mainly made in relation to the purchase of pharmacy benefit managers (PBMs) by pharmaceutical companies in the mid 1990s, leading to access to personal records that could be used for marketing. However, they are also relevant today to medical information collected as part of a DTCA marketing campaign.

Consumer privacy was also one of the issues addressed by a multi-state informal working group of state consumer protection staff in June 1994.[134] Woodward describes a case

involving the company Miles Inc, and payments to pharmacists to switch patients to its antihypertensive. A second case involved Upjohn and a diabetes drug. In both cases one of the arguments put forward by the states was that consumers' privacy interests were undermined. A condition of the settlement with Miles was that the company would not try to obtain confidential consumer information in the future.

6.2.3 Legal concerns in Canada: Charter rights

In Canada, the main legal issue discussed in relation to DTCA is freedom of commercial communication. A 1995 Supreme Court case on tobacco advertising[135] is frequently cited as evidence that the current prohibition against prescription drug advertising to the public in the Food and Drugs Act would not be upheld in a Charter challenge. In the 1995 case, the Supreme Court upheld the tobacco industry's challenge of legislation banning all tobacco advertising in a split decision, 5-4, on the basis that it was an unnecessarily extreme infringement on the industry's freedom of communication.

From a public safety perspective, the decision in this case was a reversal of the burden of proof: it was up to Health Canada to prove its case that a complete ban on advertising was necessary to protect health, as opposed to a partial ban.[136] The tobacco industry was not required to prove that partial tobacco advertising would be safer than a full ban. The relevance of this decision to DTCA remains unclear, given the different legal implications of prescription-only status and the heavily divided opinions of the justices. Additionally, one of the factors cited in the tobacco decision was Health Canada's failure to bring forth evidence from research the agency had carried out on the health implications of a partial versus total ban of tobacco advertising.

Following the 1995 court decision, new legislation restricting tobacco advertising was passed in 1997. The 1997 *Tobacco Act* prohibits ads that are deceptive, misleading or likely to create an erroneous impression, as well as testimonials and endorsements, which are defined to include the depiction of a person, character or animal (real or fictitious). It also prohibits lifestyle advertising, and restricts the industry from advertising in specific media.[137] The tobacco industry immediately challenged the new Act, leading to a

prolonged court battle. In 2002, a Quebec Superior Court upheld the constitutionality of the Act.[138] This decision may still be appealed to the Supreme Court.

Throughout this process Health Canada actively pursued a strategy in support of extensive legislated restrictions on the advertising of a marketed product when there was a public health imperative in doing so, in spite of strong industry opposition. A Health Canada fact sheet on tobacco marketing entitled "Tobacco Marketing Makes us Sick" explains to young people that U.S. laws are not as stringent as those in Canada and attempts to warn readers about the emotive messages and images in tobacco ads in U.S. magazines sold in Canada.[139] In contrast, nowhere on Health Canada's website or in other information materials is there a clear explanation of the rationale behind legal differences in prescription drug advertising regulations in Canada and the U.S. nor any comment on potential negative health effects of U.S. pharmaceutical advertising aimed at the public.

Health Canada's response to the Supreme Court case on tobacco advertising has been to continue to pursue policies limiting public exposure to advertising campaigns that promote smoking in spite of legal challenges. This contrasts dramatically with the agency's response to the 1995 case when it comes to pharmaceutical advertising. In February 2003, the Health Canada official who is responsible for legislative renewal cited the 1995 Supreme Court tobacco decision as a key reason the agency was still pursuing policy development leading towards the legalization of DTCA.[140] 'Legislative renewal' refers to plans to replace Canada's Food & Drugs Act and related legislation with a new omnibus health protection act, in the process opening up the possibility of legalizing DTCA. The federal government is hoping to introduce new legislation within 2003.[140]

In a review of Canadian law in relation to advertising contraceptives to the public, Rhonda Shirreff points out that advertising has been identified in relevant case law as lying far from the core of guaranteed freedom of expression.[141] In addition to the tobacco case discussed above, a 1998 decision also upheld freedom of commercial speech. However, this was a challenge to the Canada Elections Act involving publication of political opinion polls, and therefore not directly related to advertising rights. Only one

case has involved the Food and Drugs Act. This involved the list of serious diseases, Schedule A diseases, for which a manufacturer may not advertise a preventative or treatment. A margarine producer had advertised its product as being protective against heart disease. The Court upheld the restriction, judging the advertising campaign to be illegal because this is a Schedule A disease. The implication, legally, is that DTCA for Schedule A diseases would not survive a legal challenge.

Conclusion: Legal concerns

In addition to effects on public health and on the cost and quality of health care services, DTCA has implications for manufacturers' liability and physicians' legal responsibility in drug-induced injury, protection of individual privacy, and commercial freedom of expression.

These legal implications are part of the policy debate on DTCA, although in many cases they are being argued behind the scenes. Physicians are in a difficult position legally if they are under pressure from patients to prescribe advertised drugs, as has been reported in physician surveys, and yet they remain wholly legally responsible for the prescribing decision. The U.S. FDA has brought in regulations for broadcast advertising that send viewers and listeners to company websites, a regulatory decision that appears to have been taken without concern for potential risks to the privacy of individual patients. The degree to which some individuals avoid company websites and telephone lines because of privacy concerns, and therefore experience a barrier to access to product risk information, is unknown. In Canada, a highly divided Supreme Court decision on tobacco advertising appears to have led two branches of Health Canada to respond in diametrically opposite fashions: in the case of tobacco, Health Canada has built up its case and stood its ground; in the case of drugs it appears unwilling to uphold existing health protection legislation. At the very least, the implications of this case should be clarified to ensure a coherent and consistent policy response.

6.3 Consumer Health Information

A Case Study : esomeprazole (Nexium) radio ad

A central point in policy discussions on DTCA is the role of advertising in informing the public about the availability and characteristics of medicines. The following section examines a recent U.S. radio ad for a heavily advertised product, esomeprazole (Nexium), a treatment for ulcer and gastro-esophageal reflux disease (GERD), as a case study in the role of advertising in information provision.

6.3.1 Consumer Drug Information Standards

In order to examine the role of DTCA in information provision, it is useful to compare the information provided in DTCA to existing information standards, and studies of patient information needs.

Several organizations have developed instruments to assess the quality of consumer information on health care treatments. DISCERN, developed for the U.K. National Health Service, is an example of a systematically designed and tested instrument used to judge information quality. [142] A panel representing a range of expertise in consumer health information designed the questionnaire. Questions were generated from a random sample of information materials on three conditions: myocardial infarction, endometriosis and chronic fatigue syndrome. A draft questionnaire was tested on a second random sample of information materials, redrafted, and sent to a national sample of health information providers and members of self-help groups. They were asked both to directly judge the content of the questionnaire and to test it by analyzing a random sample of U.K. patient information leaflets. The questionnaire was judged to be a valid and reliable measure of health information quality by a broad range of users, and has also proved to be highly reliable among experienced users.

The aim of the questionnaire is to judge the quality of information materials as an aid to shared informed treatment choice. As this role is frequently claimed for DTCA, it is

relevant as a measure of DTCA information quality. Fifteen criteria form the basis of the questionnaire. These are listed in Table 6.5.

Table 6.5 : Criteria for consumer information on treatment choices

Good quality information materials on treatment choices should:
1. Have explicit aims
2. Achieve those aims
3. Be relevant to consumers
4. Make sources of information explicit
5. Make date of information explicit
6. Be balanced and unbiased
7. List additional sources of information
8. Refer to areas of uncertainty
9. Describe how treatment works
10. Describe the benefits of treatment
11. Describe the risks of treatment
12. Describe what would happen without treatment
13. Describe the effects of treatment choices on overall quality of life
14. Make it clear there may be more than one possible treatment choice
15. Provide support for shared decision-making

Summary criteria from : www.discern.org. Accessed March 27, 2003

Another initiative in the U.K. used separate groups of clinicians with relevant expertise and patients with relevant conditions to review the quality of available patient health information materials discussing ten medical conditions and treatments.[143] The ten conditions were chosen because of the availability of systematic reviews of treatment effectiveness, against which patient information materials could be compared.

The authors found that the quality of materials was often poor, information was inaccurate and out-of-date, and technical terms were often not explained and topics of relevance to patients omitted. Areas of uncertainty were either ignored or glossed over and information about the effectiveness of treatments was often missing or unreliable. The study included focus groups of patients discussing health information needs. The patients stressed their desire for information about treatment options and outcomes even if they did not wish to participate actively in treatment decisions.

In addition to the types of quality criteria covered in the DISCERN questionnaire, the authors stress the importance of using patients' questions as a starting point and involving

them in the development process. Common concerns and misapprehensions should be addressed, and the sources and strength of evidence should be discussed.

A national Canadian study of patients' drug information needs similarly found that patients wanted complete, detailed information on expected benefits and harmful effects, duration of treatment, and the range of available treatment options.[144] This study also found a divergence in patients' identified information needs and the attitudes of physicians and pharmacists', who were leery of providing too much information on drug risks and side effects for fear that it might deter patients from taking their medicines.

Thus, studies from Canada and the U.K. have identified unmet patient needs for information on medicines. A key argument made in favour of DTCA, both by pharmaceutical industry proponents[68 53] and by governments considering introduction, [100] is that it can meet patients' needs for information about available treatment options.

6.3.2 Nexium radio ad: they didn't know, and now they do

How well does DTCA meet patients' information needs? Chapter 2 describes systematic analyses of advertising information quality in the U.S. and New Zealand. In this section, a single advertisement is presented as an exploratory case study: a recent U.S. radio ad for esomeprazole (Nexium). The advertising company that produced this ad for AstraZeneca, Interep, used it as a promotional example of the advantages of radio advertising in a bid to obtain more pharmaceutical industry customers, at a conference on DTCA held in Philadelphia in the autumn of 2002.[145] It was chosen as an example because the text of the ad makes explicit references to gains in consumer knowledge.

This is a reminder ad: it states the product's name but not its indication. The ad is especially relevant to policy discussions in Canada on DTCA because under the interpretation of the Food & Drugs Act published by Health Canada in November 2000, this and other reminder ads, in any media, would be considered legal in Canada. Table 6.6 contains the full transcript.

Table 6.6 Transcript of U.S. esomeprazole (Nexium) radio ad[146]

Man: I didn't know

Woman: I didn't know

Man: You may know an awful lot about a lot of things but here's something I'll bet you didn't know. I'll bet you didn't know there's a new purple pill. Introducing the new purple pill called Nexium. Nexium: esomeprazole magnesium to be exact. It's a prescription medicine you might want to know about.

Woman: I didn't know

Man I didn't know

Woman: I didn't know there was a new purple pill 'til I went to my doctor. It's called Nexium. And you know what? They've even got a new trial offer.

Man: Prescription Nexium is the new purple pill. And if you call 1-800-4 N-E-X-I-U-M. You'll get more information and a certificate for a free trial of Nexium for qualified individuals. Is a free trial of Nexium right for you? Talk to your doctor. Nexium. It's new. It's purple and maybe you should know about it.

Woman: Now I do.

Man: Talk to your doctor. And for your Nexium free trial certificate call 1 –800-4 N-E-X-I-U-M. Nexium, the new purple pill.

Since it is a reminder advertisement, the ad is not required by law to provide any product risk information. There is nothing in the law to *prohibit* an advertiser from providing risk information in any ad, including reminder advertising; this is an advertising choice. However, a reminder ad may not mention a product's indication or make any health claims. If it does so, it is considered to be a full product ad and is therefore required by law to provide major risk statements in a radio ad, as well as specified ways the listener may obtain full risk information, such as a company phone number and website.

In this case, AstraZeneca is using the public's awareness of another advertising campaign, for omeprazole (Prilosec in the U.S. or Losec in Canada) in order to provide hints of this product's indication. Omeprazole (Prilosec) was presented as 'the purple pill' both in U.S. full product DTCA and reminder ads. Calling esomeprazole (Nexium) 'the new purple pill' suggests to listeners that it has the same indication as omeprazole. Astra Zeneca spent U.S. $236.6 million advertising omeprazole to the U.S. public as 'the purple pill' from 1998 to 2000 inclusive.[147] Thus listeners are fairly likely to have been exposed to this advertising campaign and may connect the 'new purple pill' with the idea that the drug is a newer, similar medicine to omeprazole. If a listener has taken omeprazole,

which again is not unlikely with sales of U.S. $10.6 billion from 1998 to 2000 inclusive, he or she is highly likely to be aware of the indication, to treat gastro-esophageal ulcer or reflux (GERD).

AstraZeneca is gambling on a strategy to promote the brand name of the product with hints at its indication, in order to avoid having to provide risk information that would be legally required with a full product advertisement. The listener is unlikely to be aware of this aim, as it requires knowledge of nuances of U.S. advertising regulations. Two U.S. surveys have examined consumer knowledge of more basic aspects of regulation of promotion, a national FDA survey [148]and a survey of the Sacramento public by academic researchers. [149] In both cases knowledge of regulation was poor.

The two other aims of the ad appear to be brand name recognition and to let the listener know that a free trial offer is available. In both cases the advertiser has achieved its aims. The name Nexium appears nine times in this brief ad, plus an extra two times in the spelling of the phone number. The free trial offer features prominently as the key content being communicated to the listener. But how relevant are those aims to listeners' participation in shared health care choices?

A free trial offer of an expensive medicine may not be much of a gift in the long run. In this case it is especially questionable, given the likelihood of omeprazole coming off patent soon after the launch of esomeprazole, and cheaper generic equivalents becoming available.

Esomeprazole can be viewed as the product of a generous approach to patenting, in which a new medicine that is nearly identical to an existing patented product obtains its own separate patent protection. Omeprazole is a racemic mixture of two isomers. These are chemically identical compounds that have different spatial orientations. [150] One of these isomers is esomeprazole, also called S-omeprazole. In other words, esomeprazole and omeprazole are chemically identical, except that esomeprazole has a specific spatial

orientation that is shared by half of the chemical forming omeprazole (the other isomer is called R-omeprazole).

Some differences in pharmacological activity might be expected due to the different spatial orientation of the isomers. However, in this case the two isomers are actually 'pro-drugs.' When they are ingested, they become metabolized into the same active substance that acts as a proton pump inhibitor in the body. This active substance does not have any different forms with different spatial orientations. It is a single chemical, which is identical no matter whether it is derived from esomeprazole alone, R-omeprazole alone, or the racemic mixture of the two isomers, omeprazole.

The only difference between the two forms of this chemical is in their potency. Esomeprazole is not as susceptible to metabolism by the small intestine and liver and therefore reaches higher concentrations in the blood if the same amount, in milligrams, is ingested. A 20milligram (mg) dose of esomeprazole reaches nearly twice the concentration as a 20mg dose of omeprazole. Simply put, this means that taking a 10mg pill of esomeprazole is roughly equivalent to taking a 20mg pill of omeprazole. Taking a higher dosage would not necessarily provide therapeutic advantages, but if it did, the advantages from taking either 40mg of omeprazole or 20mg of esomeprazole would be expected to be similar. The FDA medical reviewer who examined the U.S. premarketing submission for esomeprazole raised concerns that concentrations of gastrin increased with both esomeprazole and omeprazole in a dose-related manner, and that long-term exposure to elevated levels of gastrin may be associated with an increased risk of stomach cancer.[151]

If AstraZeneca had wanted to provide relevant advice to listeners of this ad, the company could have suggested that after receiving their free trial offer, users could cut their pills in half and obtain a similar treatment effect as with a whole pill of omeprazole of the same dosage. If Canadians had been listening across the border, they could have been informed that requesting the higher dosage pill (40mg, which is not approved in the U.S. due to the FDA safety concerns mentioned above) and cutting it into quarters could be an effective

cost-cutting strategy. Of course, the listener with occasional mild heartburn is unlikely to need either product in the first place.

The only information provided about this medicine, beyond the brand-name Nexium, is the generic name, esomeprazole magnesium, that it is a prescription-only product, and that this is a 'new purple pill'. Esomeprazole (Nexium) is a pill and it is purple, although the colour is hardly relevant to treatment decisions. Whether it is really new is another question. Although this is not exactly untrue, it is hardly 'the truth, the whole truth and nothing but the truth', since esomeprazole is a chemical component of omeprazole and is metabolized into precisely the same active substance in the body. Calling this product 'new' is likely to mislead a public that is unaware of its chemical and pharmacological properties.

The ad fails every question on the DISCERN questionnaire except whether it has met its aims – to market a product. It is arguably foolish even to consider applying a measure of the quality of information on treatment options to this type of advertising message.

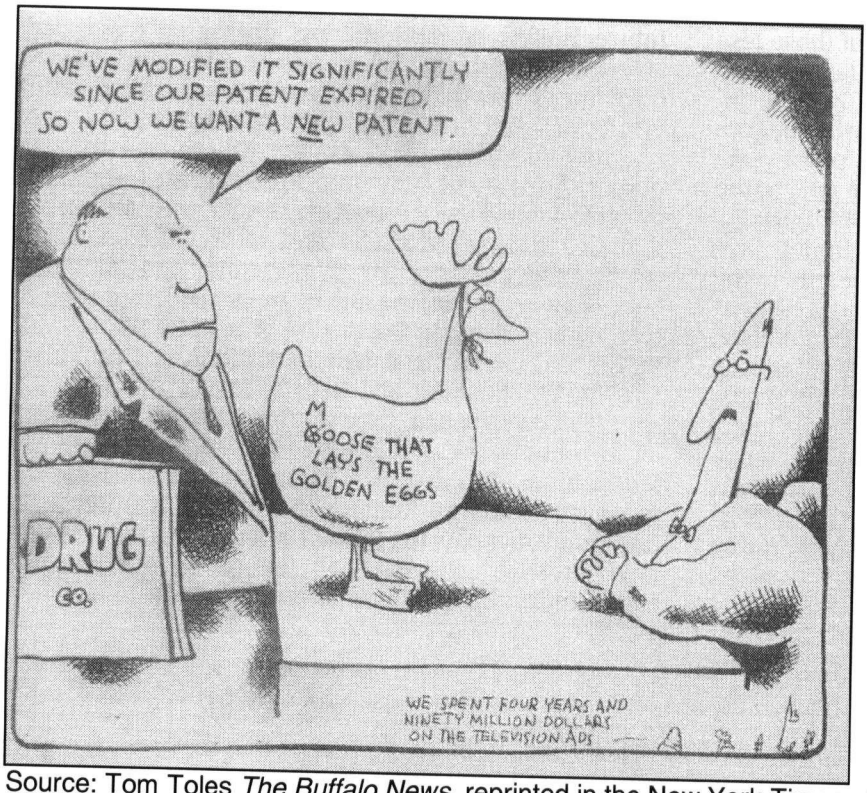
Is this a case of technical information being simplified so a lay public will readily understand it? This again is questionable. Tom Toles, cartoonist for the *Buffalo News*, provided a readily understandable explanation of esomeprazole's key characteristics (minus the product name) in a form that did not require a medical or pharmacy degree, as is illustrated below in Figure 6.2.

In spite of the frequent clash with reality, the rhetoric surrounding DTCA is that advertising provides a valuable source of information about medicines that helps to empower patients and enables them to participate in shared informed health care decisions. Canada's brand-name industry association states that: "Advertising medication would ultimately, and most importantly, give the Canadian consumer a choice. Canadians would be empowered to take charge of their health like never before... As long as roadblocks to DTC advertising remain, Canadians will lack a valuable resource in their health care decisions."[68] Alan Holmer, president of the U.S. industry association

PhRMA, similarly presents DTCA as a means of informing and educating the public: "Direct-to-consumer (DTC) advertising is an excellent way to meet the growing demand for medical information, empowering consumers by educating them about health conditions and possible treatments."[152] Similarly, the New Zealand industry group, RMI states that: "The growth in New Zealand of prescription medicines' advertising indicates a realisation by companies that the public has an increasing 'appetite' for knowledge about, and information on, health matters and treatment options including medicines."[153]

As Lewis Carroll said in *The Hunting of the Snark*, [154] "I have said it thrice. What I tell you three times is true."

Figure 6.2: the Moose Goose: esomeprazole and U.S. patent policies



Source: Tom Toles *The Buffalo News*, reprinted in the New York Times, June 9, 2002, WK 6

Appendix 6.1:

Members of Medicines in Europe Forum/ Membres du Collectif Europe et Médicament, October 14, 2002

Consumers groups/Associations et organisations familiales et de consommateurs
- Conseil National des Associations Familiales Laïques (CNAFAL), France
- Confédération Syndicale des Familles (CSF), France
- Familles Rurales, France
- Health Action International (HAI), Europe/NL
- Institut National de la Consommation (INC-60 Millions de Consommateurs), France
- KILEN Consumer Institut for Medicines and Health, Sweden
- Organisation Générale des Consommateurs, France
- Social Audit, U.K.
- UNAF (Union Nationale des Associations Familiales), France
- Union Fédérale des Consommateurs (UFC-Que Choisir), France
- Union Féminine, Civique et Sociale, France

Patient groups/ Associations de malades:
- Act Up Paris, France
- Act Up Toulouse, France
- Actions Traitements, France
- AIDES, France
- Association Française des Polyarthritiques (AFP), France
- Association de Lutte, d'Information et d'Etudes des Infections Nosocomiales (Le Lien), France
- Association pour le Recherche, la Communication et l'accès aux Traitements (ARCAT), France
- Conseil National des Associations Familiales Laïques (CNAFAL), France
- Dessine-moi un mouton, France
- European Federation of Asthma and Allergy Associations (EFA), Europe
- Federacion Estatal de Escuelas de Prevencion de Sida (FEES), Spain
- Fédération Française des Associations et Amicales d'Insuffisants Respiratoires (FFAAIR), France
- Fédération Nationale des Accidentés du Travail et des Handicapés (FNATH), France
- Fédération Nationale des Associations d'(ex) Patients PSY (FNAP-PSY), France
- Fédération Nationale des Associations de Malades Cardiovasculaires et Opérés du Cœur (FNAMOC), France
- Grupo de Trabajo sobre Tratamientos del VIH/SIDA (GTT), Spain
- HIV I-Base, United Kingdom
- Ligue des Diabétiques de France et Diabète & Nutrition, France
- Ligue Nationale Contre le Cancer (LNCC), France
- Lilia CEDIUS - Centre for human rights and public health, Italy
- Le Collectif Migrants contre le sida, France
- Réseau D.E.S. France, France
- Réseau Hospitalier des Usagers (REHSUS), France
- Sida info Service, France
- Sol en Si, France
- TRT-5 (groupe interassociatif de 8 associations de lutte contre le sida), France
- Union Nationale des Amis et Familles de Malades Mentaux (UNAFAM), France

Members of Medicines in Europe Forum – continued

Health insurers/ Organismes d'assurance maladie:
- Agencia de Cooperacion Internacional farmacéutica, Spain
- Association Internationale de la Mutualité (AIM), Bruxelles
- La Mutualité Française, France
- Union Nationale des Mutualités Socialistes, Belgium

Health professional groups/ Associations et organisations de professionnels de santé
- Arznei-telegramm, Germany
- Association Mieux Prescrire (AMP) et la revue Prescrire, France
- BUKO Pharma-Kampagne, Germany
- CRIM Rennes (Centre Régional d'Information sur le Médicament), France
- Der Arzneimittelbrief, Germany
- Dialogo sui farmaci, Italy
- Fundació Institut Català de Farmacologia, Spain
- Geneesmiddelebulletin, the Netherlands
- Groupe de Recheche et d'Action pour la Santé (GRAS), Belgium
- Informazioni sui Farmaci, Italy
- International Society of Drug Bulletins (ISDB)
- Mario Negri Sud, Italy
- Pharmaca and Bilten O lijekovina, Croatia
- Réforme & Santé, France
- RELIS Ost Drug Information Centre, Norway
- Ricerta & Pratica, Italy
- Syndicat de la médecine générale et la revue Pratiques, France
- Union des Syndicats de Pharmaciens d'Officine, France

Source: http://www.prescrire.org/aLaUne/dossierEuropeCollectif.php. Accessed March 20, 2003

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Chapter 7

Opinion survey of pharmaceutical policy experts in Canada

7.1 Introduction

Chapter 6 examined policy development on DTCA both in Canada and internationally. The main emphasis was on potential legislative and regulatory changes that are currently under discussion in countries where DTCA is currently legal as well as where it is not.

Canada is in a unique position among countries where DTCA is illegal, in terms of the degree of population exposure to cross-border advertising from the U.S. Thus pharmaceutical policy experts working in sectors likely to be strongly affected by full legal DTCA, should the law be changed, already have considerable experience with this form of pharmaceutical marketing. The federal government first began to discuss potential legislative change to introduce DTCA in 1996, and thus many with expertise in pharmaceutical policy have been involved in discussions of potential legislative change, either as 'stakeholders' or as government representatives.

This chapter reports on a survey carried out in February 2001 to solicit the opinions of pharmaceutical policy experts in sectors directly affected by direct-to-consumer advertising (DTCA) in Canada.* What are their opinions of the likely effects of direct-to-consumer prescription drug advertising (DTCA) on public understanding of drugs and diseases, quality of health care, and health care costs? Do they think that prescription drug advertising aimed at the public should be allowed, and if so, to what extent?

Four types of organizational sectors were included, reflecting a range of relationships to prescription drug advertising:

- *Health care payers, managers and regulators:* governments and private payers
- *Health care service providers:* health professional organizations

* The original survey also included pharmaceutical policy experts from the USA (N=24) and New Zealand (N=22); however as the aim of this chapter was specifically to examine policy development on DTCA in Canada, results of the Canadian arm of the survey are presented separately. The full survey results are posted at: www.chspr.ubc.ca

- *Health care users*: non-profit/consumer groups and disease/patient groups
- *DTCA producers and disseminators*: advertising and pharmaceutical industries.

The questionnaire was designed to probe respondents' views on DTCA information quality, and potential impacts on knowledge, quality of health care services, and direct costs. Additionally, respondents were asked their opinions on regulatory issues, including the types of advertising that should or should not be allowed, and appropriateness of different target groups and advertising media. These topics were derived from a literature review and informal individual interviews.

DTCA is controversial, with many claims made about benefits and risks and often very little empirical research to back those claims. This survey included questions about what type of evidence respondents had seen to support stated opinions. The questionnaire addressed direct effects of DTCA on patient knowledge, and use of health care services. It did not attempt to assess indirect effects of DTCA on hospitalization, morbidity or mortality because these hypothesized effects have not been researched and cannot be ascertained through personal observation alone.

7.2 Methods

Claimed benefits and harms of DTCA were compiled on the basis of the literature review described in Chapter 2, combined with informal individual interviews of experts working in sectors affected by DTCA in New Zealand and the U.S. Draft versions of the questionnaire were then circulated for review among Canadian researchers with expertise in pharmaceutical policy who had not been identified as potential survey participants.

Health Canada personnel working on drug policy and advertising regulation were invited to participate in the survey, as were representatives of the three pharmaceutical industry associations (representing branded and generic prescription drug manufacturers and OTC manufacturers), and national physician, pharmacist, nursing and consumer associations. Participants in the following committees and advisory groups were also invited to participate:

Non-governmental (industry, health professionals, consumers, patient groups):

- Multi-stakeholder consultation on DTCA held by Health Canada in April 1999
- Therapeutic Products Programme Advisory Panel on Drug Licensing
- *Government (provincial and federal):*
- Federal/Provincial/Territorial Advisory Committee on Health Services' Pharmaceutical Issues Committee (PIC)

In Canada, provincial governments administer health services, including publicly financed drug benefit plans. PIC included drug plan managers and policy experts from provincial and territorial ministries of health, as well as from a federal plan covering aboriginal people (Non-Insured Health Benefits), and federal policy-makers working on pharmaceutical policy issues. Additional names of provincial personnel were suggested by provincial government contacts in Manitoba and Quebec, and Health Canada provided names of policy experts from national industry associations.

A librarian with expertise in fugitive literature searches carried out an Internet search for additional unpublished reports on DTCA. Within the course of that literature search, she identified Canadian groups within selected sectors that had written policy papers on DTCA or on consumer medicines information, as well as individuals within each organization working on pharmaceutical policy.

Seventy-nine people were invited to participate (80 were identified, but one could not be reached). Contacts received a faxed questionnaire and cover letter explaining the survey (See Appendix 7.1), asking them to reply as soon as possible. Non-respondents received up to two additional questionnaires, by fax and e-mail, over a three-week period.

Results are reported by sector only, with individual responses kept confidential. If there were fewer than four responses in a sector, responses were combined with another related sector in order to maintain confidentiality. Analysis of results is purely descriptive. The aim of this survey was to solicit opinions of those directly working within sectors affected by DTCA and actively involved in policy discussions in Canada. It is not possible to accurately define a larger group of policy experts represented by this sample; neither can they be assumed to represent, for example,

health professionals or pharmaceutical industry personnel in general; thus statistical comparisons were inappropriate.

Ethics approval was obtained from the University of British Columbia's Research Ethics Board.

7.3 Results

7.3.1 Questionnaire Responses

The response rate was 76%, with 60 of 79 questionnaires returned. Table 7.1 presents a breakdown of respondents' affiliation by sector. There were three respondents with academic affiliations. Their responses were grouped with the closest relevant sector: marketing professors were included with the advertising industry, medicine or pharmacy professors with health professionals. Similarly, if a non-profit organization was associated with a specific sector, it was classified accordingly. For example, pharmaceutical industry trade associations were classified with the pharmaceutical industry. Private sector agencies mandated to review pharmaceutical advertising were classified with the advertising industry. As there were only two private insurance respondents (private drug payers), and confidentiality could not have been maintained with separate reporting, they were grouped together with government respondents, as this sector included public drug payers.

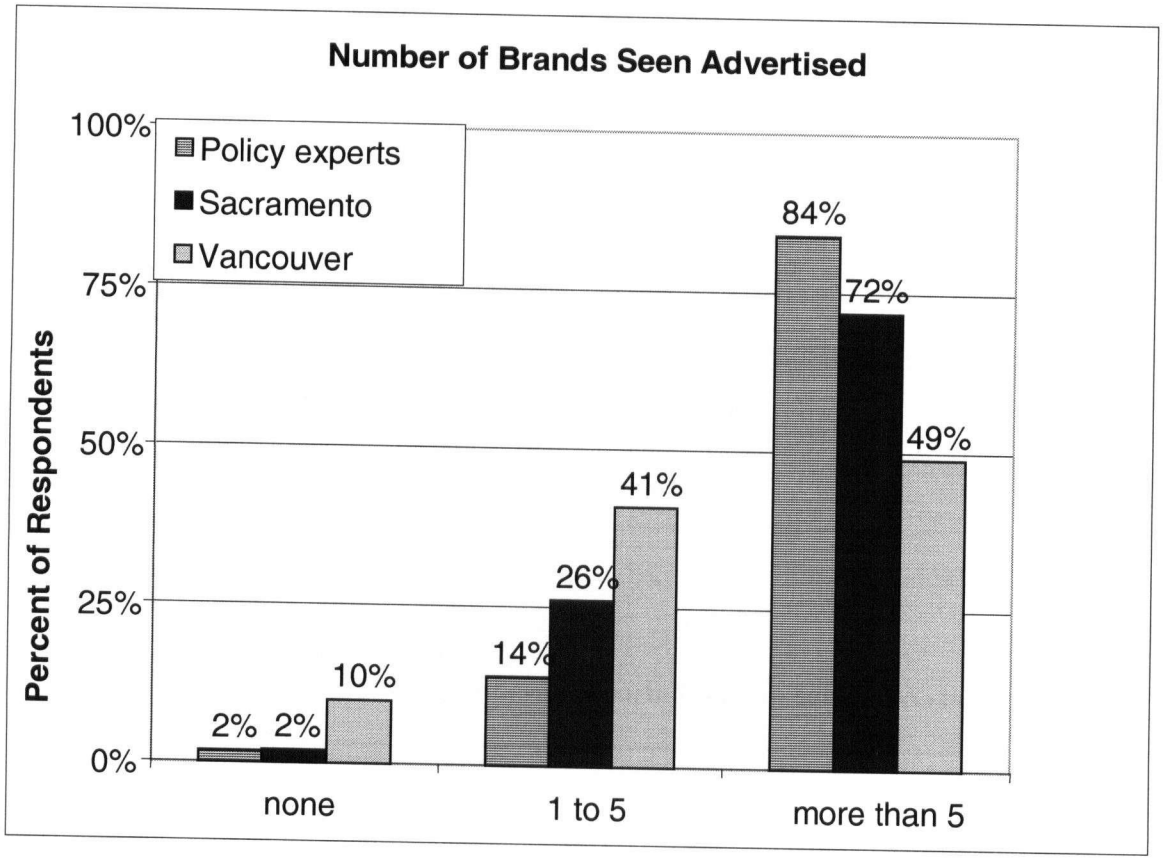
Table 7.1 Affiliation of survey participants

Type of affiliation	No. of respondents	Response rate
Payers, managers and regulators		
Government agency (5 federal; 19 provincial)	24	80%
Private insurance	2	67%
Health care providers		
Health Professional Organization	11	69%
Health care users		
Consumer and public interest non-profit group	9	75%
Disease-specific patient group	5	63%
DTCA producers and disseminators		
Pharmaceutical industry	5	83%
Advertising industry	4	100%
Total	***60***	***76%***

7.3.2 Exposure to DTCA

The questionnaire began by asking how many different prescription drugs respondents had seen advertised to the public during the last year. The aim of this question was to focus respondents' attention on concrete examples of DTCA as well as to compare the rates of exposure reported by pharmaceutical policy experts to those reported by patients in the comparative patient-doctor survey (Chapter 5) The policy experts reported greater exposure than Canadian patients enrolled in the patient-doctor survey, and slightly greater exposure than U.S. patients (Figure 7.1). Over half reported having seen more than 10 brands advertised within the last year (data not shown).

Figure 7.1: Number of brands respondents reported having seen advertised in previous year.



7.3.3 Effects on organizations' work

Those most likely to mention that DTCA had a substantial effect on their work were either in advertising (including advertising industry self-regulatory bodies), in the public sector, or private insurers (Table 7.2). Over 85% of those in the "public sector and private insurers" category of respondent reported that DTCA had a moderate or substantial effect. Interestingly, no pharmaceutical industry respondents reported it having a substantial effect, and over half indicated "little or no effect". Industry respondents were mainly from trade associations, and none were marketing managers, so this lack of perceived effect could also reflect their positions within the industry.

Table 7.2 Extent to which DTCA is affecting organizations' work

Sector	Substantial Effect	Moderate effect	Little to no effect
Advertising industry (n=4)	75%	-	25%
Public sector & private payers (n=26)	42%	46%	12%
Non-profit/consumer groups (n=9)	25%	50%	25%
Disease-specific patient groups (n=5)	20%	60%	20%
Health Professionals (n=11)	10%	40%	50%
Pharmaceutical industry (n=5)	0	40%	60%

7.3.4 Quality of Information on Drug Benefits and Risks

Three-fourths of respondents judged the quality of information on drug benefits and risks in DTCA to be poor or very poor, 20% found the quality to be good, and none judged it to be excellent (Figure 6.2). One respondent commented that risk information was generally much lower quality than benefit information. Several others mentioned that the quality varied for different types of DTCA.

Figure 7.2: Assessment of drug information quality in DTCA

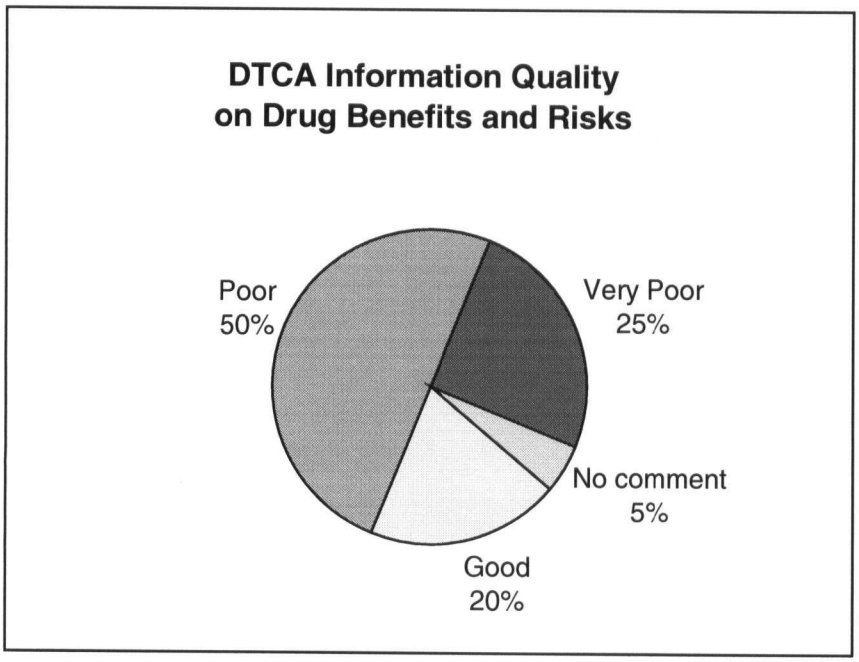


Table 7.3 provides the breakdown by sector, with the majority opinion per sector in bold. There were large differences in opinion between the two industry sectors that produce and disseminate DTCA and all other sectors. Even 40% of pharmaceutical industry respondents rated the quality to be poor to very poor.[†]

Table 7.3 What is the quality of information on drug benefits and risks in DTCA?

	Poor to very poor	Good	No comment
Mainly negative opinion			
Disease-specific patient groups (n=5)	**100%**	-	-
Health Professionals (n=11)	**81%**	9%	9%
Public sector & private payers (n=26)	**81%**	12%	8%
Non-profit/consumers (n=9)	**78%**	22%	-
Mainly positive opinion			
Pharmaceutical industry (n=5)	40%	**60%**	-
Advertising industry (n=4)	25%	**75%**	-

[†] Pharmaceutical industry respondents included both the brand-name and generic sector, and on many questions there were differences of opinion between these sectors. No generic

7.3.5 Effects on knowledge and appropriateness of health care

Table 7.4 presents the respondents' opinions on the effects of DTCA on the public's understanding of drug therapy and disease risks. Again, opinions were divided between sectors affected by DTCA and those producing it.

Table 7.4 How does DTCA affect understanding of drug therapy and disease risks?

	Improves	Worsens	No effect	No comment
Disease-specific patient groups (n=5)				
Drug therapy	-	**80%**	20%	-
Disease risks	-	**80%**	20%	-
Health professionals (n=11)				
Drug therapy	-	**73%**	18%	9%
Disease risks	-	**64%**	27%	9%
Non-profit/consumer (n=9)				
Drug therapy	11%	**67%**	11%	11%
Disease risks	-	**78%**	22%	-
Public sector & private payers (n=26)				
Drugs therapy	19%	**62%**	4%	15%
Disease risks	16%	**42%**	19%	23%
Pharmaceutical industry (n=5)				
Drug therapy	**60%**	20%	20%	-
Disease riks	**60%**	20%	-	20%
Advertising industry (n=4)				
Drug therapy	**75%**	-	25%	-
Disease risks	**75%**	-	25%	-
Total Drug therapy	***20%***	***58%***	***12%***	***10%***
Disease risks	***17%***	***50%***	***20%***	***13%***

There was greater diversity of opinion on the likely direction of effect of DTCA on doctor/patient communication (Table 7.5). One doctor remarked that DTCA improved communication because you can't communicate with a patient who doesn't come in to the office. Another thought it worsened communication by shifting the focus away from the patient's health problem and onto whether a specific drug was needed.

Table 7.5 How does DTCA affect doctor-patient communication?

	Improves	Worsens	No effect	No comment
Public sector & private payers (n=26)	16%	**58%**	4%	22%
Non-profit/consumer (n=9)	22%	**56%**	11%	11%
Health professionals (n=11)	27%	**55%**	9%	11%
Disease-specific patient groups (n=5)	**40%**	**40%**	20%	-
Advertising industry (n=4)	**75%**	25%	-	-
Pharmaceutical industry (n=5)	**80%**	20%	-	-
Total (n=60)	***30%***	***50%***	***5%***	***15%***

Most public sector respondents believed that DTCA worsened appropriateness of physicians' prescribing decisions, but nearly half expressed no opinion on effects of DTCA on patients' use of drugs. Claimed benefits of DTCA have included for example the suggestion that DTCA increases compliance.[1] Many health professional respondents also did not comment on these questions, but those that did comment were more likely to believe the effect of DTCA was negative than positive.

Pharmaceutical industry responses were mixed, but advertising industry respondents mainly believed that DTCA has a positive effect on both prescribing and drug use. Only four respondents (7%), two from the public sector and two from the pharmaceutical industry, believed that DTCA would have no effect on the appropriateness of drug use. However, as shown on Table 7.6, one fourth to one third of respondents overall chose not to comment on these two questions.

Table 7.6
How does DTCA affect the appropriateness of physicians' prescribing and patients' drug use?

	Improves	Worsens	No effect	No comment
Public sector & private payers (n=26)				
Physicians' prescribing	-	**81%**	-	19%
Patients' drug use	8%	**39%**	8%	46%
Non-profit/consumer (n=9)				
Physicians' prescribing	11%	**78%**	-	11%
Patients' drug use	11%	**89%**	-	-
Health professionals (n=11)				
Physicians' prescribing	9%	**55%**	-	36%
Patients' drug use	9%	**55%**	-	36%
Disease-specific patient group (n=5)				
Physicians' prescribing	20%	**40%**	-	**40%**
Patients' drug use	20%	20%	-	**60%**
Pharmaceutical industry (n=5)				
Physicians' prescribing	**40%**	20%		**40%**
Patients' drug use	**40%**	-	**40%**	20%
Advertising industry (n=4)				
Physicians' prescribing	50%	-	-	50%
Patients' drug use	**75%**	25%	-	-
Total Physicians' prescribing	***12%***	***62%***	***-***	***27%***
Patients' drug use	***17%***	***43%***	***7%***	***33%***

Table 7.7 reports responses on appropriateness or inappropriateness of visits to doctors. Again many respondents chose not to comment. Non-profit consumer groups, government and private payers mainly believed that DTCA would decrease appropriateness of doctor visits; other sectors had mixed opinions.

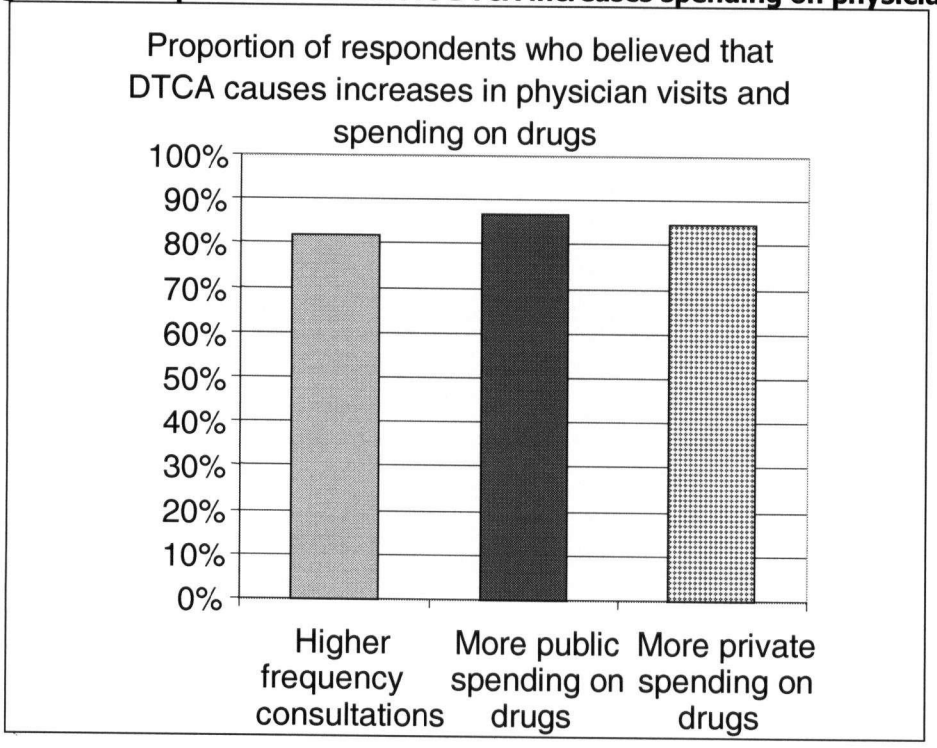
Table 7.7 How does DTCA affect the appropriateness of visits to doctors?

	Improves	Worsens	No effect	No comment
Non-profit/consumer (n=9)	-	**89%**	11%	-
Public sector & private payers (n=26)	4%	**62%**	4%	31%
Health professionals (n=11)	18%	27%	9%	**45%**
Disease/ patient groups (n=5)	20%	**40%**		**40%**
Pharmaceutical industry (n=5)	**40%**	**40%**		20%
Advertising industry (n=4)	**50%**	-	-	**50%**
Total	***13%***	***52%***	***5%***	***31%***

7.3.6 Effects on Health Care Costs

The survey included three questions related to the impact of DTCA on direct health care costs: expected effects on frequency of physician consultations and on public and private spending on prescription drugs. As shown in Figure 7.3, over 80% of respondents expected DTCA to drive up private and public drug costs and frequency of physician consultations. None believed that it would lead to lower drug costs or less frequent physician visits; and none believed it would fail to affect drug costs. Four respondents (7%) believed DTCA did/would not affect frequency of physician visits. They were from a variety of sectors: consumer groups (1), health professionals (1), public sector/private payers (2).

Figure 7.3: Proportion who believe DTCA increases spending on physician visits and drugs



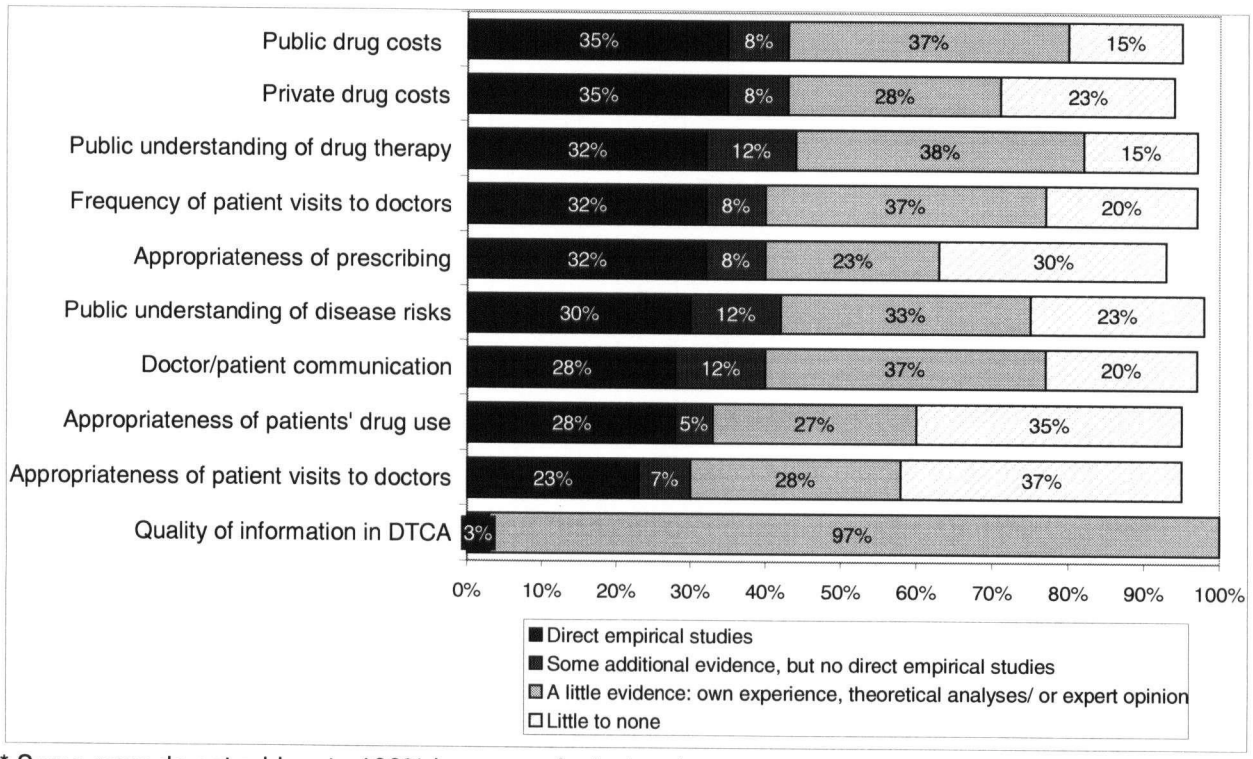
7.3.7 Levels/Types of Evidence Cited to Support Opinions

Figure 7.4 compares the proportion of respondents citing different types of evidence for the nine questions concerning DTCA information quality and its effects on appropriateness and cost of care. The breakdown of categories in Figure 7.4 is as follows:

- **Little to none:** those who marked 'little to no evidence' or only marked 'no comment or don't know' and left the question on degree of evidence blank;
- **A little evidence:** those who either marked only 'own experience' or only 'theoretical analyses or expert opinion'. Given that this is an expert survey, the two responses were considered equivalent;
- **Some additional evidence**: an intermediate category, those who marked indirect empirical evidence alone, or two to three different types of evidence. This category **excludes** anyone who marked 'little to no evidence' and/or 'direct empirical evidence'
- **Direct empirical evidence:** any response that included 'direct empirical studies of DTCA', whether or not other types of evidence were also mentioned.

As Figure 7.4 illustrates, nearly all respondents (97%) cited their own experience as the basis for opinions on DTCA information quality. Direct empirical evidence was cited more often as the basis for opinions on effects on drug costs than on other questions, but respondents were almost equally likely to mention their own experience as the reason they believed costs would increase.

Figure 7.4: Levels/types of evidence cited by respondents*



* Some rows do not add up to 100% because of missing data.

DTCA's effects on appropriateness of visits to doctors, prescribing and drug use have not been directly studied, and many respondents referred to the lack of evidence available on these outcomes. In most cases, a similar proportion of respondents cited empirical evidence, irrespective of whether they believed that DTCA improved or worsened the quality of care. Half of those who thought that DTCA improved public understanding of drug therapy, versus 34% of those who believed that it worsened understanding, stated that their views were based on direct empirical evidence. For effects on public understanding of disease risks, the proportion who cited empirical evidence as the basis for their opinion was remarkably similar regardless of that opinion: 30% of those who believed DTCA improved public understanding versus 37% of those who believed it worsened understanding and 33% of those who believed it had no effect.

Was there variation across sectors in the strength of empirical evidence on which different respondents believed their responses to be based? Table 7.8 provides a breakdown by sector of the proportion of respondents on average citing weaker or stronger evidence to support their responses to all 10 questions listed in Figure 7.4. Those representing health professional organizations were most likely to characterize the evidence as weaker, whereas those representing non-profit consumer groups, the pharmaceutical industry and disease-specific patient groups tended to characterize the evidence as stronger.

Table 7.8 Average level of evidence cited by respondents, by type of affiliation

Proportion of respondents per sector:	*Stronger* → → → *Weaker*			
	Direct empirical evidence	Some additional evidence	A little evidence (mainly own experience)	Little to no evidence
Non-profit/consumer (n=9)	**56%**	22%	22%	
Pharmaceutical industry (n=5)	**40%**	**40%**		20%
Disease-specific patient groups (n=5)	**40%**	20%	20%	20%
Advertising industry (n=4)	25%	25%	**50%**	
Public sector & private payers (n=26)	12%	**35%**	27%	27%
Health professionals (n=11)	9%	9%	**46%**	36%
Total (n=60)	***23%***	***28%***	***27%***	***22%***

7.3.8 Opinions on the regulation of DTCA

The questionnaire included two types of questions on the regulation of DTCA: possible limitations on advertising in settings where it is allowed; and whether or not Canada should allow various forms of advertising, including full DTCA.

- How soon following market launch should advertising to the public be allowed?
- Should limits be placed on which products are advertised to the public?
- Should advertising campaigns be allowed to target specific population groups?
- Are specific media appropriate for prescription drug advertising?

Limits on timing of DTCA campaigns

Table 7.9 presents the breakdown by sector on whether respondents thought that there should be limits on the timing of DTCA campaigns post market launch, and if so, what those limits should be. The responses varied considerably by sector, with most of the consumer and patient groups, and almost half of the health professional and public sector/ private payer respondents who registered an opinion, believing that advertising campaigns should begin at least 5 years post

product launch, and most pharmaceutical and advertising industry respondents suggesting that campaigns begin within the first year post launch.

Table 7.9 When should advertising first be allowed?

	Immediately (no limit)	6 months to one year post launch	Five or more years post launch	No comment don't know
Non-profit/consumer (n=9)		11%	**78%**	11%
Disease-specific patient groups (n=5)	20%	20%	**60%**	
Public sector & private payers (n=26)	8%	**31%**	**31%**	**31%**
Health professionals (n=11)	9%	27%	27%	**37%**
Pharmaceutical industry (n=5)	**40%**	**40%**	20%	
Advertising industry (n=4)		**100%**		
Total (n=60)	***10%***	***32%***	***37%***	***20%***

Limits on which drugs may be advertised

Over 80% of respondents, including all of those from non-profit/consumer groups and over half of respondents from the advertising and pharmaceutical industries, believed that there should be limits on which prescription drugs may be advertised to the public in settings that allow DTCA (Table 7.10).

Table 7.10 Should limits be set on which drugs are advertised to the public?

	Yes	No	No comment
Non-profit/consumer (n=9)	**100%**	-	-
Health professionals (n=11)	**82%**	-	18%
Public sector & private payers (n=26)	**81%**	12%	8%
Disease-specific patient groups (n=5)	**80%**	-	20%
Pharmaceutical industry (n=5)	**60%**	40%	-
Advertising industry (n=4)	**50%**	**50%**	-
Total (n=60)	***80%***	***12%***	***8%***

Those who thought that limits should be set (N=48) were asked to specify whether health condition, drug profile or payment method should be the basis for those limits. Table 7.11 presents a breakdown of their responses. Nearly all of those who thought that limits should be set (representing 75% of the entire study sample), believed that advertising should be limited on the basis of drug safety profile, followed by drug efficacy (65% of entire sample).

Table 7.11 Limits to DTCA should be based on these factors

Criterion to limit DTCA	Percent (n=48)
Drug Safety	45 (94%)
Drug Efficacy	39 (81%)
Patients' Health Condition	33 (69%)
Private or public payment	8 (17%)

Targeting of specific population groups

Six population groups were listed and respondents were asked whether DTCA campaigns should specifically target each group. Taken together, these categories include the entire population except infants, who are unlikely to be the direct targets of DTCA campaigns (although their parents may be). Table 7.12 presents responses by sector, as well as the proportion that either checked off 'yes' or 'no' to all listed groups. Responses for whether women or men should be targeted were identical and are therefore presented together as 'one sex'. Very few people believed that children or adolescents – the most vulnerable among the listed groups – should be targeted, 3% and 7% respectively. These were all pharmaceutical and advertising industry respondents.

Table 7.12 Should the following groups be targeted in DTCA campaigns?

	*Proportion who believe this group should be targeted:**						
	Children	Adolescent	Elderly	One sex	Low income	ALL	NONE
Public sector & private payers (n=26)	-	4%	8%	8%	-	-	85%
Non-profit/ consumer (n=9)	-	-	-	11%	-	-	78%
Health professionals (n=11)	-	-	-	9%	-	-	73%
Disease-specific patient groups (n=5)	-	-	20%	20%	20%	-	60%
Pharmaceutical industry (n=5)	40%	40%	60%	60%	60%	40%	40%
Advertising industry (n=4)	-	25%	75%	75%	25%	-	25%
Total (n=60)	***3%***	***7%***	***15%***	***18%***	***8%***	***3%***	***72%***

*all = all listed groups marketed 'yes', should be targeted; none = all marked 'no', should not be targeted.

Four types of media that are commonly used for DTCA were listed (magazines, television, billboards and the Internet) and respondents were asked to judge how appropriate each medium was for prescription drug advertising. Table 7.13 presents the proportion of respondents who judged that each medium was either appropriate or very appropriate for DTCA. Larger proportions of respondents judged magazines and Internet to be appropriate than billboards or

television ads. Billboards provide very limited information on advertised products (often only the name, an advertising image and the suggestion to 'ask your doctor'). Television ads can provide more information but this remains limited within a 30-60 second slot. Magazines and the Internet can provide more detailed information.

Table 7.13
Proportion who judged the following media to be 'appropriate' or 'very appropriate' for DTCA

	Billboards	Television	Magazines	Internet
Non-profit/consumer (n=9)	-	**11%**	**11%**	-
Public sector & private payers (n=26)	4%	4%	**27%**	**27%**
Health professionals (n=11)	9%	9%	**27%**	18%
Disease-specific patient groups (n=5)	20%	20%	20%	**40%**
Pharmaceutical industry (n=5)	20%	20%	**80%**	**80%**
Advertising industry (n=4)	50%	75%	**100%**	**100%**
Total (n=60)	***10%***	***13%***	***33%***	***32%***

Should Canada allow prescription drug advertising?

Respondents were asked whether Canada should allow five different types of prescription advertising aimed at the public, all of which are allowed in the U.S. and New Zealand:

- Full DTCA, including product name and health claims
- Full DTCA which also includes 'free trial offers' or price reductions
- Disease-oriented advertisements with no product name
- Reminder ads, which include brand names and images but no health claims
- Comparative price advertising (listings of name, price and quantity only; no images or advertising text; joint listings of competing products).

All but price advertising are currently illegal under Canada's *Food & Drugs Act*, if the aim of a campaign is to stimulate sales of a specific prescription-only medication.

Respondents who were more positive about the quality of information on drug benefits and risks in DTCA were also more likely than others to believe that full DTCA should be allowed (8/12 or 67% of those judging that the information was good). Nine of the 45 respondents, or 20%, of those who believe that the information on drug benefits and risks was poor or very poor, nevertheless believed that full DTCA should be allowed in Canada. These included four public sector/private payer, one advertising industry, one pharmaceutical industry, two patient group, and one health professional respondent. The latter had judged the information on drug benefits

and risks to be 'very poor'. Respondents were not asked to offer explanations for why they believed that full DTCA should or should not be allowed. However, this discrepancy could reflect beliefs in freedom of commercial communication, regardless of information quality, or perhaps the belief that in spite of poor information provision, there are other benefits associated with full, legal DTCA.

Table 7.14
Proportion who believe the following types of DTCA should be allowed in Canada*

	Full DTCA with free trial offers	Reminder ads	Full DTCA	Price advertising	Disease oriented ads
Non-profit/consumer (n=9)	0	0	11%	**44%**	33%
Disease-specific patient groups (n=5)	0	0	**40%**	**40%**	20%
Public sector & private payers (n=26)	0	23%	19%	39%	**54%**
Health professionals (n=11)	9%	18%	27%	36%	**46%**
Pharmaceutical industry (n=5)	20%	60%	**80%**	40%	60%
Advertising industry (n=4)	25%	75%	75%	25%	**100%**
Total (n=60)	***5%***	***23%***	***30%***	***38%***	***50%***

*each question was a separate 'yes/no' answer; respondents did not need to choose between different types of DTCA.

Federal and provincial/territorial views on allowing DTCA

Given their different roles in policy development on DTCA in Canada, responses from federal respondents were analysed separately from those of provincial and territorial government respondents. This disaggregation is presented in Table 7.15. There were 24 respondents from the public sector, 19 provincial or territorial and 5 federal.

Table 7.15
Proportion in public sector who believe these types of DTCA should be allowed in Canada

	Full DTCA	Reminder ads	Price advertising	Disease oriented ads
Federal government (n=5)	40%	60%	60%	**100%**
Provincial/territorial government* (n=19)	11%	16%	32%	**42%**

*2 were not government employees: one was a provincial representative on PIC (academic), and one was working in a provincial government office on a 2-year contract (pharmaceutical information policy)

Organizational policies on DTCA

Twenty-four respondents, or 40% of the sample, said that their organization had a position on DTCA (Table 7.16). These can be roughly divided into policies supportive of DTCA, neutral or

opposed. The latter included respondents supporting restrictions on the content of DTCA or the types of advertising allowed. Three respondents who work for federal or provincial governments responded to this question by citing the current restrictions in the Food & Drugs Act as their organization (the government)'s position in opposition to DTCA.

Table 7.16 Types of organizational policies, by sector

Policies on DTCA	Opposed	Supportive
Non-profit/consumer (n=9)	6	
Disease-specific patient groups (n=5)	3	
Public sector & private payers (n=26)	9	
Health professionals (n=11)	2	
Pharmaceutical industry (n=5)	1	2
Advertising industry (n=4)		1
Total with stated policies (N=24)	***21 (88%)***	***3 (13%)***

7.4 Discussion

These results were based on a survey of Canadian pharmaceutical policy experts from sectors most strongly affected by prescription drug advertising: health professionals, patients, consumers, public and private payers and managers of health care services, and the advertising and pharmaceutical industries. Most respondents reported considerable exposure to prescription drug advertising, i.e. they had seen more than 10 brands advertised during the last year.

The survey was carried out in February 2001. Health Canada had held several recent consultations, in 1996-1999, on whether the federal *Food & Drugs Act*, which currently prohibits DTCA, should be changed in order to allow this form of advertising. Policy briefs on prescription drug advertising targeting the public, aiming to inform the pharmaceutical industry of the scope currently allowable under the law, had been published in 1996,[2] and most recently in November 2000. [3] At the time this survey was carried out, Health Canada officials were discussing plans for legislative renewal, including an overhaul of health protection legislation and introduction of some form of DTCA, with details not yet made public. The first federal government statement that DTCA would not be introduced was made a full year after the survey, in March 2002, at which time Canada's Health Minister expressed opposition to the introduction of DTCA.[4] Thus legalization was actively under consideration during the survey period (and, in fact, despite the Minister's declaration to the contrary, may still be so).[5]

In addition to these discussions of potential legislative change, large changes have occurred in Canada in population exposure to DTCA, following the August 1997 U.S. FDA relaxation of regulations governing broadcast ads. This U.S. regulatory change has led to an increase in Canada in cross-border exposure to U.S. television programming. Companies have also begun direct television advertising campaigns in Canada. In at least two cases in 2000, television ads that were eventually judged to be illegal were broadcast for several months.[6] There were also billboard advertising campaigns featuring prescription drug names in some cases (reminder ads), and in other cases an indication for a newly approved drug coupled with the suggestion to 'ask your doctor' about treatment options (disease-oriented ads).[7]

The survey respondents were not just passive observers of this shift in regulatory environment in Canada. They were directly involved in highly charged discussions over whether Canadian law should be changed in order to allow DTCA, and in how the current law should be enforced, as policy analysts within Health Canada, managers of provincial drug benefit schemes, and as representatives of stakeholder organizations involved in consultations and advisory committees.

For example, the provincial and territorial respondents in this survey included managers and policy analysts for provincial and territorial drug plans. Only 2 (11%) supported legalization of full DTCA, and for each listed type of DTCA, fewer provincial or territorial respondents agreed with legalization than federal employees. Given the small number of federal employees surveyed, any differences between the two sectors are suggestive only. However, provincial and territorial governments would be expected to be concerned about the effects of DTCA on drug costs, especially if no compensatory cost savings are expected, given their role in health care financing and administration of health care services. As regulation of pharmaceutical advertising is largely delegated to the industry and to a multi-stakeholder third party (the Pharmaceutical Advertising Advisory Board, or PAAB), regulatory change to allow DTCA would not be seen as an immediate fiscal risk at a federal level, as the cost of providing drugs is primarily a provincial responsibility, and increased costs of regulation of advertising could be borne by self-regulatory bodies. PAAB currently charges a fee to companies to pre-screen ads for health professionals. This type of system could be extended to DTCA, and any increase in the volume of ads would result in more fees, and thus additional financing would be available to offset cost increases.

There are some exceptions to this federal/provincial/territorial divide in responsibility for drug financing including the non-insured health benefits (NIHB), the federally managed drug plan covering prescription drugs for aboriginal people (status Indians) in Canada. The federal government also covers federal government employees, the Royal Canadian Mounted Policy, the military service, and federal prisoners. However, provincial governments bear a much larger responsibility for public financing of pharmaceuticals than the federal government, and thus can be expected to be more sensitive to the consequences of any direct increases in pharmaceutical costs associated with legalization of DTCA.

DTCA information quality and effects on health care quality

Three-quarters of respondents judged the quality of information on drug benefits and risks in DTCA to be poor or very poor. The only sectors primarily judging the information quality to be good were the advertising and pharmaceutical industries, i.e. producers and disseminators of advertising. Most respondents assessed the effects of DTCA on knowledge and appropriateness of care to be negative or at best neutral, with the exception of doctor/patient communication, where opinions were fairly evenly divided among representatives of disease-specific patient groups, but other non-industry respondents were more likely to judge the effects to be negative than positive. Most advertising and pharmaceutical industry respondents believed that DTCA was likely to have positive effects on health care quality. This was true for all measures of health care quality included on the questionnaire.

The results indicate considerable polarization of opinion about the quality of information on drug benefits and risks in DTCA and on the effects of DTCA on public understanding and appropriateness of care. There is considerable empirical evidence suggesting that quality is frequently poor, both on the basis of published systematic analyses of information quality and regulatory reviews. This is described in detail in the literature review in Chapter 2.

Interestingly, although the empirical evidence on DTCA information quality is more extensive than other DTCA research and is based on sound methodology for sampling and analysis (at least in terms of the quality of U.S. print advertising), most respondents stated that their beliefs about DTCA information quality were based on their own experience. This experience, however, was largely consistent with the research evidence.

When this survey was carried out, there were no published direct or indirect empirical studies on DTCA's effects on prescribing appropriateness. An article describing the combined results of the patient-doctor survey described in Chapter 5 has since been published, and provides indirect evidence, in terms of physicians' confidence or ambivalence in treatment choice, on effects of DTCA on prescribing appropriateness.[8]

A number of empirical studies have looked at the effects of doctors' reliance on promotional information on prescribing appropriateness, [9 10 11 12 13 14 15] and a systematic review has examined the effects of physicians' interactions with the pharmaceutical industry.[16] This is the most relevant body of indirect empirical evidence on the likely direction of DTCA's effects on prescribing appropriateness. Four of the five respondents who based their replies on indirect empirical studies said that DTCA decreased prescribing appropriateness, which is consistent with this research evidence; the fifth marked 'no comment or don't know'.

Although DTCA's effects on the appropriateness of patients' use of medicines have not been directly studied, one frequent claim is that DTCA increases patient compliance. *Prevention* magazine's consumer surveys asked members of the public who were taking a drug that they had seen advertised whether they were reminded to take the drug or to refill a prescription.[17] Around a third of those currently taking advertised drugs said that they were reminded, leading to claims of a beneficial effect on compliance. This finding raises a number of questions concerning actual behaviours, what products respondents were using, whether advertising led to increased frequency of medicine use, and if so, whether this increase was linked to health benefits. In some cases of symptomatic drug treatment, being reminded to take a medicine by advertising may be neutral or even harmful, as for example in the case of NSAID users who continue to take prescribed treatments in spite of symptoms of adverse effects. [18]

Most respondents in this survey did not believe that published or unpublished empirical studies on DTCA had shown that it increased appropriateness of use. Only three respondents, two from the advertising industry and one from the pharmaceutical industry, cited empirical studies as indicating an improvement in patients' use of prescription drugs.

Nearly all respondents from all sectors believed that DTCA increases direct health care costs in the form of private and public spending on prescription drugs and frequency of physician visits. In the U.S., the National Institute of Health Care Management has found that a large proportion of annual increases in retail prescription drug spending was attributable to increased prescribing and sales of the most heavily-advertised drugs, suggesting a strong link between DTCA and increased drug costs.[19]

In summary, most respondents judged DTCA information quality and effects on public understanding of drugs and diseases, and health care quality to be negative, and expected costs of drugs and physician services to increase. Respondents from the pharmaceutical and advertising industries were much more likely to believe that DTCA information quality and effects on knowledge and health care quality were positive than respondents from all other sectors.

Evidence cited to back opinions

One interesting survey finding was the degree to which respondents with contradictory views reported that those views were based on direct empirical evidence. For example 30% of those believing that DTCA improved public understanding of disease risks, 37% of those who believed that it worsened public understanding, and 33% of those who believed that it had no effect said that their opinions were based on direct empirical evidence. These contradictory views are unlikely all to be based on the same interpretation of a single body of empirical evidence.

A number of things may be happening. Respondents may inaccurately believe, on the basis of secondary reports, that empirical evidence is available to back stated views. They may be selectively choosing specific empirical findings to back a stated opinion, or they may interpret studies with stronger or weaker methodological designs differently. For example, much of the research on consumer awareness of DTCA in the U.S. focuses on opinions and attitudes rather than knowledge, and thus only limited conclusions may be drawn from it. Only one study, by Kaiser Family Foundation, included a comparison of knowledge among respondents who had and had not viewed specific product ads,[20] and the results of this study were equivocal. Viewers did know more about the drugs than non-viewers, but unfortunately this included more misinformation as well as correct information about the drugs' characteristics.

These discrepancies highlight the relevance of Hadorn's recommendation[21] for explicit, formal rules, guiding both the *admissibility* and *relevance* of evidence, as occurs within a courtroom, to decisions concerning the introduction of public health interventions (or, as in the case of advertising, interventions with expected public health effects). In this survey, those representing health professional organizations were most likely to characterize the evidence as weak, followed by those in government, whereas representatives of non-profit consumer groups, the pharmaceutical industry and disease-specific patient groups tended to characterize the evidence as strong.

This may again reflect a number of factors. Some organizations that oppose DTCA are concerned about potential harm to public health and to the sustainability of public health care services and strongly support a precautionary approach in the absence of conclusive evidence.[22] In this case, empirical evidence – although imperfect – would be considered strong enough to back stated opinions. On the other hand, multinational pharmaceutical manufacturers operating in Canada also market their products in the U.S. and thus are actively carrying out DTCA campaigns. They would be expected to have a vested interest in believing and/or stating that the effect of DTCA on the public is positive. This survey was carried out as part of a Health Canada research project investigating potential effects of DTCA (See Appendix 1 for cover letter). Thus the type of evidence cited may also have reflected a desire to convey the seriousness of concerns or solid grounding for beliefs in positive impacts of DTCA. The pharmaceutical industry has been actively seeking a change in Canadian legislation to allow introduction of full DTCA.[23] In other words, reported strength of evidence may match strength of convictions. This points to the key role of social values in the interpretation of empirical evidence, particularly when the evidence is ambiguous or imperfect, as is the case with research on outcomes of DTCA.

Another possible explanation for the observed difference is that the respondents with the most training in the health disciplines (health professionals) were the most likely to be skeptical of existing empirical research and to recognize methodological weaknesses.

Regulatory Recommendations

Given the current policy review in Canada, respondents were also asked to make regulatory recommendations on a range of issues associated with the introduction of DTCA, the types of

products, media and target audiences that might or might not be considered acceptable, and timing of advertising campaigns relative to market launch.

Limits in timing of campaigns

Marketers might be expected to support a short delay in introduction of public advertising campaigns, such as six months, since products can be promoted to physicians before patients, helping to increase the likelihood of a prescription following a request. All advertising industry respondents supported a six-month to one-year delay, and 80% of pharmaceutical industry respondents supported either immediate marketing or a brief (6 months) delay.

There are also health reasons for delaying advertising of new drugs, when relatively little is known about rare or longer-term health risks. Stimulation of rapid increases in population exposure may be ill advised, especially in the absence of evidence of a significant therapeutic advantage over older and better-understood therapies. A systematic review by the US General Accounting Office found that over 50% of newly marketed drugs had serious risks that were discovered only post-approval, usually in the first few years.[24] As a result, a U.S. non-profit organization, Public Citizen Health Research Group, suggests avoiding using new drugs until they have been on the market five years unless they are true breakthrough products. [25] The rationale behind this suggestion is that slower growth in population exposure to a new chemical is prudent. If serious adverse events are discovered at a later date, fewer people will have been exposed to the chemical before regulatory action is taken. This is especially relevant to the lag period between when adverse events are first suspected, and when the public is notified and regulatory action is taken.

The second rationale for delayed advertising is cost. Allowing DTCA only post patent expiry would address concerns that DTCA leads to a substitution of costlier patented products for products of equivalent therapeutic value that are off-patent and therefore unlikely to be advertised to the public. Seventy-eight percent of the consumer group and 60% of patient group respondents believed that DTCA should only be allowed five or more years post product launch, versus a minority of respondents from all other sectors. This is consistent with a focus on drug safety. Among the 12 respondents who believed that advertising should not be allowed until after

patent expiry, 8 were from the public sector and private payers (31% of respondents in this category).

Product-specific limits

Most respondents thought that there should be product-specific limits to which drugs are advertised to the public, and the most commonly cited rationale was drug safety profile. This is similar to the rationale behind Canada's current legal framework limiting advertising to the public to over-the-counter products. The limitation on the basis of patient's health condition, supported by 33 (55%) of respondents, reflects a similar logic to the list of Schedule A diseases in the Food & Drugs Act, for which treatments may not be advertised to the public.

If advertising is limited on the basis of product safety or efficacy, but advertising of some prescription-only drugs is allowed, in practice this means establishing an intermediate tier of products with prescription-only status but better-established safety and efficacy profiles than other products. For example, ads might be allowed only for products with clear evidence of a therapeutic advantage compared to alternatives and/or a well-established safety record.

The possibility of product-specific restrictions was raised at a national multi-stakeholder consultation on DTCA held in Ottawa by Health Canada in April 1999. [26] Neither proponents nor critics of DTCA embraced this option. Industry representatives were concerned that it would introduce an extra layer of complexity in regulation and potentially lead to unfair competition. Critics saw it as partial deregulation in an environment where promotion aimed at health professionals is already inadequately regulated.

Targeting of specific population groups

Most respondents disagreed with targeting of children in advertising campaigns: only two pharmaceutical advertising respondents believed that children should be targeted, and only four respondents (pharmaceutical and advertising industry) believed adolescents should be targeted. The majority of respondents (72%) felt that none of the listed population groups should be targeted although the listed groups included the entire population in one or more categories, minus infants, who are unlikely to be direct targets in DTCA.

All advertising campaigns have a target audience, whether it consists of a broad segment of the population, such as ads for allergy drugs, or a more restricted audience, such as ads for acne drugs. There have been both negative and positive commentaries in the press about targeting of specific population groups in DTCA. In the US, targeting of young children in a campaign for azithromycin, "Z is for Zithromax" on a Sesame Street programme, has been criticized.[27] In Canada women's groups have objected to the targeting of adolescent girls in billboard and television/cinema campaigns for two combined hormonal products: estradiol and cyproterone (Diane-35) and estradiol and levonorgestrel (Alesse).[28] In New Zealand, women's groups have raised concerns about the images of women and social ramifications of a campaign for an anti-obesity drug, orlistat (Xenical).[29] Authorities in San Francisco raised concerns about ads for AIDS drugs targeted at gay men after a survey of men attending STD clinics indicated that those with highest self-reported exposure were also more likely to report unsafe sex and to believe that HIV infection was no longer as serious a problem as in the past.[30]

Targeting of specific population groups has also been highlighted as a positive feature of advertising campaigns. RMI, the New Zealand industry association, has suggested that television campaigns are especially useful as a means to reach Maori people who might otherwise not obtain diagnosis or seek ongoing care for chronic conditions such as diabetes or asthma. [31] They argue that broadcast DTCA meets public health objectives in reaching a lower income disadvantaged population group, those most likely to suffer from under-diagnosis and under-treatment, and also more likely to be in poorer health than higher income population groups. A UK pharmaceutical industry commentator similarly suggested that television advertising could fill a gap in access to health information among low-income groups.[32] In this survey as well, four out of the five respondents who believed that low income and disadvantaged patients should be targeted in advertising campaigns were from the pharmaceutical and advertising industries; nearly ten times as many respondents (n=49) thought that they should not be targeted.

Use of different media for prescription drug advertising

Billboards were considered the least appropriate medium for DTCA, with only 10% of respondents considering them to be appropriate or very appropriate. Similarly, few respondents thought that television is an appropriate medium. Since late 1997, when the US FDA relaxed regulatory requirements for risk information presentation in broadcast ads, television advertising in the US has expanded enormously, with $1.1 billion spent on television ads in 1999, a 70% increase over 1998. [33]

Types of DTCA that should or should not be allowed in Canada

Only 30% of respondents believed that Canada should allow full DTCA, i.e. advertising that includes both product name and indication. These included the majority of pharmaceutical and advertising respondents. Only 11% of consumer/non-profit group respondents and 19% of government and private payers were in favour of legalization of full DTCA. Twenty-four of the 60 respondents have organizational policies concerning DTCA, 21 opposed to legalization (including those that believe that the current Canadian law should be maintained and others who believe that stricter regulation and enforcement are needed), and three supportive.

Few respondents (3 or 5%) believed that financial incentives such as free trial offers and price reductions should be included in advertising. A ten-year review of print DTCA in major consumer magazines in the US found that 17% of print ads contained such financial incentives.[34] The offer of monetary incentives to physicians to prescribe certain products is generally considered unethical[35] and is prohibited under most national regulatory guidelines or codes governing drug promotion.

In the U.S., the Office of the Inspector General issued a notice to pharmaceutical manufacturers in October 2002 warning that payments made to influence the choice of medication in federally financed health programmes would be subject to regulation under anti-fraud and kickback legislation. [36] Although this concerns influences on decisions concerning prescribing and dispensing of publicly financed drugs, not offers of free trials or price reductions to patients, in both cases a financial incentive is being used by a manufacturer to influence a choice of medical treatment.

Reminder ads have been the subject of recent controversy in Canada, with divergent opinions voiced about their legality under the Food & Drugs Act, mainly centring over the interpretation of Section C.01.044: *"Where a person advertises to the general public a Schedule F Drug, the person shall not make any representation other than with respect to the brand name, proper name, common name, price and quantity of the drug."* Reminder ads contain elements other than name, price and quantity, including emotive advertising images and text and suggestions to 'ask your doctor' about the product. However, a November 2000 Health Canada policy paper stated that reminder advertising was allowed in Canada.[37] Respondents may therefore have had differing understandings of the legal status of reminder advertising.

In the U.S., when the FDA brought in a new guidance for broadcast advertising in 1997 relaxing the regulations for risk information provision, the agency referred to the confusion caused by televised reminder ads as one of the reasons new regulations were needed.[38] Reminder ads often leave viewers guessing what the advertised product is used for, and may seem odd to viewers who are unaware of the regulatory reasons a manufacturer has chosen to advertise its product in this way, i.e. to avoid legislated requirements governing risk information provision in full product advertising. From a marketing perspective, the main justification is to create brand-name recognition and loyalty, often through the use of emotive imagery. It is difficult to reconcile this aim with the type of information needed to make informed decisions about medicine use. Reminder ads have continued to be common on U.S. television following the 1997 FDA guidance, as the guidance did not include any restrictions on reminder ads.

Most respondents opposed comparative price advertising, which is currently allowed in Canada, with only 36-40% of respondents stating that the Canadian government should allow such advertising. The proportion did not differ between sectors, although more consumer group representatives favoured this form of advertising than other sectors. A recent review of Australian health protection legislation recommended against introduction of full DTCA, but in favour of introduction of comparative price advertising.[39] Although price advertising is allowed under the *Food & Drugs Act*, it is rare to non-existent in Canadian media. Some respondents may have been unaware of its current legal status.

Half of respondents supported disease-oriented advertising. These are ads that mention a health condition but not a specific product. Pharmaceutical companies are allowed to pay for advertising to inform the public about specific diseases or health conditions, in Canada and in other countries that do not allow DTCA, as long as it is not product-specific advertising.

Disease-oriented advertising is subject to few regulatory controls. Messages about diseases are sometimes strongly linked to a treatment model involving only drug therapy, for example in biochemical descriptions of depression,[40] which can also be treated through psychotherapy. At times the link to a specific product may be obvious to the public, as in Pfizer campaigns involving sports celebrities urging men to discuss erectile dysfunction with their physicians.[41] The World Health Organization cautions against advertising that exaggerates risks, stating that advertising aimed at the public "...should not take undue advantage of people's concern for their health."[42] Disease-oriented advertising has also been criticized as contributing to unnecessary medicalization of healthy life events such as menopause and ageing.[43]

One of the differences between mass media advertising and brochures in doctors' offices or promotional Internet sites is the ability of mass media to reach a public that does not already define itself as needing the product or necessarily having the treated condition. This has been viewed both positively and negatively, with proponents of DTCA claiming an effect in reaching under-treated and under-diagnosed people and critics raising concerns about fear-mongering and feeding into people's anxieties about their health, or "creating a nation of hypochondriacs".[44]

Relevance to Canadian policy discussions

The individuals in government included in this survey were closely involved in policy discussions on DTCA in Canada, both on a provincial and federal level. One provincial government respondent raised concerns about DTCA in a press release on health policies,[45] but in general there has been little public commentary on expected positive or negative effects of DTCA on the quality of health care services, on health care costs, or on public understanding of drugs and diseases, at either a provincial or federal government level. Additionally, discussions on introduction of DTCA in Canada have tended to focus only on one of the three main forms of prescription drug advertising, full product ads, and not on reminder ads or disease-oriented

advertising, although the latter two forms of DTCA also have ramifications for the quality and cost of health care services, and public understanding of drugs and diseases.

This was an opinion survey carried out within the context of a review of DTCA policy in Canada. Respondents reported high exposure levels to DTCA in spite of its legal status in Canada; thus their opinions reflect some degree of experience with prescription drug advertising. Whether or not these opinions reflect a broader consensus among policy experts is unknown. An attempt was made to reach those working directly on DTCA policy in Canada, but some sectors may have been missed. For example, because the focus was on effects on health care services, policy experts working within health ministries were invited to participate, but those in finance, foreign affairs or industrial affairs, for example, were not. However, policy development on DTCA may not originate only within the health sector.[5] Additionally, although the response rate was high and was broadly similar between different sectors, opinions of non-respondents may differ from those of respondents.

6.5 Conclusions: quality expected to suffer and costs increase

The survey indicates a great deal of concern about the quality of information in DTCA, and the effects of prescription drug advertising on appropriateness of care as well as direct health care costs. No attempt was made to solicit opinions on indirect effects on health care, such as hospitalization rates, or effects on health -- morbidity and mortality -- as there is no research evidence linking DTCA to longer-term impacts. However, most respondents from the health professions, consumer and patient groups and governments believe that DTCA has a negative impact on public understanding of drug therapy and disease risks, appropriateness of prescribing, drug use and physician consultations. Short-term harm is unlikely to lead to long-term benefit.

There was strong support for the introduction of direct-to-consumer advertising of prescription drugs (DTCA) in Canada among respondents from the advertising and pharmaceutical industries, but very little support among those from the health professions, consumer/non-profit groups or disease-specific patient groups. The majority of public sector/private payer respondents supported disease-oriented advertising, but not other forms of DTCA.

The strongest recommendation, in terms of numbers of respondents, was against allowing full DTCA with monetary inducements such as free trial offers or reduced prices. Such prescription drug advertising is common in the U.S. Additionally, many respondents said that reminder advertising should not be allowed and that both billboards and television are inappropriate media for prescription drug advertising. Canada has recently seen a plethora of billboard and television reminder advertising,[6] highlighting the need to clarify current regulatory restrictions as they apply to reminder advertising, and if necessary introduce an additional amendment to the *Food & Drugs Act.* Most respondents believed that drug safety and efficacy profiles should be criteria for allowing product-specific DTCA in jurisdictions where DTCA is allowed. This could be interpreted in two ways: either support for the rationale behind current advertising being restricted to OTC drugs; or the suggestion of a 3rd tier in drug regulation, in which some prescription-only drugs known to be safer and/or more effective than others might be advertised to the public. The latter suggestion, interestingly, was not popular at a 1999 national multi-stakeholder consultation on DTCA. [26]

This is an opinion survey, not a direct assessment of the empirical literature on outcomes of DTCA. The conclusions should therefore be taken as a reflection of expert opinion only. However, the survey raises serious concerns about the introduction of DTCA as a direction for policy change in Canada, particularly given the opinions expressed by respondents in provincial and federal governments, as well as Canadian health professional and public interest organizations. From a public policy perspective, a shift leading to increased drug and physician costs might be considered if health care quality was expected to improve. If the result of relaxing current DTCA regulations is to increase health care costs while simultaneously leading to deteriorating quality of care, as the majority of these experts believe, it seems hard to justify such a shift.

Appendix 7.1 – invitation letter

Centre for Health Services and Policy Research
429 - 2194 Health Sciences Mall
University of British Columbia
Vancouver, BC V6T 1Z3

Facsimile Cover Sheet

Date: June 24, 2003

To:
Organization:
Fax:

From: Barbara Mintzes, DTCA Project Coordinator
Phone: (604)822-0565
Fax: (604)822-5690

Pages including this cover page: 5

Dear _____,

Canada is reviewing its legislation on prescription drug advertising aimed at the public and considering options for change. Direct-to-consumer prescription drug advertising (DTCA) is under debate, with many claims made about potential public health benefits and risks.

We are sending this survey to experts in the health professions, consumer and disease groups, the pharmaceutical and advertising industry, media, government, private insurance and health care management. You were identified as someone with specific expertise and interest in pharmaceutical policy. We are interested in your observations and opinions, as well as how DTCA has affected your organization or institution's work.

The survey is funded by Health Canada and is being carried out by the Centre for Health Services and Policy Research, University of British Columbia.

We ask for your participation in this policy review by completing the enclosed survey, which should take ten minutes of your time. Please fax it back as soon as possible to **(1 604) 822 5690.**

The return of the completed questionnaire indicates your willingness to participate in the survey, although you are under no obligation to do so.

The report to Health Canada will include a respondent list, but the survey results will be reported by sector only (such as government, industry etc.). Individual responses will be kept confidential. We invite you to report your personal opinions and experiences, whether or not they reflect your organization's official position. All participants will receive a report of the survey results.

If you have any questions or would like to discuss this further, please feel free to contact me by phone at (604) 822 0565 or by email at bmintzes@chspr.ubc.ca

Thank you very much for your help,

Barbara Mintzes
DTCA Project Coordinator

Centre for Health Services and Policy Research
429 - 2194 Health Sciences Mall
University of British Columbia
Vancouver, BC V6T 1Z3

Appendix 7.1 - continued: Survey Questionnaire

SURVEY ON DIRECT-TO-CONSUMER ADVERTISING OF PRESCRIPTION DRUGS (DTCA)

After Completion Please fax back to: ***1 604 - 822 5690***

Note: 'DTCA' refers to all ads for prescription-only medicines aimed at the public, i.e. print, TV, radio, billboards etc.

1. How many different brands of prescription drugs have you seen advertised to the public in the last year?

- ☐[1] None
- ☐[2] 1 to 5
- ☐[3] 6 to 10
- ☐[4] More than 10
- ☐[5] *No comment or don't know*

2. Since the mid 1990's, the volume of spending on prescription drug promotion aimed at the public has grown enormously. How much has this growth affected the work of your organization and/or its members?

- ☐[1] Substantial effect on organization/members' work
- ☐[2] Moderate effect on organization/members' work
- ☐[3] Little to no effect on organization/members' work
- ☐[4] *No comment or don't know*

3. Overall, what is the quality of information on drug benefits and risks in DTCA?

- ☐[1] Excellent
- ☐[2] Good
- ☐[3] Poor
- ☐[4] Very poor
- ☐[5] *No comment or don't know*

→ ***What evidence have you seen to support this view? [Please mark all that apply]***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

4. How do you think DTCA affects the public's understanding of drug therapy?

- ☐[1] Improves public understanding
- ☐[2] Worsens public understanding
- ☐[3] No effect on public understanding
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

5. How do you think DTCA affects the public's understanding of disease risks?

- ☐[1] Improves public understanding
- ☐[2] Worsens public understanding
- ☐[3] No effect on public understanding
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

6. How do you think DTCA affects doctor/patient communication?

- ☐[1] Improves communication
- ☐[2] Worsens communication
- ☐[3] No effect on communication
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

7. How do you think DTCA affects the frequency of

What evidence have you seen to support this view?

patient visits to doctors?

- ☐[1] Increases the frequency of visits
- ☐[2] Decreases the frequency of visits
- ☐[3] No effect on frequency
- ☐[4] *No comment or don't know*

→

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

8. How do you think DTCA affects the *appropriateness* of visits to doctors?

- ☐[1] Increases the appropriateness of visits
- ☐[2] Decreases the appropriateness of visits
- ☐[3] No effect on appropriateness
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

9. How do you think DTCA affects prescribing?

- ☐[1] Increases the appropriateness of prescribing
- ☐[2] Decreases the appropriateness of prescribing
- ☐[3] No effect
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

10. How do you think DTCA affects *patients' use* of prescription drugs?

- ☐[1] Increases appropriateness of use
- ☐[2] Decreases appropriateness
- ☐[3] No effect
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

11. How do you think DTCA affects *public* spending on prescription drugs?

- ☐[1] Increases spending
- ☐[2] Decreases spending
- ☐[3] No effect
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

12. How do you think DTCA affects *private* spending on prescription drugs? (out-of-pocket, private insurance and health care companies)

- ☐[1] Increases spending
- ☐[2] Decreases spending
- ☐[3] No effect
- ☐[4] *No comment or don't know*

→ ***What evidence have you seen to support this view?***

- ☐[5] own experience with DTCA
- ☐[6] published or unpublished empirical studies on DTCA
- ☐[7] indirect empirical studies [not on DTCA]
- ☐[8] theoretical analyses or expert opinion
- ☐[9] little to no evidence

13. In settings where DTCA is allowed, how soon after a drug is first marketed should advertising to the public be permitted?

- ☐[1] Immediately
- ☐[2] Six month post market launch
- ☐[3] One year post market launch
- ☐[4] Five years post market launch
- ☐[5] Following patent expiry
- ☐[6] *No comment or don't know*

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14. In settings with DTCA, should limits be set on which prescription drugs may be advertised to the public?

15. Should DTCA campaigns specifically target the following population groups?

☐[1] *No comment or don't know*
☐[2] No
☐[3] Yes → If yes, base limits on: *[mark all that apply]*
- ☐[3] health condition
- ☐[4] drug safety profile
- ☐[5] drug efficacy profile
- ☐[6] whether payment is public or private

A. The elderly	☐[1] Yes	☐[2] No
B. Women	☐[1] Yes	☐[2] No
C. Men	☐[1] Yes	☐[2] No
D. Adolescents	☐[1] Yes	☐[2] No
E. Children	☐[1] Yes	☐[2] No
F. Low income people, disadvantaged groups	☐[1] Yes	☐[2] No

16. How appropriate or inappropriate are the following types of media for DTCA?

	Very appropriate	←	Neutral	→	Very inappropriate
A. Magazines	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]
B. Television	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]
C. Billboards	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]
D. Internet	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]

17. In your opinion, should the Canadian government allow the following types of prescription drug ads?
Note: Canada is currently considering legislative change.

	YES	NO
A. Full DTCA, including product name and health claims	☐[1]	☐[2]
B. Full DTCA as above, with 'free trial offers' or price reductions	☐[1]	☐[2]
C. Disease-oriented advertisements with no product name	☐[1]	☐[2]
D. Reminder ads [*brand name, images, but no health claims*]	☐[1]	☐[2]
E. Comparative price advertising [*name, quantity and price only; no images or advertising text; joint lists of competing products*]	☐[1]	☐[2]

18. Does your organization have an official policy or position on DTCA?
☐[1] No
☐[2] Yes → Please briefly describe: _____

19. Have you or your organization researched DTCA's effects on costs, health, or use of health care services?
☐[1] No
☐[2] Yes → Please explain: _____

Type of organization
[please mark best fit]

- ☐[1] health professional organization
- ☐[2] consumer group
- ☐[3] disease-specific patient group
- ☐[4] pharmaceutical industry
- ☐[5] advertising industry
- ☐[6] media / publishing
- ☐[7] government agency
- ☐[8] private health or drug insurance
- ☐[9] other, please specify_____

20. Comments?

PLEASE FAX THIS QUESTIONNAIRE TO: (1 604) 822 5690

Appendix 7.2

Additional Written Comments on Questionnaires, by sector

NON-PROFIT/CONSUMER GOUPS
DTCA should never be allowed for historical reasons, the experience with thalidomide. There is also experience with the heavy marketing of thalidomide overseas, leading to increased sales and increasing negative results. The fear is that history would repeat itself.
DTCA should be banned, except for comparative price advertising.
We are against all DTCA.
We are opposed to the introduction of DTCA in Canada.
We support the current prohibition and urge more stringent monitoring and enforcement.
DISEASE/ PATIENT GROUPS
The present Canadian situation is a maximum. We would prefer better control of what is allowed.
The quality of DTCA is currently poor. That is why I marked 'no effect' on public understanding of drug therapy. It needs to be improved so it can improve doctor/patient communication. What DTCA should be is not what it is now.
We are opposed to DTCA. More funding is needed for education. Tighter controls are required, mandatory transparent review process for advertisements, as well as a mandatory transparent reporting system for violations.
GOVERNMENT: FEDERAL, PROVINCIAL AND TERRITORIAL, AND PRIVATE PAYERS
An extra comment on the question about appropriateness/ inappropriateness of various media: all media are inappropriate for publicly funded drugs.
We have consistently supported a position of opposition to DTCA and support for regulation by Health Canada.
We have certainly seen a significant increase in client demand for products based on DTCA. Physicians and pharmacists also indicate to us concerns over patient demand as a result of DTCA.
We oppose DTCA.
We are strongly opposed – unless there is evidence to support the use of DTCA.
Advertising=marketing=selling drugs. In the US, where DTCA is permitted, what are the costs of policing regulations, in terms of money and staff? This needs to be considered. More general information on diseases is warranted ahead of prescription drug ads. More emphasis should be placed on prevention and non-drug therapies.
DTCA has no proven health benefits and real potential for harm. If you want to see the impact of DTCA on consumers, look at what direct-to-doctor marketing has done to prescribing.

GOVERNMENT: FEDERAL, PROVINCIAL AND TERRITORIAL, AND PRIVATE PAYERS – CONTINUED
In terms of research on DTCA, we review products with high utilization growth which usually also have DTC advertising. Pharmaceutical CEO's are now being chosen for their experience marketing products to the public (press clipping example enclosed). A second enclosed US press clipping draws the link between high drug prices and spending on promotion. "The subcommittee found, however, that the 22 largest pharmaceutical manufacturers were spending 24 cents of every revenue dollar on promotion. This was approximately four times their spending on research." [Mintz M. What's new about prescription... Washington Post, Feb 10, 2001 pB01]
I doubt DTCA helps prescribers to better prescribe and patients to better use drugs. It increases drug utilization, sometimes for the best, but also with costs and risks of inappropriate prescribing and use. My comments are based on my own analysis and my understanding of determinants of prescribing following about 15 years of observation.
I believe there should be DTCA with EQUAL TIME AND EQUAL SPACE for a balancing message from Health Canada. This would be permissible under the Charter of Rights & Freedoms, as are health warnings on cigarettes.
I disagree with DTCA
I support the current federal government position.
DTCA usually worsens understanding of drug therapy and disease risks but there have been a few exceptions, where it improves public understanding. It is likely to decrease appropriateness of visits more than increase appropriateness, but both are likely to occur.
It would have been useful to have a no comment/ don't know option on the targeting of specific population groups.
The effect of DTCA on doctor/patient communication is likely to depend on the specific therapy and disease. We need to consider the current underutilization of drug therapies for some diseases. DTCA may help in patient education in these situations.
We are opposed to DTCA as it exists in the US.
DTCA must be oriented towards patient empowerment to take care of his or her health condition.
HEALTH PROFESSIONALS
Too much information is presented in too short a time to be absorbed by the listener. DTCA places increased pressure on doctors to prescribe newer and more costly treatments. Doctors are under pressure to spend more time with patients and explain new therapies. The outcome would be positive it this were done; the more discussion of their therapy, the better. DTCA may not lead to the most cost-effective treatment of their condition, however. There should be ample evidence from third party programs in the US for the demand for new drugs stimulated by DTCA. On the organization's policy: while there is discussion on this policy and concern over increasing costs of drug therapy and change in the traditional channels of distribution for drug information (less to health professionals and more to the public), no policy has been enunciated at this time.
The Canadian Medical Association opposes the legalization of DTCA.

HEALTH PROFESSIONALS - CONTINUED
DTCA increases awareness of new drug therapies. I'm not sure that this leads to increased understanding. It is likely to lead to more dialogue between doctors and patients. On its own, I am not sure that DTCA improves communication. Prescription rates do go up. I would hope they are appropriate. If DTCA goes ahead how will this be monitored and policed and how will the industry be held accountable?
We oppose DTCA, but support the need for better health and drug related information for consumers to make informed choices.
I found it difficult to answer some questions because I do not approve of DTCA because the present quality of prescribing is generally poor, in terms of appropriate use of medicines, and will be worsened by DTCA. The industry favours it because it will increase sales, and not appropriate use.

PHARMACEUTICAL INDUSTRY
American ads are seen in Canada. Canadian policies should be harmonized with the USA.
We are against expanding DTCA and support full enforcement of the existing legislation.
The consumer has a right to be informed. Shifts away from self-care due to prescription drug advertising should be considered during policy development. Prescription drug advertising should indicate that the product only available by prescription, following consultation with a doctor.

ADVERTISING INDUSTRY
By allowing access to drug information/advertising provided by the source of most available drug information, the pharmaceutical industry, consumers would be in a better position to participate in their own health care. We do not need to use the US system, we can take the best parts of it and add whatever we want to make it work within a Canadian context.
With the growing spill effect of DTCA from the US into Canada, we believe strongly that 'made in Canada' guidelines could reduce confusion, aid in Canadian understanding and perhaps even improve on the US model. Regulated DTCA will assist public in gaining information on prescription drug treatments.
I believe DTCA is a good communication tool to the consumer as long as the information is presented in a balanced manner, that is, equal emphasis on both the risks and benefits of the product. Mandatory review should be enforced to avoid dissemination of inaccurate and unbalanced information. This is especially true for DTCA on TV or radio where the consumer is referred to a toll-free line or an Internet site. Content of both media must be carefully reviewed so that the consumer is not misdirected to bad information. DTCA should be allowed after a minimum of 3 months after launch, so health care professionals have the time to digest new information.

Appendix 7.3: Organizational affiliations of survey respondents

Advertising Standards Canada
Alberta Health
Alliance for Access to Medical Information
BC Ministry of Health and Ministry Responsible for Seniors
Canadian Cancer Society/National Cancer Institute of Canada
Canadian Diabetes Association
Canadian Health Coalition
Canadian Nurses Association
Canadian Pharmaceutical Association
Canadian Pharmacists Association
Canadian Society of Hospital Pharmacists
Canadian Treatment Advocates Council
Canadian Veterinary Medical Association
Canadian Women's Health Network
CIHI (Canadian Institute for Health Information)
Compagnie d'Assurances SSQ
Conseil Consultatif de Pharmacologie, Quebec
Consumers Association of Canada
D.E.S. (diethylstilbestrol) Action Canada
Department of Medicine, University of Toronto; Canadian Medical Association
Drug Plan and Extended Benefits Branch, Saskatchewan Health
Extended Benefits and Pharmaceuticals Program, Yukon Territorial Government
Faculty of Medicine, Memorial University
Faculty of Pharmacy, University of Montreal
Financial and Management Services, Northwest Territory Department of Health and Social Services
Green Shield Canada
Home Care and Pharmaceuticals Division, Health Canada
National Association of Pharmacy Regulatory Authorities
National Drug Manufacturers Association of Canada
Non-Insured Health Benefits Medical Services Branch, Health Canada
Nova Scotia Department of Health
Ontario Lung Association
Ontario Teachers' Insurance Plan
Pharmaceutical Advertising Advisory Board
Pharmaceutical Consultant Group, Manitoba Health
Pharmaceutical Issues Committee (Manitoba, P.E.I., Nova Scotia representatives)
Pharmaceutical Programmes, Alberta Health
Physicians for a Smoke Free Canada

Prescription Drug Program, Department of Health and Wellness, New Brunswick
Provincial Drug Program, Manitoba Health
Rhoxalpharma
Rx&D, Canada's Research Based Pharmaceutical Companies
School of Business, Concordia University
Stroud Consulting Inc.
Thalidomide Victims Association of Canada
Therapeutics Initiative
Therapeutics Products Programme, Health Canada
Unité Coordination des Affaires Pharmaceutique, Ministère de Santé et des Services Sociaux
Working Group on Women and Health Protection

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Chapter 8

Conclusion

In 2002, Dr. Henry Haddad, president of the Canadian Medical Association, described a Canadian television ad for sildenafil (Viagra) as indicative of a dangerous trend, which "makes light of the serious nature of prescription medicine in Canada."[1] John Calfee, writing on behalf of the Fraser Institute, a Canadian business think tank, argued instead that, "Under-treated medical conditions are the focus of a large proportion of DTC ads... DTC advertising is filling an informational void, reaching out to consumers and patients and their families to provide essential information and urge them to talk to their physicians (which is, of course, the only way to obtain advertised drugs)."[2]

On the one hand DTCA is seen as a threat to public health in Canada; on the other it is seen as a means to meet as-yet-unmet patient needs, and therefore as a boon to health. Within the policy debate on the introduction of DTCA in Canada, such competing claims are common. DTCA exists at present to some extent in Canada, and full legalization remains on the policy agenda. However, little research has been carried out on the effects of DTCA in Canada, and there are considerable gaps in evidence on outcomes in the two countries where it is currently legal, the U.S. and New Zealand.

An important shift in health care policy, such as the introduction of patient-directed prescription drug advertising, should be based on evidence that likely public health benefits clearly outweigh the possibility of harm. The aim of this study was to move the debate on DTCA beyond competing claims about likely effects. It contributes to discussions in Canada on potential legislative change and current enforcement standards, through a comprehensive overview of the existing empirical evidence on outcomes of DTCA, a survey of policy experts in Canada and a review of international policy developments, and through an original study that aims to fill a gap in knowledge about the effects of patient-directed advertising on prescribing in primary care.

Is DTCA likely to lead to a net cost or benefit to society? The empirical evidence available to date, and the original research carried out within this study, point unequivocally in the same direction: the costs to the public, to the patient-doctor relationship and to publicly financed health care services are likely to far outweigh *alleged* benefits (with the emphasis on **alleged** since, to date, no evidence of significant benefit have emerged, except to shareholders of advertising agencies, the brand-name pharmaceutical industry, and the media that receive advertising dollars).

In 2002, a U.S. advertising company promoted its services to pharmaceutical companies with the claim that: "Today's patients are the new spokespeople for your brand. Their active voice influences the medications physicians prescribe and the profits you make."[3] Fortunately for the advertiser but unfortunately for the patient, the results of this study suggest that such claims are not without substance.

8.1 What this study adds

This study includes four key components:

- A critical review of the empirical research evidence on outcomes of DTCA
- A comparative patient-doctor survey on the effects of DTCA on prescribing decisions, carried out in physicians' offices in a Canadian and U.S. setting;
- A review of international DTCA policy developments
- An opinion survey of Canadian pharmaceutical policy experts.

8.1.1 DTCA literature review

The aim of this literature review was to examine the current state of knowledge on the effects of DTCA, through a comprehensive literature search of medical, health sciences, economics, business, law and current affairs databases, as well as the fugitive literature (as accessed through the Internet and electronic list serves). The literature search covered the period from 1991 to 2001, and included studies measuring health, behaviour and knowledge, provision, use and quality of health care services, and effects on health care costs. Four key types of studies were identified: analyses of the content and accuracy of advertisements; consumer surveys of advertising exposure, opinion and behaviours (both

actual and hypothetical); surveys of health professionals' opinions, experiences and behaviours; and restrospective data analyses on advertising spending, prescribing, sales and use of physician services.

Content and Accuracy of Advertisements

U.S. print advertising information quality has been studied to a greater extent than U.S. television advertising or than either print or television advertising in New Zealand. Around one-third of ads published between 1993 and 1995 failed to provide adequate risk information, and 15% had no risk information in advertising copy.[4] An analysis of the educational content of 10 years' worth of ads in major magazines (1989 to 1998) found that most failed to provide the information consumers need to make informed choices, such as the likelihood of treatment success, how a drug works, or any other possible treatments.[5] Regulatory reviews, similarly, indicate that violations are common, with over 90 DTCA campaigns found to have violated U.S. FDA regulations from 1997 to 2001, and repeat violations for the same product occurring commonly.[6] A New Zealand regulatory review in 2000 found that 83% of voluntarily submitted television ads and 24% of print ads violated the Medicines Act, mainly because of inadequate or missing risk information. [7]

Consumer Surveys

U.S. general population surveys based on random nationally representative samples indicate that a substantial minority of the public responds to prescription drug advertising by speaking with their doctors about advertised drugs and conditions, and 5-19% directly request drugs.[8 9 10] These surveys are based on recall and self-reported behaviour and thus may be subject to recall bias. However, patients consistently report that they respond to DTCA by discussing advertised drugs with their physician, and by requesting prescriptions. Most patients who report having requested prescriptions also say that they received them.[8] Some patients also report that they would switch doctors if they could not obtain a desired prescription.[9]

Many consumers also believe that they are better protected by regulation than is the case: in a national survey, 28% thought that only the safest prescription drugs could be advertised on U.S. television [10]; in a California survey, 43% believed that only prescription drugs 'found to be completely safe' could be advertised to the public, and half thought that the ads were pre-approved by the government.[11]

Surveys of health professionals

Fewer surveys have been carried out of physicians' experiences, and the only study published in a peer-reviewed journal was carried out in 1994, when exposure to DTCA would have been considerably lower than it is currently:[12] 89% of respondents at that time did not feel that DTCA enhances the patient-physician relationship and 71% believed that they were pressured to prescribe specific drugs. A more recent U.S. FDA survey asked physicians about their most recent consultation with a patient who mentioned DTCA.[13] Patients asked about a brand-name drug in nearly 9 out of 10 of these consultations, and directly asked for a prescription just over half the time. Many physicians reported pressure to prescribe; if the patient had directly asked for a prescription for a specific brand, 61% reported pressure, and half of those said they felt somewhat or very pressured.

Retrospective analyses of sales and prescribing

Retrospective database analyses have examined the relationship between DTCA and prescribing volumes and cost. The National Institute of Health Care Management has published three analyses of the relationship between DTCA and annual increases in retail prescription drug expenditures in the U.S. [14 15 16] They found that increases in the sales of drugs that were heavily advertised to the U.S. public were responsible for a large proportion of the annual increases in spending on prescription drugs. For example, in 2000, 50 drugs that had been advertised to the public were responsible for U.S. $9.9 billion of the $20.8 billion increase in retail spending over 1999 levels. The number of prescriptions for these drugs rose by 25% over the one-year period versus a 4% increase for all other drugs. These products are also heavily promoted to physicians, so DTCA is

unlikely to be responsible for the entire increase; however, there is no doubt that it is a contributing factor.

Physician consultations

Pharmaceutical market research reports also indicate that patient visits for conditions treated by advertised drugs increase during an advertising campaign, and the Dutch Health Inspectorate reported a large increase in visits for toenail fungus during an unbranded advertising campaign for terbinafide (Lamisil).[17] However, no research has been carried out on the health status of patients seeking care after seeing DTCA, or the appropriateness of self-diagnosis and subsequent physician diagnoses.

In summary, there is evidence that the U.S. public is aware of DTCA, that patients request advertised medicines from their physicians in response to DTCA, and that physicians prescribe most requested medicines. Additionally, there is evidence that a proportion of these physicians experience feelings of pressure to prescribe. And finally, there is evidence of an association between DTCA and increases in U.S. prescription drug costs. Less research has been carried out in New Zealand. There is no reliable evidence that DTCA improves compliance, that it leads to more appropriate early diagnosis of under-treated conditions, or that it prevents hospitalizations and serious disease consequences.

8.1.2 Patient-doctor survey

This is the first study to collect comparative data on requests for drugs, and prescribing in response to requests, in environments with and without legal DTCA. A survey was carried out in the offices of 78 primary care physicians, involving 1431 patients in Vancouver, B.C. and Sacramento, California. The unit of analysis was a matched set of patient and physician questionnaires covering a single consultation. The primary hypothesis was that patients in Sacramento, in an environment with full, legal DTCA, would request and receive more advertised drugs than patients in Vancouver, in an environment where DTCA is illegal, but where there is exposure to cross-border advertising. Additionally, patients in each setting with higher self-reported advertising

exposure were hypothesized to request more advertised medicines than patients with lower exposure.

This study used a conceptual framework based on Andersen and Newman's behavioural model of health care service utilization. [18] Within this model, DTCA is hypothesized to be one of many individual and environmental factors affecting patient behaviours, rather than an isolated determinant of care-seeking behaviours. By modelling the effects of DTCA within the context of established determinants of health care use, it is possible to explore the extent to which patient requests for advertised drugs follow or diverge from established patterns associated with use of health care services.

Results

In a single consultation in primary care, Sacramento patients were nearly twice as likely to request prescriptions from their doctors as patients in Vancouver: 15.8% versus 9%. They were also more than twice as likely to request advertised drugs: 7.3% versus 3.3% in Vancouver.

Patients reporting higher individual advertising exposure in both settings requested more DTC-advertised medicines. Effective advertising exposure was measured in three ways: the number of products a patient reported having seen advertised; whether or not they identified themselves as having a condition treated by an advertised medicine; and whether they reported using advertising as an information source. When these individual advertising exposure measures were entered into a General Estimation Equation model together with location of residence (Sacramento or Vancouver), the influence of location became attenuated and non-significant, although individual advertising exposure measures remained significant. This suggests that differences between patient request rates were more strongly associated with DTCA exposure than with underlying cultural or health system differences between the U.S. and Canada. Such unmeasured differences between settings are likely to exist in spite of model adjustments for sex, age, income, education, drug payment method, and self-reported health status, but they appear unlikely to account for most of the observed variation in the rate of requests for advertised drugs.

To what extent does DTCA stimulate health-seeking behaviour (such as requests for medicines) that follows established patterns of determinants of health care use and patient health needs? There was no significant relationship between sex, age or self-reported health status and the likelihood that a patient would request a DTC advertised drug. In other words, patient requests for advertised medicines diverged from traditional care-seeking patterns expected to reflect health care needs. In contrast, requests for non-advertised medicines did occur more frequently among patients with poorer self-reported health status.

Approximately three quarters of patients who requested DTC advertised drugs in both settings received prescriptions for the drugs they requested. **Thus the difference in effect on prescribing in the two settings was attributable to differences in patient request rates, not in prescribing rate in response to requests.**

Patients who requested advertised drugs were also highly likely to leave consultations with one or more new prescriptions, regardless of which product was prescribed: 86% of such patients received one or more new prescriptions. In contrast, in the two sites combined, physicians provided one or more new prescriptions to only 26% of patients who had not requested medicines.

Although physicians prescribed most requested medicines, they were often ambivalent about treatment choice. They judged half of these medicines to be a 'possible' or 'unlikely' choice for other similar patients with the same health condition, rather than a 'very likely' choice. In contrast, only one in eight prescriptions not requested by patients was judged to be a 'possible' or 'unlikely' choice for other similar patients. Taken together with the high prescribing rate in response to patient requests, this suggests that DTCA has a negative effect on prescribing appropriateness.

Physicians were ambivalent nearly as often about prescriptions for requested non-advertised medicines. However, many of these requests were for drug classes recognized

as frequently being problematic in terms of prescribing appropriateness in primary care: antibiotics, anxiolytics/hypnotics, and analgesics.

This survey is the first to document an effect on patient requests for medicines and prescribing patterns from exposure to DTCA in a Canadian setting. This is likely to reflect both cross-border advertising and 'made-in-Canada' reminder and disease-oriented advertising. Twenty-nine percent of the requests for advertised drugs in Vancouver were for products that had been advertised to the Canadian public, including one drug not advertised in the U.S.

The rate of requests for advertised drugs was lower in Vancouver than that in Sacramento, as was the rate of requests among patients with less versus more self-reported advertising exposure. Thus the survey results suggest both that current exposure levels in Canada are affecting prescribing in primary care, and that a legal change would be expected to result in higher population exposure and thus in a higher volume of prescriptions affected by advertising.

Relevance to other empirical research on DTCA

The Sacramento rate of requests for advertised prescription medicines in a single observed consultation was remarkably similar to rates reported in U.S. nationally representative consumer surveys. The prescribing rate in response to DTCA drug requests in both settings was also similar to that reported in other U.S. consumer surveys.

U.S. analyses of print advertising content indicate that educational content is poor, particularly in terms of providing the public with any indication of the likelihood of treatment success, and the use of vague, emotive claims of benefit rather than specific outcomes is common. This research on DTCA content suggests that the public often does not obtain the type of information from DTCA needed to participate in informed treatment decision-making. If physicians are prescribing most requested advertised drugs, often in spite of their own ambivalence about the choice of treatment, and patients are absorbing misleading, or at least very incomplete, information on the products they are

requesting, prescribing appropriateness may suffer. Patients may be unaware of the range of available treatment options, and how an advertised medicine compares to treatment alternatives. Additionally, patients may or may not accurately self-diagnose, as information on medical conditions in DTCA is also frequently inadequate.[5] A second related concern is that if DTCA leads to a shift in prescribing choice, physicians may be prescribing medicines with which they are less familiar. This raises concerns about attention to contraindications, interactions with other medicines or foods, and appropriate administration and dosage.

The results of this survey suggest that, in addition to product-specific effects, DTCA is likely to lead to increases in prescribing volume: nearly nine out of 10 patients requesting an advertised drug left the consultation with one or more new prescriptions, as compared to under three in 10 patients not requesting medicines. The health consequences of an increased volume of prescription drug use stimulated by DTCA are unknown. However, a systematic review of studies of adverse drug reactions in U.S. hospitals identified adverse drug reactions as being between the 4th and 6th leading cause of death in the U.S.[19]

The effects of patient requests on prescribing decisions observed in this study are consistent with the results of an extensive and rapidly growing body of research on social influences on prescribing decisions. Physicians are affected by their perceptions of patient expectations of a prescription, and are more likely to prescribe medicines if they believe their patients desire them. The study results are also consistent with the economic rationality of pharmaceutical manufacturers' decisions to invest increasing amounts in this marketing technique: if it did not have an effect on sales over and above that generated from promotion aimed solely at physicians, companies would be expected to abandon DTCA, or at the very least to limit rather than expand investment into this marketing technique.

Limitations of this study

The primary care survey was cross-sectional in nature, carried out at a single point in time for each site. Therefore causality cannot be inferred. Additionally, there was a ten-

month delay between the Vancouver and Sacramento portions of the study, due to unanticipated difficulties with identifying a U.S. comparison group. Given the increase in spending on DTCA and hence population exposure over time, this delay may have exaggerated exposure differences between the two settings. However, it would not have affected the association between higher individual exposure levels within each setting and requests for DTC advertised medicines. Nor would it have affected the relationship between requests and prescriptions granted.

The patient population in this study had higher than average income and education. This limits generalizability to other population groups. Additionally, this was a cluster sample of patients of primary care physicians who had agreed to participate in the study. Generalizability to broader regions or patient populations cannot be assumed. A volunteer bias would have been expected among physicians. Although the study procedures aimed to minimize disruption of physicians' workday, some disruption was inevitable, in part due to the requirement that physicians complete brief questionnaires after each patient contact. Additionally, most invited physicians had some association with a medical faculty. In both cases, the likely direction of bias would be expected to be towards more cautious, appropriate prescribing. Whether physicians' opinions tended to be more favourable or more opposed to DTCA than family physicians in general is unknown, as we did not ask physicians their opinions.

Although patient attitudes to the doctor-patient relationship and to medicine use were similar between the two settings, and adjustments were made for age, gender, income, education, drug payment and self-reported health status, it is not possible to control for all likely U.S./ Canadian cultural differences or differences in organization of health care services. Thus some unmeasured differences in the two comparison groups were likely to remain, and may have affected results. For example, differences in health insurance coverage in the U.S. partially determine who is and is not in the physician's office, whereas in Canada there is universal access to primary care services. Whether this affects the rate of requests for advertised drugs is unknown, and it is conceivable that it could affect not only who is at the physician's office but what they do when they are there.

However, the consistent relationship observed in the two settings between individual patients with higher self-reported advertising exposure and DTCA drug requests suggests that exposure plays an important role regardless of the influence of other social factors.

Finally, this study compares two levels of population exposure to DTCA. It does not compare environments with and without DTCA. U.S./Canadian differences observed in the study are likely to represent an underestimation of differences between settings with and without DTCA. During the period in which the study was being planned, two policy changes occurred which affected population exposure to DTCA. The first, which affected both settings, was the U.S. FDA's decision to open up full product advertising on television and radio in the U.S., by limiting requirements for risk information provision within a broadcast ad. This affected both U.S. exposure levels and Canadian cross-border exposure. Secondly, Health Canada began to allow reminder advertising in addition to disease-oriented advertising in 1999 and 2000, and chose not to pursue aggressive enforcement in several cases judged to be in violation of the law. During this period, the industry began advertising more prescription-only products to the Canadian public, using a variety of media. The Canadian population's exposure to DTCA is likely to be third in intensity internationally, after the U.S. and New Zealand. Although in one sense this limits the applicability of the results to settings that do not allow DTCA, it also allowed for exploration of a dose-response relationship within each setting, adding to the evidence that differences in outcome were related to advertising exposure, rather than other unmeasured U.S./Canadian differences.

8.1.3 International policy discussions on DTCA

The patient-doctor survey was carried out within the context of research on the potential impacts of full legalization of DTCA in Canada. DTCA is highly controversial, both in the U.S. and New Zealand, where it is legal, and where it is not allowed. Canada is not alone in considering legislative change: Australia, the European Union and South Africa have all carried out policy reviews during the last few years and discussed the possibility of introducing DTCA. In contrast, New Zealand has considered the possibility of imposing a ban or restrictions on advertising activities.

These policy reviews share a number of characteristics: where DTCA is currently prohibited on public health grounds, recommendations to introduce it have been made in the absence of evidence of public health benefit or of assurance of lack of harm. This is the case both in terms of patient health and of the effect of DTCA on the quality of health care services. There is evidence that DTCA increases costs, and in countries with public financing of prescription drugs in outpatient settings, policies recommending introduction of DTCA conflict with the need to manage limited health care resources cost-effectively. This is reflected in national policy discussions on DTCA, with drug benefit managers in Canada, New Zealand and Europe expressing opposition to introduction. Proposals to introduce DTCA have come both from federal health ministries, as in Canada, and from industry ministries (DG Enterprise in Europe).

Policy discussions on DTCA are remarkably similar across jurisdictions. One of the key arguments made in favour of introduction is that DTCA will provide patients with needed information about medicines, and lead to greater empowerment, patient autonomy and involvement in decision-making. This line of argument tends to blur the distinction between patient information needs – as identified mainly through consumer surveys and focus groups– and advertising goals. Both the content and the aims of DTCA differ from criteria for good quality patient health and drug information.

Another argument made in favour of DTCA is that it will improve the quality and outcome of health care services by stimulating the under-diagnosed and under-treated to seek care. This has not been tested empirically, and the flip side of this claim is a concern that DTCA will lead to over-treatment, and that it contributes to unnecessary medicalization of healthy individuals and life processes, such as ageing, baldness or menopause. Any research on care-seeking behaviours stimulated by DTCA needs to investigate both the benefits and risks of stimulating patients to seek care. This should include an analysis of the types of conditions identified, accuracy of diagnoses, and appropriateness of treatment decisions. In order to understand the net direction of effect of DTCA, a comparison group would also be needed.

DTCA policy also has legal ramifications. For example, there are differences of opinion within Canada on whether advertising restrictions can be maintained in the light of corporations' rights to freedom of expression. The effect of DTCA on confidentiality of medical records and on patient privacy is also controversial. Marketing databases for patient-directed advertising of prescription drugs differ from databases for other consumer products, in that they may include sensitive information on disease diagnoses. A third legal concern is the effect of DTCA on manufacturers' liability for injuries caused by advertised prescription drugs. Traditionally, manufacturers have been protected by the learned intermediary defense. As long as they have warned physicians of product risks, physicians act as 'learned intermediaries' who are legally responsible for prescribing decisions and for informing the patient about potential risks. With an increasing shift towards patient-directed advertising, manufacturers may begin to face greater liability.

Finally, in all jurisdictions the pharmaceutical and advertising industries strongly support the introduction of DTCA. This has led a British commentator, Annibel Ferriman, to suggest that with large potential profits at stake, the DTCA debate in Europe, "...is not likely to end until the drugs industry gets its way."[20] The European Commission's resurrection of a proposal for partial introduction of DTCA, despite a nearly 12-1 vote against this proposal by the European Parliament, would tend to support this view. [21] Similarly, Canada has already seen a partial introduction of DTCA (disease-oriented and reminder advertising) without any legislative change, and the possibility of full introduction of DTCA has been under active consideration since at least 1996.

8.1.4 Survey of Canadian pharmaceutical policy experts

Within the context of discussions of potential introduction of DTCA in Canada, this study included an opinion survey of pharmaceutical policy experts working within sectors expected to be affected by DTCA. The survey canvassed:

- *Health care payers, managers and regulators:* governments and private payers
- *Health care service providers:* health professional organizations
- *Health care users*: non-profit/consumer groups and disease/patient groups

- *DTCA producers and disseminators*: advertising and pharmaceutical industries.

Potential participants were identified through membership lists of pharmaceutical policy committees, a national DTCA consultation, and an Internet search carried out by a librarian to identify organizations within relevant sectors. Seventy-nine people were faxed a questionnaire, 60 of whom participated (76% response rate).

Most survey respondents believed that the information quality of DTCA is poor, across all sectors. This is consistent with the research evidence. The results indicated a great deal of concern about effects of prescription drug advertising on appropriateness of care and direct health care costs. Most respondents from the health professions, consumer and patient groups and governments believe that DTCA has a negative impact on public understanding of drug therapy and disease risks, appropriateness of prescribing, drug use and physician consultations. In contrast, most respondents from the pharmaceutical and advertising industries believed that the effects of DTCA on health care quality were positive. No attempt was made to solicit opinions on indirect effects, such as hospitalization, morbidity or mortality, as these effects have not been researched.

Results of the survey were highly polarized, with strong support for the introduction of DTCA in Canada from advertising and pharmaceutical industry respondents, but very little support among experts from the health professions, consumer/non-profit groups or disease-specific patient groups. The only responses that were not polarized were on likely cost impacts: almost all respondents, from all sectors, believed that DTCA would lead to increased prescription drug costs and increased volume of physician consultations. Few respondents supported targeting of children (3%) or adolescents (7%) in DTCA campaigns, and many recommended against targeting of any listed population group (covering everyone except infants).

Most supported product-specific limits on DTCA, and drug safety profile was the most commonly cited rationale. Magazines and the Internet were considered to be appropriate

for DTCA by a third of respondents; however, only 10% believed that billboards and 13% that television were appropriate media.

Opinions on legalization differed by sector, with around 30% overall supporting legal change to allow full DTCA. Few were supportive of advertising that included financial inducements, such as free trial offers. The majority of public sector/private payer respondents supported disease-oriented advertising, but not other forms of DTCA.

The results of this survey, in terms of opinions on information quality in DTCA, and the expected direction of DTCA on the quality and cost of health care services, were broadly consistent with the research evidence on outcomes of DTCA, as described in the literature review. The expected direction of effect on prescribing appropriateness reported by most pharmaceutical policy experts in all sectors, except the pharmaceutical and advertising industries, is also consistent with the results of the doctor-patient survey.

This was an opinion survey only, but it was a survey that included individuals who have actively participated in policy development on DTCA, particularly those involved from provincial and federal governments. The degree of skepticism with respect to expected outcomes of DTCA was remarkable: from a public policy perspective, a shift leading to increased drug and physician costs might be considered if health care quality was expected to improve. If the result of relaxing current DTCA regulations is to increase health care costs while simultaneously leading to deteriorating quality of care, as the majority of these experts believe, it seems hard to justify such a shift.

8.2 Recommendations

Taken together, the results of the four components of this study suggest that the effect of DTCA on health care quality is more likely to be negative than positive. The results of the patient-doctor survey, specifically, suggest both that DTCA is having a negative

impact on prescribing appropriateness in a U.S. setting, where it is allowed, and in a Canadian setting, where it is not allowed.

8.2.1 No justification for legislative change to introduce DTCA

Given the lack of evidence of benefits to health or the quality of health care services from DTCA, there is no current research-based justification, from a public health perspective, to legalize this form of pharmaceutical marketing in Canada.

Consumer drug information needs cannot be met by advertising, which aims to sell a product. However, the public does have a legitimate need for accurate, unbiased and comparative information on alternative approaches to treatment, including information on all available treatments, drug and non-drug, and including the option not to treat. This information should be publicly financed and be integrated into existing health care and information services. The types of methods used by independent drug bulletins to evaluate the strength and quality of evidence of drug safety, effectiveness and/or therapeutic advantage in comparison to existing alternatives can also be applied to consumer drug information. [22] No change to pharmaceutical advertising legislation would be required.

8.2.2 Reminder and disease-oriented advertising: better controls are needed

If a clause in Canada's *Food & Drugs Act* that was introduced to allow comparative price advertising is ambiguous, and thus allows for reminder and disease-oriented advertising, clarifying language should be added to close off this loophole. There is no justification from a public health perspective for a policy shift to allow branded reminder ads under a provision introduced in 1978, before the advent of DTCA, to allow comparative price advertising.

Disease-oriented advertising can have either a negative or positive impact on health, depending on the condition that is advertised and the message conveyed. Manufacturers have an incentive to choose specific conditions on the basis of marketing priorities; these do not necessarily match public health priorities. For example, they may have an

incentive to exaggerate the prevalence of conditions, and to extend the domain of pharmaceutical treatment beyond true health care needs, as was recently described in an exposé in the *British Medical Journal* on the role of pharmaceutical companies in the redefinition of female sexual dysfunction as a disease.[23] In addition to having negative social consequences, marketing priorities may skew the allocation of health care resources away from medical problems with a greater public health impact.

One option is for public health authorities to engage advertising companies in developing disease-oriented campaigns to meet identified health needs. In order to maintain a public health orientation, and to maintain public trust in such campaigns, any private funding should be sought from corporate sectors without a financial stake in selling a product to those afflicted by the disease in question.

8.2.3 U.S. Cross-border advertising: not an entirely inevitable flow

Cable television providers serving Canadian audiences should be required to replace advertising that is illegal in Canada. This is technically feasible and is consistent with existing regulations governing split-run magazines, which are not allowed to contain advertising that is illegal in Canada even if they have a U.S. publisher.

8.2.4 Overall, better regulation of pharmaceutical advertising is needed

A key outcome of the patient-doctor survey was the finding that non-enforcement of the law has consequences: exposure to DTCA was widespread in Vancouver and was found to affect prescribing decisions in primary care. The effect on prescribing appropriateness was most likely negative, as physicians prescribed most requested advertised drugs, in spite of frequent ambivalence about treatment choice. Patients requested drugs that had been advertised to the public in Canada, including two drugs that had been advertised in campaigns judged by Health Canada to contravene the law: bupoprion (Zyban), and estradiol and levonorgestrel (Alesse). In both cases regulatory action was slow, allowing ads to run for many months, and involved no financial or other consequences for the offending companies.

The inadequacy of regulatory response to DTCA in part reflects the lack of resources devoted to this activity, since Canada mainly depends on industry self-regulation of prescription drug promotion aimed at physicians, and of OTC drug promotion aimed at the public. Therefore the staffing, resources and regulatory expertise needed to deal with illegal DTCA has not been allocated to this activity in-house. A cynical view is that this reflects the federal/provincial split in responsibility for pharmaceutical policy: the federal government does not enforce the law adequately; the provincial governments bear the brunt in terms of less cost-effective prescribing.

Another reason frequently cited for the lack of adequate enforcement is a 1995 Supreme Court case on tobacco advertising, which Health Canada lost on the grounds that it had not provided convincing evidence that a full ban on tobacco advertising met public health needs to a greater extent than a partial ban. This has now been addressed for tobacco and Health Canada has proceeded with an extensive tobacco-advertising ban, despite legal challenges from the industry. Rather than choosing not to enforce the law in order to avoid a legal challenge on pharmaceutical advertising, such a case would help both to clarify the current legal discussion, and to stimulate the type of public debate on pharmaceutical advertising that is sorely needed in Canada.

8.3 Further research needs

There are a number of gaps in existing knowledge about the effects of DTCA. No systematic analyses have been published on the content of television and other broadcast advertising, or on print or broadcast advertising in New Zealand, the only country with DTCA that relies on industry self-regulation. The latter is especially relevant to policy discussions in Canada and in European countries that rely on industry self-regulation. Research is needed on the health impacts of both physician and patient-directed pharmaceutical advertising. Such research has not been carried out thus far and is complicated to design in a way that avoids systematic biases. Essentially, any follow-up of a self-selected group of users of medicines will be affected by confounding by indication. If there are systematic differences that lead some patients to choose to request advertised drugs, and these differences also affect health outcomes, then it is very

difficult to know whether it was the drug, or baseline patient characteristics, that caused observed differences. Health service research designs, extending the type of conceptual framework used in this study, could address some of these differences. A key factor affecting the validity of research results would be the choice of comparison group.

Research using administrative databases could also be carried out, looking at effects of advertising campaigns on prescribing patterns at a population level. Although this type of research cannot distinguish between individual prescribing decisions stimulated by patient-directed or physician-directed advertising, it can examine shifts in population patterns of prescription drug use associated with specific advertising campaigns.

Another less direct approach to research on health outcomes of DTCA would be through systematic analyses of randomized controlled trials examining the effects of advertised drugs on clinically important health outcomes, in comparison to treatment alternatives. Clinically important health outcomes would include all serious adverse events as well as differences in symptoms and quality of life. They would exclude intermediate physiological measures that are risk factors for future disease, such as cholesterol lowering or bone density effects, as these outcomes are only of importance clinically if they are linked to a lower subsequent rate of disease and disability. The aim would be to establish the extent to which therapeutic advantages exist, particularly for heavily advertised drugs, over existing treatment alternatives.

Ultimately, the aim of regulation should be to support cost-effective and high quality prescribing and medicine use, so that the patients who are most likely to benefit from the use of a medicine receive it, and those for whom potential benefit is unlikely to outweigh potential harm do not. Research is needed into the types of regulatory bodies, regulatory standards and enforcement procedures that could best meet these aims.

8.4 Conclusion

The aim of the original research component of this study, the patient-doctor survey, was to investigate the effects of patient-directed prescription drug advertising on prescribing decisions in primary care. DTCA was found to affect prescribing: if a patient asked for an advertised medicine, the physician usually prescribed the drug. And the greater the patient's exposure to advertising, the more likely he or she was to ask.

These results are unsurprising: advertising does stimulate sales. However, this is advertising for prescription drugs. Prescription-only status is a restriction on manufacturers' rights to sell certain pharmaceuticals freely, based both on product characteristics and the types of conditions treated. It is reserved for medicines that are known to have greater risks of toxicity or to have a less well-understood toxicity profile than those that may be sold directly to the public. Additionally, prescription-only drugs generally treat health conditions that cannot be easily self-diagnosed and self-managed.

In many parts of the world, prescription-only status is more of a myth than a reality. The public can buy nearly any medicine directly, whether or not it is officially available by prescription only, often from unlicensed drug venders. The uncontrolled sale of potent pharmaceuticals has been identified as a public health concern and a major barrier to rational medicine use in developing countries.[24] In these settings, prescription-only status is essentially meaningless as a health protection measure.

In industrialized countries, even with full prescription drug advertising, a person cannot see an ad and then go to the corner store and buy a prescription-only drug.* However, if a company advertises to a patient, the patient asks a physician for the drug, and the physician almost always writes the requested prescription (or the patient tries again with another physician), how different is this from going to the corner store and buying the drug? In stimulating sales and shifting product choice, DTCA also leads to an erosion of the protection offered by prescription-only status.

* He or she can, however, go to the Internet to buy some advertised prescription drugs directly.

Such a shift in health protection policy would be justified if prescription-only status had been found to be unnecessary, for example if prescription-only drugs were generally innocuous. Instead there is growing evidence that adverse drug reactions are a major cause of morbidity and mortality. DTCA primarily stimulates sales of the newest prescription-only drugs, at a time when less is known about longer term and less common risks, and often when questions remain about longer-term benefits. Some drugs advertised to the U.S. public have already been withdrawn from the market for safety reasons, or have been the subject of safety advisories as new serious risks emerge post-approval. Additionally, if strong and well-established evidence of health benefits for DTCA existed, clearly outweighing potential risks, then such a policy shift might be considered justified. No such evidence exists. From a health perspective, there is no rationale for a policy change to introduce prescription drug advertising to the public.

This leaves only one convincing explanation for national and regional policy developments in support of legislative change to introduce direct-to-consumer advertising of prescription drugs: "It's not about health," said Charles Medawar of Social Audit U.K. "It's overwhelmingly about money." [1]

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