General Practitioners' Reasons for Not Participating in a Pharmacy-Initiated Randomized Comparison of Community Pharmacy and Physician-based Warfarin Management

by

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Date Sep 03, 02
Objective: To determine General Practitioners’ reasons for not entering patients into a clinical trial comparing the safety and effectiveness of outpatient anticoagulation management by community pharmacists and physicians.

Methods: A prospective, randomized comparison of community pharmacy and physician-based warfarin management was developed. All General Practitioners practicing on the North Shore were invited to participate. After eighteen months of physician recruitment, only eight had agreed to participate. To determine reasons for physicians’ non-participation in this research, a comprehensive survey was developed. Surveys were mailed to all General Practitioners (n=118) who had been invited to participate in the original clinical trial: 8 who had agreed to participate and 110 who had not. Physicians were asked the extent to which they agreed to specific statements describing potential concerns with the study and to rank the most important reasons why they did or did not participate in the clinical trial. A $50 cheque was included with all surveys, and reminders were sent at one and four weeks. Responses were anonymous.

Results: The response rate from physicians who had not participated in the clinical trial was 78 out of 110 (73%). Sixty-four of 78 respondents (83%) had five or more warfarin patients in their practice, and only one had no eligible patients. Thirty-nine (51%) had participated in 1 to 5 clinical trials in the past, while twenty-nine (38%) had no previous trial participation. The three most important reasons for not entering patients were “concern about the issue of legal liability” (40%), “concern about healthcare professionals taking over physician responsibilities” (33%), and “desire to remain responsible for patients” (29%). The response rate for the eight physicians who agreed to enter patients was 100%. The most important reason for agreeing to participate was the belief that “research advances the profession” (87%).

Conclusion: General practitioners were reluctant to enter patients in a clinical trial that involved pharmacists taking on additional responsibility for patient care. Issues of responsibility and legal liability, as well as concern about other health care professionals taking over physicians’ duties need to be clearly addressed.
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<td>Deep Vein Thrombosis</td>
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<td>GP</td>
<td>General Practitioner</td>
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<td>INR</td>
<td>International Normalized Ratio</td>
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<td>LGH</td>
<td>Lions Gate Hospital</td>
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<td>MD</td>
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Preamble

The original clinical trial intended for this thesis was a prospective, randomized, controlled trial comparing outpatient anticoagulation management by community pharmacists and physicians. Over a period of eighteen months, our repeated attempts at physician recruitment were unsuccessful. It was determined, at this point, that the study was no longer viable and we chose to conduct a survey to determine reasons for non-participation. Therefore, this thesis contains two chapters: chapter one describes the original randomized, controlled study and the results of recruitment efforts; and chapter two describes the survey research.
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Chapter 1: Study One: A Prospective, Randomized Comparison of Community Pharmacy and Physician-Based Warfarin Management

1.1 Background

Warfarin is the mainstay of therapy for treatment and prevention of thromboembolic events. The intensity of warfarin’s anticoagulation is affected by many drugs, foods and disease states. Warfarin’s anticoagulation response is measured in terms of International Normalized Ratio (INR), and should be maintained within a specified narrow therapeutic range for optimal results. The risk of thrombosis from under-dosing and risk of bleeding complications from overdosing make it necessary to monitor INR levels routinely. In addition, thorough patient assessment and follow up in terms of diet, concurrent drug therapy, and disease states are required in order to manage patients effectively. Warfarin therapy is typically initiated in a hospital setting, but may continue after discharge from hospital for a prolonged period of time. Studies have shown that in the community setting, there is a lack of a consistent and a reliable system for monitoring the many possible influences on warfarin anticoagulation, and ensuring appropriate dosage adjustments. The idea for this study was developed at Lions Gate Hospital (LGH) after a proposal for a hospital-based anticoagulation clinic was rejected due to funding restrictions. Some LGH physicians informally proposed a pharmacist-run warfarin management program modeled after a successful pharmacist-run heparin management program within the hospital. This provided the stimulus to develop a study to test the feasibility and benefits of establishing a community based anticoagulation program utilizing the existing infrastructure of local community pharmacies. There are reports
describing community pharmacist-managed anticoagulation programs, but there is no research evaluating health, economic and satisfaction outcomes.\textsuperscript{4} Specifically, this randomized prospective controlled study was designed to compare warfarin therapy managed by physicians and community pharmacists with respect to specific warfarin-related outcomes including accuracy of dose adjustments, the incidence of adverse effects, and the number of warfarin-related hospitalizations.\textsuperscript{5,6}

1.2 Objectives

1.2.1 Hypothesis

There is no statistically significant difference in the safety and effectiveness of warfarin anticoagulation managed by a community pharmacist-run anticoagulation program versus usual care.

1.2.2 Study objectives

The primary outcome of this study was the mean number of INR values outside the target range per patient. The secondary outcomes of this study were:

1) The number of hospital admissions due to re-thrombosis or warfarin-related bleeds.
2) The number of minor bleeds as reported by the patient.
3) The number of physician office visits related to warfarin therapy.
4) A pharmacoeconomic analysis accounting for monitoring costs, physician office visits, dispensing costs, hospital admissions (and associated costs).
5) Patient satisfaction assessed by means of a survey.
1.3 Progress

1.3.1 Approval

UBC and LGH ethics committees both reviewed and approved the proposal (approval # C99-0065). A presentation was made to the College of Pharmacists of BC board members. The College approved the study.

1.3.2 Recruitment

The study design required the participation of patients, physicians, pharmacists and laboratory personnel. Physicians and patients were required to sign a consent form. Pharmacists practicing in Northmount and Davies pharmacies were recruited to participate in the study as treatment providers. The two pharmacies are independently owned and are located close to LGH. A training session was held for all pharmacists (n=5), which included a presentation of study procedures as well as anticoagulation management. A resource binder was developed as reference for each pharmacy. The binder was to be kept in each pharmacy at all times (see Appendix 1).

Northmount and Metro Laboratories agreed to provide INR reports to participating pharmacy or applicable GP depending on the arm of study to which patients were randomized. Special requisition forms were developed for the study.

Prior to initiating recruitment, study investigators visited five GP offices in order to evaluate support for the proposal. All five physicians received the proposal positively.
After recruitment was initiated, letters were sent to all physicians practicing on the North Shore inviting them to participate and enroll patients in the study. A presentation was made to approximately fifty GPs attending a monthly GP meeting at LGH. The majority of physicians attending this meeting didn’t receive the presentation positively. Follow-up letters were sent to all physicians practicing on the North Shore. In addition, study investigators visited thirteen physicians' offices describing the study and asking for participation. After eighteen months of attempts to recruit physicians and patients into the study, three physicians had agreed to participate.

1.3.3 Revised recruitment strategy

Due to low recruitment and on the advice of the research supervisory committee, a telephone poll was carried out to evaluate the potential impact of compensating physicians for participating in the study. Prior to conducting the telephone poll, a thorough literature search was carried out in order to evaluate efficacy and ethics of paying such a fee. Based on the literature search, study budget, and the fact that physicians were paid $60 for a routine twenty-minute office visit, $50 was offered to physicians for each patient enrolled in the study. This compensation was not contingent upon patient completion of the study. A telephone poll was conducted to assess the effect of such a fee on enrollment (see results section for further detail).
1.4 Results

The following table summarizes the number of physicians who agreed to participate in the study:

Table 1- Numbers of physicians and patients agreeing to participate in the anticoagulation management study

| Number of physicians agreeing to participate prior to the offer of a monetary incentive | 3 |
| Number of physicians agreeing to participate after the offer of monetary incentive | 8 |
| Number of informed consents obtained from physicians (obtained by BB) | 3 |
| Number of patients contacted to participate in the study | 29 |
| Number of informed consents obtained from patients (obtained by BB) | 8 |

Eight informed consents were obtained from patients: all eight patients were enrolled and randomized. Three out of four patients randomized to the study arm withdrew from the study before the first dosage adjustment. The reasons given for their withdrawal were patient illness, physician’s preference for continuing care, and termination of warfarin therapy.

The results of the telephone poll conducted to assess the potential impact of reimbursement on enrollment are summarized in the following algorithm:
Figure 1- Telephone poll results

110 GPs contacted by phone

49 responses

5 “yes” responses 39 “no” responses 5 “maybe” responses

+ 3 GPs agreed to participate prior

8 GPs agreed to participate
1.5 Options considered after the original warfarin management study was terminated

Overall, eight physicians and eight patients agreed to participate in the study. Based on the original sample size calculation, the study required at least 121 patients per treatment arm to address the original hypothesis; therefore, it was decided to terminate our attempts at recruitment (Appendix 1).

Several options were considered after the original warfarin management study was closed: 1) exporting the study protocol to a different geographic area, 2) extending the geographic location to include a wider area, 3) continue with the study without randomization, 4) permitting long-term care patients to participate, and 5) conducting a survey to assess reasons for low enrollment. After close review of each option, we determined that the original study design was no longer viable; and, on the advice of the research supervisory committee, chose to identify the reasons physicians failed to participate in this study. It was assumed that such findings would be useful as background information for other researchers assessing feasibility of studies involving GPs, as well as those assessing the feasibility of studies involving community pharmacist managed anticoagulation service. It was also assumed that the results of this survey would help those planning to provide pharmacist-managed clinical services in the community setting, including anticoagulation programs.
Chapter 2- General Practitioners’ reasons for not entering eligible patients into a clinical trial comparing pharmacy and physician-based anticoagulation management

2.1 Rationale

The original study leading to this survey was a randomized, controlled trial designed to compare the safety and effectiveness of outpatient anticoagulation management by community pharmacists and physicians practicing on the North Shore. This study was designed in such a way that it depended on physicians, who normally manage anticoagulation in the community, to enroll their consenting patients in the study. Unfortunately, once the recruitment phase started, a number of physicians who had originally expressed their support for the study were no longer interested in participating, and we were unable to accrue enough additional physicians to continue with the study. Over a period of eighteen months, North Shore physicians were contacted by letters, telephone, and presentations and asked to participate in the study. A telephone survey of physicians indicated that offering monetary reimbursement for physicians’ time involvement in the study would not increase the total number of physicians willing to participate in the study enough to achieve the target numbers (Appendix 2). While eight physicians agreed to participate, the majority of physicians \( n=110 \) did not participate.

2.2 Objective

The objective of this survey analysis was to determine and compare physicians’ reasons for participation or non-participation in a proposed randomized clinical trial comparing
outpatient anticoagulation management by general practitioners and community pharmacists.

2.3 Applicability of results

Unsuccessful study proposals are frequently abandoned and no further formal enquiry into the reasons for their demise is undertaken. Indeed, it is difficult to locate such studies in the published literature. As a result, other researchers may unnecessarily repeat the same research projects with little chance of successful completion. It is hoped that the results of this study will be useful as background information to other researchers assessing feasibility of future studies involving General Practitioners (GPs), as well as those assessing the feasibility of future studies involving community pharmacist-managed anticoagulation service. These results may be particularly useful for researchers planning projects on related topics carried out in the same geographic area as this project. It is also hoped that the results of this survey will help those planning to provide pharmacist-managed clinical services in the community setting, including anticoagulation programs.

2.4 Background

2.4.1 Survey Design

Survey research is a powerful scientific tool aimed at gathering accurate and useful information to describe, explain or influence some phenomenon. Its idea comes from drawing random samples from a large population in order to make conclusions. It is also a tool that can frequently be misused. Survey methods are not appropriate for many
research topics, nor do they provide the best approach to many research questions. However, survey research is an appropriate method when the goal is to determine what percentage of a population has a particular attribute or opinion.  

The goal of any survey research should be to gain accurate information. Accuracy in surveys refers to results that are as close to the true population value as possible. In order to get accurate results, four kinds of error should be avoided: coverage error, sampling error, measurement error, and non-response error. Coverage error is made when the list of people from which a sample population is chosen is incomplete. Complete and accurate lists can be difficult to obtain. In addition to being incomplete, lists sometimes contain duplicate entries or entries that are no longer members of the target population. Sampling error is made when only a subset or sample of the target population is surveyed rather than conducting a census. Measurement error occurs when a respondent’s answer to a given question is inaccurate, imprecise, or not comparable to other respondents’ answers. Non-response error occurs when significant numbers of the sample population do not respond and are different from those who do in a way that is important to the study.  

Although none of the four errors can be completely eliminated, each has the power to render results invalid. Therefore, correct decisions have to be made and quality procedures have to be in place at all stages of the process in order to optimize the survey quality. Surveys are conducted either in person, by phone, or using a mail questionnaire. Each survey method should be considered against the specific study objective and resources available to the researcher. It is important to note how sensitive
each method is to various kinds of errors. Therefore, the choice of survey method used also depends on what kind of error is more likely to be encountered.\textsuperscript{15}

Mail surveys require the least amount of resources. Since they are not costly, they allow researchers to minimize sampling error. Mail surveys are easy to answer and are considered more private than a face-to-face or telephone interview especially when dealing with a sensitive subject matter. Mail surveys are also less sensitive to biases introduced by interviewers compared to face-to-face or telephone surveys. One weakness of mail surveys is their sensitivity to coverage error. Samples are usually drawn from a published list, which is almost never complete. A second weakness of mail surveys is the possibility of non-response error since some people are more likely to respond to a questionnaire than others. Mail surveys give potential respondents a chance to examine the questionnaire before they decide to answer it. Since respondents usually have an interest in the topic, respondents differ from non-respondents in a way that can affect the survey results. Another weakness of mail surveys is the fact that researchers have little control over the questionnaires once they have been mailed. The questionnaires may not be delivered to the person it is directed to, or the respondents may fail to answer all questions in the questionnaire. In summary, mail surveys are best suited for surveying people for whom a reliable address list is available and those who are likely to respond accurately and completely.\textsuperscript{15}

The use of mail surveys has been traditionally limited by low response rate. In 1978, Dillman proposed a mailed survey methodology based on social exchange theory, which
he called Total Design Method (TDM). In this theory, Dillman suggests that researchers must pay close attention to details of the questionnaires including wording of letters, length of the questionnaire, personalization, multiple follow-ups, and offering incentives to those who complete and return the questionnaires. Dillman claimed that obtaining response rates as high as 70% to 75% were possible by following this method. Many surveys have since been conducted using the TDM method. Meta-analyses conducted by Yammarino et al. and Fox et al. also concluded that preliminary notification, follow-up, stamped return envelop, and monetary incentives are effective in increasing the response rate by 2 to 31 percent.

2.4.2 Types of Information

There are four possible types of information that one can seek in a survey: attitudes, behavior, beliefs, and attributes. It is important to distinguish between the different kinds of information in order to meet the objectives of a survey accurately. The kind of questions being asked in a survey must match the kind of information being sought by the overall objective.

2.4.2.1 Attitudes

Attitude surveys are evaluative in nature and describe how respondents feel about a given issue (e.g. whether they favor tax cuts or not). Attitude questions typically ask whether respondents have positive or negative feelings about the subject. Words used in an attitude question are designed to assess direction of ones feelings such as favor versus oppose, desirable versus undesirable, or should versus should not.
2.4.2.2 Behavior

Questions in this category assess respondents’ behavior about a given subject (e.g. whether they smoke cigarette or not). It is important to note that questions regarding behavior can sometimes elicit respondents’ beliefs about their behavior. Therefore, it is necessary to ask respondents to describe their behavior, rather than asking them for their view on something that they have only experienced in a cognitive sense.\(^1\)

2.4.2.3 Beliefs

Questions regarding respondents’ beliefs assess what they think is true or false (e.g. whether they believe that photo radar saves lives). Choices that are included in this type of question are correct vs. incorrect, and what happened vs. what did not happen. At times, it is difficult to distinguish between questions designed to elicit beliefs from those that are designed to measure attitudes. In such cases, the investigator is in fact trying to measure both in one question (e.g. whether they think that marijuana use should be legalized).\(^1\)

2.4.2.4 Attributes

The fourth kind of information that is sought in surveys is personal and demographic information (e.g. age, gender). The reason for asking this kind of information is to explore how the other kinds of information (e.g., attitudes, beliefs, and behaviors) differ for people with various attributes.\(^1\)
2.4.3 Question Structure

Three different formats can be used to ask survey questions: open-ended, close-ended, and field-coded questions.

2.4.3.1 Open-ended question

Open-ended questions are designed to let respondents create their own answers and state these answers in their own words, for example:

In your opinion, what problems face practice of pharmacy in B.C.?

These questions are often used when a precise piece of information is requested and there is a large number of possible answers. They are used to stimulate free thought, clarify positions or when investigators cannot anticipate all the possible answers. They also give the respondents a chance to vent their frustrations and state strong opinions.\(^{15,18,21}\)

Moreover, these questions ensure that researcher's assumptions do not inhibit the answers; respondents choose their own words and choose what to express and what to ignore. Finally, by quoting the words of lucid or candid respondents, research reports can be improved.\(^{14}\)

There are also some disadvantages associated with the use of open-ended questions. Respondents often give responses that differ widely and therefore are not comparable. Also, answers are often too vague to fully answer the questions and it is hard to construct meaningful variables for statistical analysis.\(^{14}\) The biggest disadvantage of open-ended questions is that they are time-consuming to answer. They require the respondents to recall events in the past, and then formulate and articulate an answer. The non-response
rate in these questions can be high and investigators often end up comparing a few people whose views on a topic are known against the vast majority whose views are not known.

2.4.3.2 Close-ended questions

Close-ended questions can be formatted in two different ways: close-ended with ordered choices, and close-ended with unordered choices. An example of close-ended question with ordered choices is: How do you feel about this statement? “This community needs more pharmacies.” (Please circle the number of your response.)

1 - Strongly disagree
2 - Mildly disagree
3 - Neither agree nor disagree
4 - Mildly agree
5 - Strongly agree

An example of a close-ended question with unordered choices is: Which best describes the type of automobile you drive? (please circle the number.)

1 - SUV
2 - Compact
3 - Luxury
4 - Sports

Ordered choices represent graduation of a single dimension of a concept. Questions of this type tend to be quite specific, and are appropriate when the investigator has a clearly defined issue and knows exactly what dimension of that issue is being investigated. These
questions are good for measuring intensity of feeling, degree of involvement, and
frequency of participation; therefore, they are useful for inquiring about attitudes and
beliefs. The response categories listed must be exhaustive and mutually exclusive. The
responses to these questions are well suited for statistical measurements, such as
regression analysis. In this form of questioning, the respondents consider all possible
alternatives and do not have to rely on memory to come up with the answers. Also, these
questions are less demanding; hence, a better response rate can be achieved. If the list of
alternatives does not adequately capture the respondents' point of view, however, they
may feel that a single answer does not fairly represent the complexity of the issue.\textsuperscript{14,15,18}

Close-ended questions with unordered answer choices do not limit respondents to
choosing among gradation of a single concept. In fact, each choice is an independent
alternative representing a different concept. Questions of this format are usually used to
decide among alternatives or establish priorities. These questions, however, are more
difficult to answer and can be mentally demanding, as they require respondents to
evaluate each alternative in relation to others. Careful attention must be made to list all
possible alternatives in the answers or useful results cannot be obtained. Other
shortcomings of these questions are very much the same as discussed above for close-
edended questions with ordered choices.\textsuperscript{15,18}

2.4.4 Formulating questions

If a survey contains the wrong questions, decisions cannot be made based on the
information. Writing good questions is the most influential factor in the success of any
survey. It has been said, "no survey can be better than its questionnaire" which
emphasizes the fact that no matter how sophisticated the design or analysis of the survey, vague questions will produce vague answers, and leading questions biased answers. In addition to avoiding emotional or biased words, special attention must be paid to ensure that the questions will produce credible information, and that respondents will be willing to provide the information. Unfortunately, writing and interpreting questions about attitude and behavior, such as in this survey, can be challenging. Respondents don’t possess attitudes and beliefs the same way they possess attributes; therefore, their opinions cannot be easily measured as they can be imprecise, change from day to day, and may not be well thought out in advance. For these reasons, it is recommended that researchers use different kinds of question structures and look for patterns on how respondents have answered questions on the same topic. The objective of writing good questions is to eliminate measurement error. The following checklist has been proposed in order to ensure proper wording of the questions:

1- Is the question too vague?
2- Will the words be uniformly understood?
3- Is the question too precise?
4- Is the question biased?
5- Is the question objectionable?
6- Is the question too demanding?
7- Is it a double question?
8- Does the question have a double negative?
9- Are the answer choices mutually exclusive?
10- Has too much been assumed about respondents’ behavior?
2.4.5 Pre-testing

The purpose of pre-testing is to learn whether the survey would work to researcher's satisfaction. This process involves reviewing individual questions as well as the total effect of the survey. Even though this process is time consuming, it is essential to the success of the survey. It is also important to pre-test the survey with potential respondents as well as stakeholders or people who will use the results of the survey. The following questions are asked during the pre-testing phase in order to reduce measurement error and increase response rate:\textsuperscript{15}

1- Is each question capturing the information it is intended?
2- Are all the words understood?
3- Are the questions interpreted the same by all respondents?
4- Do all close-ended questions have an answer that applies to each respondent?
5- Does the questionnaire create a positive impression that motivates people to respond?
6- Does any part of the questionnaire suggest researcher bias?

2.4.6 Optimizing response

Response rate of a survey determines the extent of non-response bias.\textsuperscript{19} A good questionnaire should make the task of responding as easy as possible and minimize respondents' burden. To do so, one must decrease the time required to complete the questionnaire, make questions easy to answer, and show respect for respondents. This can be difficult since mail questionnaires are unique in that they stand on their own and none of the investigators are present to convince respondents that they should fill out the
questionnaire. Different authors have described various methods of increasing response rate including personalization, follow-ups, type of postage used, university sponsorship and monetary incentives.

2.4.7 Personalization

Success of mail surveys relies heavily on personalization throughout the implementation process. The overall effect that is produced by personalization will convey the message that the survey is important and that the respondent's participation is important to its success. A well-written cover letter conveys this message to some degree. It is also important to personalize as many parts of the package as possible such as printing individual names on the cover letter and envelopes. It is hoped that these measures would produce an overall effect that makes respondents feel that they are accorded individual attention.

2.4.8 Financial incentives

Traditionally, response rates among mail surveys of physicians have been low, around fifty percent, probably due to high demands on professional time, difficulty in making direct contact via office staff, and a resistance to surveys in general. According to Dillman, based on the social exchange theory, people engage in any activity because of the rewards they hope to receive; all activities incur some costs (monetary, time and others) and people attempt to keep their costs below the expected rewards. Therefore, there are three things that must be done to increase survey response: minimize the costs for responding, maximize rewards, and establish trust that those rewards will be
delivered. Dillman suggests that following this methodology one can achieve response rates exceeding 70 percent. While intangible rewards such as expressing appreciation or making the respondent feel like a “consultant” can be incorporated into the cover letter, providing financial incentives are particularly effective for increasing response rate.\textsuperscript{18} It is believed that monetary incentives are effective not so much because they compensate respondents, but because it establishes an element of trust and the feeling that they should return the favor.\textsuperscript{28}

Many authors have described the benefits of financial incentives. Gunn et al experimented with 0, $25, and $50 incentives in a telephone interview with family physicians. They found that the group offered financial incentive produced higher response rates (58\% vs. 69\% vs. 77\%, p<0.05 and p<0.08, respectively).\textsuperscript{29} Asch et al tested the effect of incentive size on physicians’ response rates to a mail survey. One thousand family physicians were randomly assigned to receive a survey with either a $5 bill or a $2 bill. The response rate among those who received the $5 bill was 61\%, while 46\% of those who received the $2 bill responded (p<0.001).\textsuperscript{28}

Similarly, many have investigated the role of timing of payments on response rates and cost effectiveness. Berry et al tested timing of payment in a mail survey of 2147 physicians, general practitioners and specialists. Half of the physicians received $20 with the questionnaire, and the other half were promised $20 upon completion of the survey. The response rate among those who received the $20 was 72\%, significantly higher than the 66\% response rate achieved from the post-payment group (p<0.05).\textsuperscript{24}
Schweitzer and Asch investigated the cost effectiveness of the pre-payment when compared to post-payment in a group of 400 university employees. They found that pre-payment was less expensive per response and more cost effective. Twenty-six subjects completed the questionnaire and did not cash the cheque, while only 2 subjects cashed cheques and did not complete a questionnaire. Moreover, pre-payment was accompanied with higher response rate after the first mailing (53 vs. 48%), and fewer subsequent follow up mailings were required. Also, there was no need for a separate mailing of the cheque. Although any subject, regardless of timing of payment, has the option of not cashing the cheque, the observed lower rate of cheque cashing may be explained by the fact that people feel more entitled to the money after they have worked for it. Flset et al, also report that providing the cheque in advance increases the response rate and is cost effective. Eleven percent of the respondents did not cash their cheques in their study, more than offsetting those who cashed their cheques but did not respond.

2.4.9 Follow-up

According to Dillman's TDM, one postcard reminder should be sent to all survey recipients one week after the initial mailing. This postcard should serve as a thank you note to those who have responded and a friendly reminder to those who have not. Dillman also suggests that three weeks after the initial mailing, a letter and a replacement questionnaire should be sent to non-respondents. This mail out should contain a replacement questionnaire, in case the first one was misplaced, as well as a cover letter. A fourth mailing, using certified mail, can be carried out as a final measure if a good
response rate has not been achieved by the first three mailings. The success of a forth mailing is, however, questionable. Dillman suggests that follow-up mailing can double the response rates of well-designed surveys. In their meta-analysis of response rates to mailed surveys, Asch et al. report that those studies which included follow-up reminders had higher response rates by about 13%. Kasprzyk et al. report, in their review of 60 physician surveys, that studies that included follow-up or telephone reminders had on average 10% higher response rate than those that did not use reminders (60% versus 50%).

2.4.10 Ethical considerations

All researchers have clear ethical responsibilities; however, there are some ethical considerations unique to surveys. First, one has to ensure that participation is completely voluntary, and respect those who decide not to take part in the survey. Survey research almost always is an intrusion into the lives of the respondents. Coercion and perceived coercion must be avoided, and researchers must respect respondents' choices in all the follow up letters that are sent out.

The second important ethical issue is that of confidentiality and anonymity. It is often difficult to maintain anonymity when follow-up mailings are utilized. Confidential survey design allows the researcher to identify the respondent, although the researcher promises not to. In this case, each questionnaire will have an identification number. Once the questionnaire is returned, the name associated with that number will be taken off the list and only non-respondents will be sent a follow up letter. There will be one master list that
links respondents’ names with questionnaire identification number, and the list will be destroyed when it is no longer needed. A confidential survey is less complicated, easier to send proper follow up mailings than an anonymous survey. Moreover, in a confidential survey, one can ensure that each respondent has returned only one answer.

In an anonymous survey, the researcher has no way of linking respondents to responses. One way to achieve this goal is to send an identifiable postcard in addition to the unmarked questionnaire and ask respondents to mail the postcard and the questionnaire separately. Once the postcards are received, the respondent’s name will be taken off the list and no more follow-up letters will be sent to that person. The questionnaires are returned unmarked and will therefore remain anonymous. One disadvantage of this method is that it could be confusing to the respondents. Some may return the questionnaire without returning the post card, and some may do the reverse. Also, this method is more demanding than the previous one as it asks respondents to follow more steps. Following this method can also increase the cost of the survey because of the extra postage, envelops, and postcards required. 14, 15, 18

2.4.11 Statistical Considerations

2.4.11.1 Non-response

Not everyone who is surveyed completes and returns the questionnaire, and non-response potentially introduces bias. 15, 17, 18 There are usually two reasons for non-response:

1- The questionnaire may not reach the respondents for various reasons,
2- Those asked to provide data actually refuse to do so.
The effect of non-response on the survey results depends on the response rate and the extent to which those not responding are biased. If the response rate is high, results are reasonably accurate even if non-respondents are heavily biased. There is, however, no agreed upon standard for a minimum acceptable response rate. Generally, those who have a particular interest in the subject matter are more likely to return questionnaires than those who are less interested. Therefore, data resulting from returns of 20 to 30 percent will likely not be indicative of the sampled population. When there is a low response rate, results will almost invariably be biased in ways that are related to the purpose of the research.\textsuperscript{17}

Not all non-response is biased. Some questionnaires may not get returned because they never reach respondents. Typically this process is random therefore, unlikely to lead to bias. Furthermore, non-respondents may have similar characteristics to those who do respond. Unfortunately, other than comparing early to late respondents, it is generally difficult to ascertain the level of bias associated with non-response. Following procedures to optimize response rate, as outlined above, is the best method for avoiding biased results.\textsuperscript{17}

2.4.11.2 Missing data

Some respondents may refuse to answer specific questions or may inadvertently skip questions. Missing answers can be dealt with in a variety of different ways. Some researchers have assigned the average value from the sample to the missing data, and then included that value in the overall analysis.\textsuperscript{31} Some, on the other hand, exclude the
missing values from calculations. Each missing value is assigned with a specific code that will be recognized by the computer as missing data. The computer will then take percentages based on the number of people who have answered that question.15

2.4.12 Literature Review: Physicians' Reasons for Not Enrolling Patients Into Clinical Trials

There is little literature specifically addressing physicians' reasons for not entering eligible patients in randomized clinical trials. Taylor et al. studied the reasons surgical principal investigators chose not to enter their eligible patients in a large, multi-center, clinical trial on breast cancer.32 Following a mail survey, the physicians offered the following explanations: 1-concern that the doctor-patient relationship would be affected by a randomized clinical trial (73%); 2-difficulty with informed consent (38%); 3-dislike of open discussions involving uncertainty (22%); 4-percieved conflict between roles of scientist and clinician (18%); 5-practical difficulties following procedures (9%); 6-feeling of personal responsibility if treatments were found to be unequal (8%).32 Other investigators have reported physicians' refusal as the main reason for non-enrollment in clinical trials.33-35 Begg et al. and Hunter et al. have both reported physicians' preference for one treatment option as a major contributing factor toward non-enrollment.34,35 The survey reported by Hunter et al. suggests that physicians’ conflict between their responsibility to the patients and their role as scientists inhibits some clinicians from entering patients in studies. Some clinicians viewed the enrollment of a patient in an experimental study as a compromise of their responsibility to look after the welfare of their patients.34 Kotwal et al. prospectively recorded reasons for non-entry in a
randomized clinical trial for breast cancer. The most common reasons for not entering eligible patients were patient refusal to participate (69.5%) and physician refusal (15%).³⁶
3. Methods

3.1 Approvals

Ethics Committee approvals for the original study were obtained from UBC and LGH Ethics Committee. A new application was submitted and approved by the UBC Ethics Committee for the survey study. LGH Ethics Committee approved of the survey study by reviewing the study proposal without requiring a full re-submission.

3.2 Sample

In selecting an appropriate sample, two different options were considered:

1- All MDs practicing on the North Shore
2- All GPs practicing on the North Shore

Including all practicing physicians in the survey was not appropriate since very few specialists on the North Shore manage anticoagulation in the community. The main focus of the recruitment in the original study was on the general practitioners; therefore, the sample frame for the survey included all general practitioners.

Two questionnaires were designed: one questionnaire (survey #1) for physicians who did not volunteer to participate in the original study (n=110), and a second questionnaire (survey #2) for those who did agree to participate (n=8) (Appendices 3 & 4, respectively). Two surveys were designed in order to satisfy research objectives. By including all practicing GPs on the North Shore in the survey, it was possible to avoid errors associated with random sampling. 16
3.3 Survey Questions

The questionnaires were composed primarily of close-ended questions in order to facilitate analysis and optimize response rate. A 5-point Likert scale was employed for response options where appropriate (e.g. 1=strongly agree, 5=strongly disagree). A 5-point Likert scale was used in oppose to a 6-point Likert scale in order to allow for a neutral position.  

A number of sources were utilized for identification of survey question themes. First, during attempted implementation of the original study, physicians had raised concerns or had explained their reasons for non-participation in office visits, presentations, or the telephone poll. All concerns or reasons for non-participation raised by physicians during these encounters were recorded in detail. The eight physicians who agreed to participate in the study were also instrumental in providing us with relevant issues pertaining to our study and this particular physician community. Secondly, we did a thorough literature review of any similar surveys. Some authors have described similar reasons for physicians' refusal to participate in studies. For example, some have reported fear of destroying physician-patient relationship or conflict between the role of physician and a scientist as the reason for not participating in studies.  

32-35
3.4 Relevant Issues

To adhere with the objective of the survey, questions were asked about the following issues:

- Concern with physician-patient relationship: Many physicians feel comfortable with the relationship they have with their patients, and may not want to jeopardize or undermine that relationship by assigning them to a study.  
- Concern with the scientific benefit of the study.  
- Concern with immediate and future economic implications of this study.  
- Confidence in pharmacists' ability to manage anticoagulation.  
- Concern with random assignment of patients to the study arm of the survey.  
- Concern about the workload associated with the study. For example, time involved in randomization, time taken to discuss the study with patients, consents forms, compiling a list of their patients, and communicating with the study investigators.  
- Concerns about relinquishing responsibility for anticoagulation management.  
- Concern about legal liability.  
- Effects of political and environmental factors  

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\[ a \] Taylor, K.M. 1984
\[ b \] Lee, J.Y. 1983
\[ c \] identified during interviews with physicians who did not participate
\[ d \] identified during interviews with physicians who agreed to participate
\[ e \] Begg, C.B. 1983
\[ f \] Hunter, C.P. 1987
\[ g \] Greenberger, P. 1999
In addition, the following questions were asked:

1- How did you first hear about the study?
2- At present, how many of your patients are on warfarin therapy?
3- Have you discussed the study with your patients?
4- How many of your patients were unable to participate?
5- How many of your patients were unwilling to participate?
6- In the past, how many clinical trials have you participated in?

3.5 Pre-testing

The purpose of pre-testing was to learn whether the survey would capture information required to meet study objectives. Assessment of pre-test results was based on answers to the following questions as recommended by Salant et al.\(^\text{15}\):

1- Is each question capturing the information for which it is intended?
2- Are all the words understood?
3- Are the questions interpreted the same by all respondents?
4- Do all close-ended questions have an answer that applies to each respondent?
5- Does the questionnaire create a positive impression that motivates people to respond?
6- Does any part of the questionnaire suggest bias on our part?

Pre-testing was done in two phases. First, the study investigators thoroughly reviewed the questionnaire and made modifications based on the above checklist. The second phase of the pre-testing involved three physicians (one specialist and two general practitioners).
The information obtained from the pre-testing was incorporated into the final version of the questionnaire.

3.6 Cover letter

A cover letter was prepared outlining the background and the objectives of the survey, its potential benefits to the physicians as a group, and the importance of the individual physician to the study’s success.18 (Appendix 5)

3.7 Personalization

We printed physicians' names on the envelopes and the cover letter as well as enclosed a cheque payable to the individual physician.18

3.8 Financial incentives

Based on the data available on advantages of offering financial incentives (discussed in the background section) and the budget available to the survey, a $50 cheque payable to individual physicians was enclosed with the survey. This money was offered as compensation for the time physicians spent on completing the questionnaire. In the province of British Columbia, GPs are paid $60 for a routine 20 minute office visit. The survey was designed to take 10-15 minutes to complete, thus adequately compensating physicians for their time. In addition, a return, stamped, self-addressed envelope was enclosed with the questionnaire in order to eliminate cost to the respondents and facilitate a fast response.
3.9 Anonymity

The survey was kept anonymous. A separate postcard that identified the physician was included with the survey (Appendix 6). Respondents were asked to return the survey and the postcard separately. Once the postcard was received, the name of the respondent was taken off the list and no more follow-up letters were sent to that physician. The survey remained anonymous since there were no identification marks on the survey.

3.10 Implementation

The survey was distributed on Aug 21st, 2000 to 118 practicing GPs on the North Shore. Each package included a questionnaire, a cover letter, a $50 cheque, a self-addressed stamped postcard, and a self-addressed stamped return envelope. The envelope containing the package, the cover letter, and the postcard were all personalized (Appendices 3-6).

3.11 Follow-up

Follow-up was conducted as per Dillman's TDM recommendations discussed in an earlier section. One postcard reminder was sent to all target physicians one week after the first mailing. It served as both a thank you note to those who responded and as a reminder for those who had not.

Three weeks past the first mailing, a letter and a replacement questionnaire were sent to non-respondents. This mail-out was the same as the original mailing, except that the
cover letter was shorter and informed non-respondents that their questionnaires had not been received. A replacement questionnaire was enclosed for those who had misplaced the original one. Since we achieved a good response rate after the third mailing, a fourth mailing was not used in this survey.

3.12 Statistical Analysis

3.12.1 Database

A database was compiled using SPSS® version 9.0 software (SPSS Inc. Chicago, Ill). All close-ended questions were coded and entered into the database as categorical data. Answers to open-ended questions were reviewed by the primary investigator (BB) and categorized for summary and descriptive analysis.

3.12.2 Analysis

Frequencies were calculated for the demographic data as well as the close-ended questions. A chi square test was used to test association between demographic criteria, namely number of patients in practice and previous study participation, and responses to the close-ended questions. For the purpose of the chi square test, the demographic data were combined to divide physicians into four categories: physicians with ten or more warfarin patients in practice, physicians with less than ten warfarin patients in practice, physicians with no clinical trial participations in the past, and physicians with one or more clinical trial participation in the past. The demographic categories were combined in this way in order to avoid cells with counts of zero. Also, the five point Likert scale in close-ended questions was condensed to a three-point scale for the same reason. The "strongly agree" and "mildly agree" categories were combined to form "agree" category,
and "strongly disagree" and "mildly disagree" categories were combined to form 
"disagree" category. A chi square test was used to explore possible associations between
demographics and survey responses, rather than for testing \textit{a priori} hypotheses. For
question #18 (Appendix 3), frequencies were calculated to rank first, second and third
most important reasons for non-participation. Frequencies were also calculated for the
combination of first, second, and third most important reasons for non-participation. Each
choice was considered an independent category. Each category was coded yes or no
based on whether it was chosen or not.

In order to test the reliability of our results, we tested how many respondents answered
questions regarding the same issue consistently. The survey was constructed such that
respondents were asked to state whether they agreed or disagreed with each concern, then
they were asked to rank the three most important reasons for non-participation from a list
that summarized all the questions in the first section. Responses to these two different
sections were compared and reported.

Responses to the open-ended questions were summarized in categories and frequencies
were calculated. No formal comparison was made between the answers to survey #1 and
survey #2 due to unequal number of respondents to each (78 versus 8). The differences in
answers were categorized and reported.

Missing values were excluded from the analysis. There was only one missing value.
4. Results

4.1 Survey #1: survey of those who refused to participate in the original study

A total of 110 surveys were delivered to physicians who refused to participate in the original study, of which three surveys were not deliverable and were returned. Seventy-eight completed surveys and two incomplete surveys were received (response rate 72.9%). Below is a diagrammatic representation of the overall response rate.

Figure 2- Survey implementation algorithm (\textsuperscript{7} see footnote)

\begin{itemize}
  \item 110 packages sent survey, cheque, postcard (110 survey\#1)
  \item 3 packages undeliverable
  \item 107 packages delivered
    \begin{itemize}
      \item 29 surveys not returned (anonymous)
      \item 78 surveys returned (anonymous)
    \end{itemize}
  \item 8 cheques cashed (name identified)
  \item 71 postcards received (name identified)
  \item 67 cheques cashed (name identified)
\end{itemize}

\textsuperscript{7} Up to seven physicians who cashed their cheques may have returned a completed survey without sending the postcard
4.1.1 Reasons for non-participation provided by close-ended questions

Demographic characteristics of the respondents are summarized in Tables 2.

Table 2 - Survey #1: practice and research characteristics

<table>
<thead>
<tr>
<th>How did you hear about this study</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Letters in the mailbox</td>
<td>59 (75)</td>
</tr>
<tr>
<td>From study presentations</td>
<td>9 (12)</td>
</tr>
<tr>
<td>Never heard of the study</td>
<td>8 (10)</td>
</tr>
<tr>
<td>From other physicians</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How many patients do you have on warfarin</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10 patients</td>
<td>34 (44)</td>
</tr>
<tr>
<td>5-10 patients</td>
<td>30 (38)</td>
</tr>
<tr>
<td>1-5 patients</td>
<td>13 (17)</td>
</tr>
<tr>
<td>None</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How many trials have you participated in before</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10 trials</td>
<td>1 (1)</td>
</tr>
<tr>
<td>5-10 trials</td>
<td>8 (10)</td>
</tr>
<tr>
<td>1-5 trials</td>
<td>39 (51)</td>
</tr>
<tr>
<td>None</td>
<td>29 (38)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did you discuss this study with your patients</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>3 (4)</td>
</tr>
<tr>
<td>No</td>
<td>74 (96)</td>
</tr>
</tbody>
</table>

* 77 respondents
<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly agree</th>
<th>Mildly agree</th>
<th>Undecided</th>
<th>Mildly disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>The relationship I have with my patients is very important to me, and I don't want to undermine this relationship by enrolling them in a study</td>
<td>2 (3)</td>
<td>16 (21)</td>
<td>11 (14)</td>
<td>26 (33)</td>
<td>23 (29)</td>
</tr>
<tr>
<td>I am concerned about the scientific benefits of this study</td>
<td>3 (4)</td>
<td>11 (14)</td>
<td>20 (26)</td>
<td>20 (26)</td>
<td>24 (31)</td>
</tr>
<tr>
<td>I am concerned about the scientific design of this study</td>
<td>3 (4)</td>
<td>6 (8)</td>
<td>39 (50)</td>
<td>13 (17)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>I am concerned about the long-economic impact of the study</td>
<td>3 (4)</td>
<td>9 (12)</td>
<td>31 (40)</td>
<td>18 (23)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>I am concerned about the short-term economic impact of the study</td>
<td>1 (1)</td>
<td>7 (9)</td>
<td>34 (44)</td>
<td>18 (23)</td>
<td>18 (23)</td>
</tr>
<tr>
<td>I don't believe that a pharmacist can efficiently and safely manage warfarin patients</td>
<td>8 (10)</td>
<td>15 (19)</td>
<td>15 (19)</td>
<td>15 (19)</td>
<td>25 (32)</td>
</tr>
<tr>
<td>I have problems with random assignment of my patients</td>
<td>9 (12)</td>
<td>19 (24)</td>
<td>6 (8)</td>
<td>31 (40)</td>
<td>13 (17)</td>
</tr>
<tr>
<td>I am concerned about the issue of responsibility. I would like to continue to be responsible for my patients</td>
<td>39 (50)</td>
<td>22 (28)</td>
<td>3 (4)</td>
<td>11 (14)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>I believe that the pharmacists should accept legal liability for the patients if they are managing warfarin therapy</td>
<td>62 (79)</td>
<td>12 (15)</td>
<td>3 (4)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td>I would feel personally responsible to my patients if one treatment group resulted in a significantly different outcome</td>
<td>23 (29)</td>
<td>21 (27)</td>
<td>14 (18)</td>
<td>13 (17)</td>
<td>7 (9)</td>
</tr>
<tr>
<td>I am concerned about other health care professionals doing the job of a physician</td>
<td>20 (26)</td>
<td>25 (32)</td>
<td>8 (10)</td>
<td>11 (14)</td>
<td>14 (18)</td>
</tr>
<tr>
<td>I would have had difficulty following the procedures involved in the study</td>
<td>12 (15)</td>
<td>22 (28)</td>
<td>29 (37)</td>
<td>11 (14)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>I would have been more likely to participate if I was confident that the NS health region was not involved in anyway and would not be informed of the results</td>
<td>9 (12)</td>
<td>13 (17)</td>
<td>21 (27)</td>
<td>15 (19)</td>
<td>20 (26)</td>
</tr>
</tbody>
</table>

\(^1\) N=78
Table 4- Summary of issues agreed to often by respondents.\(^1\)
Agree= strongly agree+ mildly agree, U= undecided, Disagree= strongly disagree+ mildly disagree

<table>
<thead>
<tr>
<th>Issue</th>
<th>Agree Number</th>
<th>Agree (%)</th>
<th>U Number</th>
<th>U (%)</th>
<th>Disagree Number</th>
<th>Disagree (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacists should accept legal liability</td>
<td>74</td>
<td>(95)</td>
<td>3</td>
<td>(4)</td>
<td>1</td>
<td>(1)</td>
</tr>
<tr>
<td>Concern about the issue of responsibility: want to be responsible</td>
<td>61</td>
<td>(78)</td>
<td>3</td>
<td>(4)</td>
<td>14</td>
<td>(18)</td>
</tr>
<tr>
<td>Concern about other health care professionals taking over</td>
<td>45</td>
<td>(58)</td>
<td>8</td>
<td>(10)</td>
<td>25</td>
<td>(32)</td>
</tr>
<tr>
<td>Would feel personally responsible if two treatment arms are unequal</td>
<td>44</td>
<td>(56)</td>
<td>14</td>
<td>(18)</td>
<td>20</td>
<td>(26)</td>
</tr>
<tr>
<td>Difficulties with procedures e.g., time constraints</td>
<td>34</td>
<td>(44)</td>
<td>29</td>
<td>(37)</td>
<td>15</td>
<td>(19)</td>
</tr>
</tbody>
</table>

\(^1\) N=78
Table 5- Summary of issues disagreed with often by respondents. ¹
Agree= strongly agree+ mildly agree, U= undecided, Disagree= strongly disagree+ mildly disagree

<table>
<thead>
<tr>
<th>Issue</th>
<th>Agree Number (%)</th>
<th>U Number (%)</th>
<th>Disagree Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Don't want to undermine my relationship with my patients</td>
<td>18 (23)</td>
<td>11 (14)</td>
<td>49 (63)</td>
</tr>
<tr>
<td>Concern about the scientific benefit of the study</td>
<td>14 (18)</td>
<td>20 (26)</td>
<td>44 (56)</td>
</tr>
<tr>
<td>Concern about the scientific design of the study</td>
<td>9 (12)</td>
<td>39 (50)</td>
<td>30 (38)</td>
</tr>
<tr>
<td>Concern about the long-term economic impact</td>
<td>12 (15)</td>
<td>31 (40)</td>
<td>35 (45)</td>
</tr>
<tr>
<td>Concern about the short-term economic impact</td>
<td>8 (10)</td>
<td>34 (44)</td>
<td>36 (46)</td>
</tr>
<tr>
<td>Problem with random assignment of my patients</td>
<td>28 (36)</td>
<td>6 (8)</td>
<td>44 (56)</td>
</tr>
<tr>
<td>Would have participated if NS health regions wasn't involved</td>
<td>22 (28)</td>
<td>21 (27)</td>
<td>35 (45)</td>
</tr>
</tbody>
</table>

¹ N=78
Table 6- Ranking of reasons for non-participation.

<table>
<thead>
<tr>
<th>Reason</th>
<th>1st, 2nd, or 3rd most important reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>The relationship I have with my patients is very important to me, and I don't want to undermine this relationship by enrolling them in a study</td>
<td>14 (18)</td>
</tr>
<tr>
<td>I am concerned about the scientific benefits of this study</td>
<td>10 (13)</td>
</tr>
<tr>
<td>I am concerned about the scientific design of this study</td>
<td>3 (4)</td>
</tr>
<tr>
<td>I am concerned about the long-economic impact of the study</td>
<td>1 (1)</td>
</tr>
<tr>
<td>I am concerned about the short-term economic impact of the study</td>
<td>1 (1)</td>
</tr>
<tr>
<td>I don't believe that a pharmacist can efficiently and safely manage warfarin patients</td>
<td>18 (24)</td>
</tr>
<tr>
<td>I have problems with random assignment of my patients</td>
<td>2 (3)</td>
</tr>
<tr>
<td>I would have had difficulty following the procedures involved in the study</td>
<td>6 (8)</td>
</tr>
<tr>
<td>I am concerned about the issue of responsibility. I would like to continue to be responsible for my patients</td>
<td>23 (29)</td>
</tr>
<tr>
<td>I believe that the pharmacists should accept legal liability for the patients if they are managing warfarin therapy</td>
<td>31 (40)</td>
</tr>
<tr>
<td>I would feel personally responsible to my patients if one treatment group resulted in a significantly different outcome</td>
<td>7 (9)</td>
</tr>
<tr>
<td>I am concerned about other health care professionals doing the job of a physician</td>
<td>26 (33)</td>
</tr>
<tr>
<td>I would have been more likely to participate if I was confident that the NS health region was not involved in anyway and would not be informed of the results</td>
<td>5 (6)</td>
</tr>
<tr>
<td>No patients in my practice take warfarin</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Never heard of this study before</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Concern about my patients willingness to participate</td>
<td>12 (15)</td>
</tr>
<tr>
<td>Concern about my patients ability to participate</td>
<td>14 (17)</td>
</tr>
<tr>
<td>Don't like to participate in studies</td>
<td>17 (22)</td>
</tr>
<tr>
<td>Others</td>
<td>20 (26)</td>
</tr>
</tbody>
</table>

The following table depicts the frequency by which respondents ranked the three most important reasons for non-participation.
Table 7- Summary of ranking of most important reasons for nonparticipation.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Most important reason (N=78)</th>
<th>2\textsuperscript{nd} most important reason (N=70)</th>
<th>3\textsuperscript{rd} most important reason (N=67)</th>
<th>1\textsuperscript{st}, 2\textsuperscript{nd}, or 3\textsuperscript{rd} most important reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacists should accept legal liability</td>
<td>3%</td>
<td>15%</td>
<td>22%</td>
<td>40%</td>
</tr>
<tr>
<td>Concern about other healthcare professionals taking over</td>
<td>13%</td>
<td>17%</td>
<td>4%</td>
<td>33%</td>
</tr>
<tr>
<td>Concern with issue of responsibility</td>
<td>13%</td>
<td>12%</td>
<td>5%</td>
<td>29%</td>
</tr>
<tr>
<td>Concern about pharmacists' ability to manage warfarin patients</td>
<td>8%</td>
<td>8%</td>
<td>8%</td>
<td>24%</td>
</tr>
<tr>
<td>Don't like to participate in studies</td>
<td>8%</td>
<td>5%</td>
<td>9%</td>
<td>22%</td>
</tr>
<tr>
<td>Concern about my patients ability to participate</td>
<td>6%</td>
<td>5%</td>
<td>6%</td>
<td>18%</td>
</tr>
<tr>
<td>No time to review material</td>
<td>18%</td>
<td>-</td>
<td>-</td>
<td>18%</td>
</tr>
<tr>
<td>Concern about my patients' willingness to participate</td>
<td>3%</td>
<td>9%</td>
<td>4%</td>
<td>16%</td>
</tr>
<tr>
<td>Concern about NS Health Region involvement</td>
<td>-</td>
<td>-</td>
<td>6%</td>
<td>6%</td>
</tr>
</tbody>
</table>

As discussed in the methods section, we compared answers to two separate, but similar sections of the survey in order to test the reliability of our results. The survey was constructed such that respondents were asked to state whether they agreed or disagreed with each concern, then they were asked to rank the three most important reasons for non-participation from a list that summarized all the questions in the first section. We compared how many respondents had ranked a concern as an important reason for non-participation yet disagreed with that same concern in the first part of the survey. Table 8 indicates the number of responses that were inconsistent between the two survey sections.
Table 8- Inter-question agreement: number of respondents who ranked a concern as important reason for non-participation and disagreed with it in the first part of the survey

<table>
<thead>
<tr>
<th>Concern</th>
<th>Most important reason (N=78)</th>
<th>2nd most important reason (N=70)</th>
<th>3rd most important reason (N=67)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concern about undermining relationship with my patients</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Concern about scientific benefits of the study</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Concern about scientific design of the study</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Concern about long-term economic impact of the study</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Concern about short-term economic impact of the study</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Concern about pharmacists' ability to manage warfarin patients</td>
<td>1</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Concern about random assignment of patients</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Difficulty following procedures</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Want to continue to be responsible for my patients</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pharmacists should accept legal liability</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Will feel responsible if treatment arms result in unequal outcomes</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Concern about other healthcare professionals taking over</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Concern about NS Health Region's involvement in this study</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

For the purpose of further analysis, physicians were stratified into subgroups according to the number of warfarin patients in their practice or previous clinical trial participation.

The chi-square test was utilized for these comparisons. In order to avoid having no more than 20% of the cells with counts less than five (one of the basic assumptions of the chi square analysis), broad demographic categories were employed, and the 5-point Likert response scale was condensed to 3 categories: "strongly agree" and "agree" were collapsed to "agree", while "strongly disagree" and "disagree" were collapsed to "disagree".38
Table 9- Summary of responses by number of warfarin patients in practice

<table>
<thead>
<tr>
<th>Concern about the scientific benefit of the study</th>
<th>Agree (N=44)</th>
<th>Undecided</th>
<th>Disagree (N=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>&lt;10 patients</td>
<td>≥10 patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concern about the scientific benefit of the study</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.011*</td>
</tr>
<tr>
<td>Don’t want to undermine relationship with my patients</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.488</td>
</tr>
<tr>
<td>Concern about issue of responsibility</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.043*</td>
</tr>
<tr>
<td>Concern about scientific design of the study</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.306</td>
</tr>
<tr>
<td>Concern about short-term economic impact of the study</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.160</td>
</tr>
<tr>
<td>Don’t believe that pharmacists can safely and efficiently manage anticoagulation</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.804</td>
</tr>
<tr>
<td>Concern about random assignment of patients</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.830</td>
</tr>
<tr>
<td>Difficulty following procedures in the study</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.448</td>
</tr>
<tr>
<td>Pharmacists should accept legal liability</td>
<td>Agree</td>
<td>Undecided</td>
<td>Disagree</td>
<td>0.093</td>
</tr>
</tbody>
</table>

* Statistically significant
<p>| Table 9- Summary of responses by number of warfarin patients in practice, cont’d… |
|---------------------------------------------------------------|----------------|----------------|-----------------|
|                                                               | &lt;10 patients   | ≥10 patients   | p-value         |
|                                                               | Number (%)     | Number (%)     |                 |
|                                                               | (N=44)         | (N=34)         |                 |
| Would feel personally responsible if treatment arm outcome   | Agree          | 23 (52)        | 21 (62)         | 0.179           |
| unequal                                                      | Undecided      | 11 (25)        | 3 (9)           |
|                                                             | Disagree       | 10 (23)        | 10 (29)         |                 |
| Concern about other healthcare professionals taking over    | Agree          | 23 (52)        | 22 (65)         | 0.413           |
| physicians’ responsibility                                   | Undecided      | 6 (14)         | 2 (6)           |
|                                                             | Disagree       | 15 (34)        | 10 (29)         |                 |
| Concern about NS Health Region involvement in the study     | Agree          | 11 (25)        | 11 (32)         | 0.514           |
|                                                             | Undecided      | 14 (32)        | 7 (21)          |
|                                                             | Disagree       | 19 (43)        | 16 (47)         |                 |</p>
<table>
<thead>
<tr>
<th>Concern</th>
<th>Agree</th>
<th>Undecided</th>
<th>Disagree</th>
<th>No clinical trials in the past (%) (N=29)</th>
<th>≥ one clinical trial in the past (%) (n=48)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concern about the scientific benefit of the study</td>
<td>2 (7)</td>
<td>5 (17)</td>
<td>22 (76)</td>
<td>12 (25)</td>
<td>14 (29)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Concern about the long-term economic impact of the study</td>
<td>2 (7)</td>
<td>9 (31)</td>
<td>18 (62)</td>
<td>10 (21)</td>
<td>22 (46)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Concern about short-term economic impact of the study</td>
<td>1 (3)</td>
<td>10 (35)</td>
<td>18 (62)</td>
<td>7 (15)</td>
<td>24 (50)</td>
<td>0.05*</td>
</tr>
<tr>
<td>Concern about issue of responsibility</td>
<td>18 (62)</td>
<td>2 (7)</td>
<td>9 (31)</td>
<td>42 (88)</td>
<td>1 (2)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Concern about issue of legal liability</td>
<td>25 (86)</td>
<td>3 (10)</td>
<td>1 (3)</td>
<td>48 (100)</td>
<td>-</td>
<td>0.03*</td>
</tr>
<tr>
<td>Don’t want to undermine relationship with my patients</td>
<td>8 (28)</td>
<td>4 (14)</td>
<td>17 (59)</td>
<td>9 (19)</td>
<td>7 (15)</td>
<td>0.660</td>
</tr>
<tr>
<td>Concern about scientific design of the study</td>
<td>3 (10)</td>
<td>13 (45)</td>
<td>13 (45)</td>
<td>6 (13)</td>
<td>25 (52)</td>
<td>0.713</td>
</tr>
<tr>
<td>Don’t believe that pharmacists can safely and efficiently manage anticoagulation</td>
<td>6 (21)</td>
<td>7 (24)</td>
<td>16 (55)</td>
<td>16 (33)</td>
<td>8 (17)</td>
<td>0.444</td>
</tr>
<tr>
<td>Concern with random assignment of patients</td>
<td>10 (35)</td>
<td>4 (14)</td>
<td>15 (52)</td>
<td>17 (35)</td>
<td>2 (4)</td>
<td>0.302</td>
</tr>
<tr>
<td>Difficulty following procedures in the study</td>
<td>12 (41)</td>
<td>10 (34)</td>
<td>7 (24)</td>
<td>22 (46)</td>
<td>19 (40)</td>
<td>0.573</td>
</tr>
</tbody>
</table>

* Statistically significant
Table 10- Summary of responses by number of clinical trials participated in previously, cont’d…

<table>
<thead>
<tr>
<th></th>
<th>No clinical trials in the past (N=29)</th>
<th>≥ one clinical trial in the past (n=48)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Would feel personally responsible if treatment arm outcome unequal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agree</td>
<td>17 (59)</td>
<td>26 (54)</td>
<td>0.739</td>
</tr>
<tr>
<td>Undecided</td>
<td>4 (14)</td>
<td>10 (21)</td>
<td></td>
</tr>
<tr>
<td>Disagree</td>
<td>8 (28)</td>
<td>12 (25)</td>
<td></td>
</tr>
<tr>
<td>Concern about other healthcare professionals taking over physicians’ responsibility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agree</td>
<td>13 (45)</td>
<td>31 (65)</td>
<td>0.069</td>
</tr>
<tr>
<td>Undecided</td>
<td>2 (7)</td>
<td>6 (13)</td>
<td></td>
</tr>
<tr>
<td>Disagree</td>
<td>14 (48)</td>
<td>11 (23)</td>
<td></td>
</tr>
<tr>
<td>Concern about NS Health Region involvement in the study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agree</td>
<td>6 (21)</td>
<td>16 (33)</td>
<td>0.386</td>
</tr>
<tr>
<td>Undecided</td>
<td>10 (34)</td>
<td>11 (23)</td>
<td></td>
</tr>
<tr>
<td>Disagree</td>
<td>13 (45)</td>
<td>21 (44)</td>
<td></td>
</tr>
</tbody>
</table>
4.1.2 Reasons for non-participation provided by open-ended questions

Responses to open-ended questions were coded, grouped and summarized in table 11.

Table 11 - Reasons for no participation provided for open-ended questions

<table>
<thead>
<tr>
<th>Reasons for not participating in the study</th>
<th>Frequency of response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of time</td>
<td>31%</td>
</tr>
<tr>
<td>No reason for change</td>
<td>16%</td>
</tr>
<tr>
<td>Lack of interest in the project</td>
<td>14%</td>
</tr>
<tr>
<td>Concern about other healthcare professionals taking over physician responsibilities</td>
<td>14%</td>
</tr>
<tr>
<td>Feeling responsible for patient welfare</td>
<td>9%</td>
</tr>
<tr>
<td>Didn't offer enough financial incentive</td>
<td>5%</td>
</tr>
<tr>
<td>Concern about pharmacists' ability to manage anticoagulation</td>
<td>5%</td>
</tr>
<tr>
<td>Practice too far from hospital/pharmacies</td>
<td>3%</td>
</tr>
</tbody>
</table>
4.2 Survey #2: survey of those agreeing to participate in the original study

This survey was sent to physicians who agreed to participate in the original study (n=8).

Eight completed questionnaires were returned (100% response rate) and all who responded cashed their cheques.

The following are practice characteristics of the group.

<table>
<thead>
<tr>
<th>How did you hear about this study</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Letters in the mailbox</td>
<td>4 (50)</td>
</tr>
<tr>
<td>From study presentations</td>
<td>4 (50)</td>
</tr>
<tr>
<td>How many patients do you have on warfarin</td>
<td></td>
</tr>
<tr>
<td>&gt;10 patients</td>
<td>4 (50)</td>
</tr>
<tr>
<td>1-5 patients</td>
<td>4 (50)</td>
</tr>
<tr>
<td>How many trials have you participated in before</td>
<td></td>
</tr>
<tr>
<td>5-10 trials</td>
<td>1 (13)</td>
</tr>
<tr>
<td>1-5 trials</td>
<td>6 (75)</td>
</tr>
<tr>
<td>None</td>
<td>1 (13)</td>
</tr>
<tr>
<td>Did you discuss this study with your patients</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (38)</td>
</tr>
<tr>
<td>No</td>
<td>5 (63)</td>
</tr>
</tbody>
</table>
As with the first survey, frequencies of responses were calculated for all close-ended questions. There was only one issue in the survey that the majority of respondents agreed with. Respondents didn't find the other issues listed as major problems for participation.

<table>
<thead>
<tr>
<th>Question</th>
<th>Agree Number (%)</th>
<th>Undecided Number (%)</th>
<th>Disagree Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The relationship I have with my patients is very important to me, and I don't want to undermine this relationship by enrolling them in a study (n=8)</td>
<td>1 (13)</td>
<td>1 (13)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>I am concerned about the scientific benefits of this study (n=8)</td>
<td>1 (13)</td>
<td>2 (25)</td>
<td>5 (63)</td>
</tr>
<tr>
<td>I am concerned about the scientific design of this study (n=8)</td>
<td>1 (13)</td>
<td>3 (38)</td>
<td>4 (50)</td>
</tr>
<tr>
<td>I am concerned about the long-term economic impact of the study (n=8)</td>
<td>1 (13)</td>
<td>1 (13)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>I am concerned about the short-term economic impact of the study (n=8)</td>
<td>-</td>
<td>2 (25)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>I don't believe that a pharmacist can efficiently and safely manage warfarin patients (n=8)</td>
<td>1 (13)</td>
<td>1 (13)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>I have problems with random assignment of my patients (n=8)</td>
<td>2 (25)</td>
<td>-</td>
<td>6 (75)</td>
</tr>
<tr>
<td>I would have had difficulty following the procedures involved in the study (n=8)</td>
<td>1 (13)</td>
<td>1 (13)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>I am concerned about the issue of responsibility. I would like to continue to be responsible for my patients (n=8)</td>
<td>3 (38)</td>
<td>2 (25)</td>
<td>3 (38)</td>
</tr>
<tr>
<td>I believe that the pharmacists should accept legal liability for the patients if they are managing warfarin therapy (n=8)</td>
<td>6 (75)</td>
<td>1 (13)</td>
<td>1 (13)</td>
</tr>
<tr>
<td>I would feel personally responsible to my patients if one treatment group resulted in a significantly different outcome (n=8)</td>
<td>3 (38)</td>
<td>4 (50)</td>
<td>1 (13)</td>
</tr>
<tr>
<td>I am concerned about other health care professionals doing the job of a physician (n=8)</td>
<td>2 (25)</td>
<td>1 (13)</td>
<td>5 (63)</td>
</tr>
</tbody>
</table>

1 N=8
Respondents were also asked to choose the three most important reasons for agreeing to participate in the trial. The next table summarizes responses to this question.

Table 14- Ranking of most important reasons for participation

<table>
<thead>
<tr>
<th>Reason</th>
<th>1&lt;sup&gt;st&lt;/sup&gt;, 2&lt;sup&gt;nd&lt;/sup&gt;, or 3&lt;sup&gt;rd&lt;/sup&gt; most important reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>I think participation in research advances the profession</td>
<td>87%</td>
</tr>
<tr>
<td>I believe that this would help establish a permanent anticoagulation program and that would be beneficial to me and my patients</td>
<td>63%</td>
</tr>
<tr>
<td>I wanted to help this student with her Masters thesis</td>
<td>50%</td>
</tr>
<tr>
<td>I would have saved time if a pharmacist followed my patients during the study</td>
<td>38%</td>
</tr>
<tr>
<td>I think MSP doesn't pay enough for each warfarin dosage adjustment</td>
<td>25%</td>
</tr>
<tr>
<td>I was interested in the financial compensation offered by this study</td>
<td>13%</td>
</tr>
</tbody>
</table>
Table 15 - Comparison of responses to survey #1 and survey #2.

<table>
<thead>
<tr>
<th>Issue</th>
<th>Responses to survey #1: survey of non-participants (N=78)</th>
<th>Responses to survey #2: survey of participants (N=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agree(^1)</td>
<td>Undecided</td>
</tr>
<tr>
<td>The relationship I have with my patients is very important to me, and I don't want to undermine this relationship by enrolling them in a study</td>
<td>18 (23)</td>
<td>11 (14)</td>
</tr>
<tr>
<td>I am concerned about the scientific benefits of this study</td>
<td>14 (18)</td>
<td>20 (26)</td>
</tr>
<tr>
<td>I am concerned about the scientific design of this study</td>
<td>9 (12)</td>
<td>39 (50)</td>
</tr>
<tr>
<td>I am concerned about the long-economic impact of the study</td>
<td>12 (15)</td>
<td>31 (40)</td>
</tr>
<tr>
<td>I am concerned about the short-term economic impact of the study</td>
<td>8 (10)</td>
<td>34 (44)</td>
</tr>
<tr>
<td>I don't believe that a pharmacist can efficiently and safely manage warfarin patients</td>
<td>23 (30)</td>
<td>15 (19)</td>
</tr>
<tr>
<td>I have problems with random assignment of my patients</td>
<td>28 (36)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>I am concerned about the issue of responsibility. I would like to continue to be responsible for my patients</td>
<td>61 (78)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>I believe that the pharmacists should accept legal liability for the patients if they are managing warfarin therapy</td>
<td>74 (95)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>I would feel personally responsible to my patients if one treatment group resulted in a significantly different outcome</td>
<td>44 (56)</td>
<td>14 (18)</td>
</tr>
<tr>
<td>I am concerned about other health care professionals doing the job of a physician</td>
<td>45 (58)</td>
<td>8 (10)</td>
</tr>
</tbody>
</table>

\(^1\) Agree= Strongly agree+ Mildly agree
\(^2\) Disagree= Strongly disagree+ Mildly disagree
5. Discussion

This survey was distributed to GPs who were asked to participate in a study comparing outpatient anticoagulation management by community pharmacists and physicians. A group of 118 GPs practicing in a community of 180,000 residents and affiliated with a non-teaching hospital were contacted. Our response rate overall was seventy two percent (72%), a high response rate compared to other published surveys of physicians. According to a recent meta-analysis of mailed surveys, the mean response rate among published surveys of physicians is only fifty four percent (54%) and that of surveys published in medical journals is sixty percent (60%).

The techniques used in this survey to increase the response rate were likely important, especially considering the fact that we were targeting a group of physicians who were non-participants in our original study. Other authors have indicated that a carefully worded cover letter, follow-up mailings, personalization, and financial incentives increase the response rate by various percentages. Furthermore, previous research has demonstrated that a higher response rate is achieved by including the financial incentive with the survey rather than promising it upon receipt of the completed survey. Although using this strategy allowed those receiving the survey to cash the cheques without completing the questionnaire, this appeared to be rare in this study (see Figure 2). There were eighty-six returned surveys and only seventy-five cashed cheques. Anonymity prevented identification of survey respondents.
The response rate of a survey indicates the extent of non-response bias.\textsuperscript{22} Although there is higher possibility for non-response bias when response rates are low, there is no clearly defined relation between response rate and bias. Nevertheless, it is customary to consider the response rate as a measure of non-response bias since it is extremely difficult to measure characteristics of non-respondents in a mail survey.\textsuperscript{22}

5.1 Survey #1

An analysis of the questionnaire responses suggests that there are six major reasons (in order of ranking) for non-participation in the original study:

\textit{Concern with the issue of legal liability}

Ninety-six percent of respondents agreed with the statement that pharmacists should accept legal liability for managing warfarin patients, and this issue was most often ranked as a primary reason for non-participation (40\%). The original study was set up such that a warfarin dose adjustment nomogram (designed based on available literature) would serve as a legal prescription. Once a patient was in the study, the physician would sign the nomogram, thereby giving pharmacists the authority to adjust warfarin dosage according to the nomogram. Pharmacists were also obligated to inform the prescribing physician of any changes to the dosage as soon as they were made. Problems arising from mistakes made when implementing the nomogram were clearly the pharmacist’s liability as would be the case with any prescription error. However, the ultimate responsibility for patient care was deemed to be physicians', as they are the principal authority for general welfare of their patients. Indeed, it was not possible in our original study, as with many other
clinical trials, for one party to assume total legal liability. It is important to note that even though the majority of physicians in the survey agreed with the statement that pharmacists should accept legal liability for managing anticoagulation patients, pharmacists were, in fact, legally liable for the portion of care they provided.

**Concern about other healthcare professionals taking over the role of physicians**

Fifty-eight percent of respondents were concerned about other healthcare professionals taking over the role of physicians. Overall, this issue was ranked as the second most important reason for non-participation. Many also have commented candidly on this issue through open-ended responses.

"...Physicians resist other healthcare professionals taking over their duties, or fragmenting the holistic care usually given by GPs...Community and hospital based pharmacists continue to attempt to intervene in physician-patient relationship...I object to further intrusion of healthcare workers to MD domain and further fragmentation of patient care....we are protecting our turf...Concern about non-medical personnel making medical decisions...loss of physicians’ role in patient management...”

It is noteworthy to mention that at about the same time the recruitment process for the original study was underway, several events were taking place in the local community that may have been perceived by GPs as encroaching upon their professional responsibilities. First, midwives were licensed to practice in B.C., an initiative opposed by various physician groups. In a survey conducted by Grace Hospital (now B.C.

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Women's Hospital), a number of GPs were decidedly territorial about the potential infringement of their turf that midwifery represented. In the comment section of the Grace Hospital survey, one physician commented on his unwillingness to "reduce or share (his) average-sized obstetrical practice." Another noted, "if we are to allow midwives to deliver patients...the family physician's role will no doubt be irreversibly eroded". The president of the Society of General Practitioners of B.C. also voiced his opposition to public funding of low-risk births attended by midwives: "we [as a group] don't feel comfortable about public funding for a small group of people who want an alternative birth experience in their home." Moreover, pharmacists in B.C. were given the authority to prescribe emergency contraception pills, despite opposition by various physician groups. While gynecologists and obstetricians supported the move as a way to reduce unwanted pregnancy and abortions, GPs were opposed to it. The president of the Society of General Practitioners of B.C. said that he was wary of such developments because once women were able to receive pills directly from a pharmacist, physicians lose the opportunity to interact with patients about other health issues. He also doubted that the one-day training program for pharmacists was sufficient. While the proposed pharmacist-run anticoagulation service may have saved the physicians' time if effectively implemented, the political environment at the time may have focused physicians' concerns on preserving professional authority.

**Concern with the issue of responsibility**

Seventy-eight percent of the respondents agreed with the statement that they would like to continue to be responsible for their patients. This was ranked by respondents as the
third most important reason for non-participation. The issue of responsibility and legal liability were two distinct but interrelated obstacles to participation in the study. These issues were included in the survey originally due to the number of times they had been mentioned in meetings with physicians. Many also commented on this issue:

"...This is an area with direct and very real implications to patients. Dangers of this therapy translate into real patients and events and I see this as abrogation of my responsibilities to look after my patients... Feeling of paramedical personnel taking over 9-5 and expecting emergency and out of hours coverage by "on-call physician" who will take medical legal responsibility yet receive no remuneration...Concern with responsibility of patient care....Feeling that warfarin management is the duty of the physician..."

On one hand it is difficult to accrue physicians who would like to continue to be responsible for their patients, and on the other hand it is more difficult to assume legal liability without having the responsibility. During the physician recruitment period of the original study, the issue of responsibility and legal liability were two, strong and emotionally charged, issues for physicians. This may have been the main reason for the lack of willingness to participate.

**Concern about pharmacists' ability to manage anticoagulation patients**

Respondents ranked this issue as the fourth most important reason for non-participation. Many also commented on this issue through open-ended responses.
"I think pharmacists aren't in the best position to manage INRs as they may not be aware of all that is happening with patients. I also think that I need to be aware of what is happening with my patients' INR and warfarin dosing....I observed a pharmacist doing counter-medicine a month ago. The patient showed the pharmacist what looked like a particularly severe cellulitis of the leg, and the pharmacist recommended an expensive bandage?! I believe there is a potential real problem with pharmacists making diagnosis and prescribing treatments..."

As mentioned in the first section of this report, pharmacists participating in the study were all trained in anticoagulation management by the study investigators. In addition, a resource manual and a study investigator were available to the pharmacists by pager at all times. There are many reports of pharmacist managed anticoagulation clinics in the literature, and it has clearly demonstrated that warfarin management by pharmacists in hospital and clinic settings results in improved outcomes. The level of training employed in the original study was equal to that of similar programs described in the literature. Moreover, the extent of pharmacist involvement in anticoagulation management in the original study was limited to the nomogram provided to them by the physicians. Nonetheless, a large number of physicians were concerned about pharmacists' ability to manage anticoagulation and did not participate in the study because of this concern.
Lack of time to participate in trials

Thirty-one percent of those who responded to open-ended questions quoted lack of time to review material or deal with paperwork associated with clinical trials as a major factor for non-participation.

"...We are so busy, and get such a large volume of mail, it just gets tossed into my "to get around to pile". Obviously, it didn't happen...No time to think about it and talk to patients about it. I'm too busy just trying to survive the nitty-gritty of everyday practice...physicians cannot be bothered to participate as we have precious little free time and do not want to spend more time with non-essential medical duties...Physicians are over-burdened as it is and therefore they don't have the time or energy to deal with the study...We are too interested in time off-it is just one more piece of paper in an avalanche...too much hassle; physicians are already busy enough without having another protocol imposed on them to think about...we are very time limited, did not take the time to review info on study and call in patients to discuss..."

It is important to note that physicians have referred to lack of time to review material sent to them in the mail as a reason for non-participation rather than considering actual procedures in the study being too time consuming. The design of the original study was such that physicians had to do little more than the usual office practice following study procedures. This was done in an effort to increase enrollment in the study. However, it appears that the material sent to physicians describing study procedures was often
overlooked, and this was typically attributed to a lack of time. In order to get a better understanding of family practice workload on the North Shore during the study time frame, we compared the number of physicians per capita, and number of services provided to other health regions with similar populations. According to MSP Information Resource Manual on fee-for-service statistics, during the 1998/99 fiscal year, the ratio of GPs per capita was one for 873 people on the North Shore, while the same ratio was 1246 for Burnaby and 1257 for Richmond. Furthermore, there were 4760 services performed per GP on the North Shore, while the same figure in Burnaby and Richmond was 6079 and 6176 respectively. Although our study only involved physicians on the North Shore, these figures indicate that physicians practicing in regions with similar population such as Burnaby and Richmond have busier practices. If excessive workload prevents participation in studies of this nature, these data suggest that implementation might also be difficult in other local regions.

Lack of interest to participate

Over nineteen percent of the respondents and a large number of those who responded to open-ended questions listed lack of interest as the main reason for non-participation.

"...No physician has sufficient time or will be paid enough to participate in the study...No valid reason for changing pattern of practice...another source of income and control to be taken away from physicians...I participate in studies if I think they will be of benefit to patients. If I'm not sure I usually couldn't be bothered to take the time unless given a very good reason and not if I think I'll be giving a good reason to someone else-
government- to take control of part of my practice... GPs are tired, low morale.... Sick of endless, stupid studies, will they never stop? Time consuming and pointless... MDs unwilling to change routine, getting new office setup... apathy: what is in it for us? ... Often the study seems rather pointless, i.e. are the results really going to be beneficial and useful? ..."

Unfortunately, a large number of physicians in our sample frame were simply not interested in participating in our study and many had general policies of not participating in studies. Thirty-eight percent of the physicians who responded to this survey had not participated in any clinical trials in the past, and fifty-one percent of respondents had only participated in one to five clinical trials over the course of their careers.

**Other issues**

Our analysis also shows that physicians with ten or more patients on warfarin were concerned about the scientific benefit, long-term economic impact of the study, and the issue of responsibility. It is possible that the proposed study will have a larger economic impact on physicians with ten or more patients. It is also possible that physicians with higher number of warfarin patients have more experience and are more competent; therefore, are more likely to question the scientific benefits of the study. Moreover, physicians with a higher number of warfarin patients might be more concerned with the issue of responsibility as it is more difficult to manage a larger group of patients. Our results also indicate that it may be difficult to recruit physicians with more than ten warfarin patients in such studies. Unfortunately, physicians with a higher number of
warfarin patients were needed to participate in the original study to achieve target sample size. Otherwise, a large number of physicians with few patients had to be recruited to obtain the same sample.

Physicians who had previously participated in clinical trials were more concerned about the scientific benefits of the study, long and short-term economic impact of the study, issue of responsibility and legal liability than those physicians without clinical trial experience. The group of physicians in our sample frame, in general, did not have extensive experience with clinical trial participation. Thirty-eight percent (38%) of respondents had no clinical trial participation in the past, and fifty-one percent (51%) had participated in one to five clinical trials. Other studies have suggested that physicians who have less experience with clinical trials are less likely to participate in them due to concerns about potential loss of patients, potential for litigation, administrative burden of referring patients, and burden of participation on their patients. However, the sub-group analysis of this survey seems to suggest that it would be difficult to recruit physicians with more trial experience.

5.2 Survey #2

This survey was also distributed to physicians who agreed to participate in the original study (n=8). All surveys were returned completed. An analysis of responses suggests that the main reasons for participation in this group were feeling that research advances the profession (87%), a permanent AC program would be beneficial to patients and doctors (62%), desire to help (50%), saving time by having a pharmacist manage anticoagulation
(37%), and MSP not paying enough for each warfarin dosage adjustment (25%). Many of the above mentioned comments were reasons behind initiation of the original study. As has been reported in the first part of this report, there is extensive research supporting the benefits of an anticoagulation program for patients and physicians. Since MSP pays physicians little for each warfarin dosage adjustment ($2.50), many physicians had suggested that they would be interested to delegate this responsibility to a pharmacist. Responses to this survey indicate that our assumptions prior to initiating the original study applied only to a minority of potential physician recruits.
6. Interpretations And Recommendations

The results of this survey suggest that the main obstacles to enrollment in the original study were the issue of responsibility and legal liability. Other important obstacles to enrollment were concern about other healthcare professionals taking over the physicians' duties, lack of confidence in pharmacists' ability to manage anticoagulation, and perceived lack of time to review study material by the physicians.

For those interested in initiating similar projects, we suggest that the issue of responsibility and legal liability should be more clearly defined. Even though we had addressed these issues in our study proposal and in meetings with physicians, many still did not participate in the study because of these issues. It should also be noted that our study was conducted in a non-teaching community setting. Similar programs may be successful in different geographic areas, physician groups, or hospitals. Timing is also an important factor in determining the success of such programs. Unfortunately, we started the study at a politically charged period when morale and willingness to cooperate were low. As published literature suggests and the results of survey #2 confirms, there are compelling reasons to start a pharmacist-run anticoagulation service in a community setting. We still believe that such program will be of benefit to patients and physicians. We also believe that a randomized controlled study is needed to properly assess and report the efficacy of such a program.
One major obstacle to recruitment in our study was the perceived lack of time to review study material by the physicians. It is difficult to contact a large group of physicians in ways other than written material. We did try to publicize our study by presenting at the GP meeting and by visiting physicians’ offices. Unfortunately, our efforts were met with presence of a vocal minority who were not in favor of the study. The success of any study is directly dependent on the initial contact with the study subjects and it is difficult to make that initial contact with physicians.

In order to keep the survey anonymous we were not able to ask many demographic questions. We don’t know the average age of our respondents, nor do we know the gender distribution or number of years of practice. The answers to these questions would help determine generalizability of our results.

Implementation of the proposed community pharmacist-managed anticoagulation service may have been more likely to succeed if a research component was not initially involved. This may have allowed physicians to become comfortable with the implications of such a program, and to separate the steps involved in participating in such program from participating in the proposed research. This may have also raised GPs’ confidence in pharmacists’ ability to manage anticoagulation. On the other hand, it may be difficult to justify implementing this service without evidence to support its effectiveness.
Reference List


7. Ferguson C: Payment of financial incentives to GPs may invalidate informed consent process. *BMJ* 1998;316:75-76.


37. Likert R: A technique for the measurement of attitudes. *Archives of Psychology* 1932;140.


42. Fayerman, P. Doctors split over morning-after pill plan: one physician fears he will lose opportunities to interact with patients about health issues. Vancouver Sun, A4. 3-23-2000.


Appendix 1- A prospective Randomized Controlled Comparison of Anticoagulation Management by Community Pharmacists and Physicians.

BACKGROUND

Physiology of coagulation

The process involved in the formation of a fibrin blood clot is referred to as thrombosis.

Following an injury, the loss of endothelium and the exposure of tissue factor, phospholipids, and collagen trigger a series of biochemical reactions that culminate in the formation of a fibrin clot. Tissue factor is a protein that is usually not found on the surface of endothelial cells but it can be expressed after exposure to endotoxins or inflammatory cytokines. It binds to the circulating factor VII, which triggers a series of events resulting in formation of a fibrin clot. A phospholipid surface is necessary in order for coagulation reactions to take place. As with the tissue factor, normal endothelial cells do not have negatively charged phospholipids on their surfaces. Negatively charged phospholipids can only come in contact with blood after tissue injury damages cell membranes. Several clotting factors, such as factor II, VII, IX, and X, bind to the negative surface of phospholipids, a process which requires vitamin K and calcium. 

The third factor that is present in the wound that initiates thrombosis is collagen. Collagen is also not normally in contact with the flowing blood; however, upon exposure, it binds and activates platelets, a process that contributes to clot formation. Moreover, activated platelets have negatively charged phospholipid surfaces, which can serve as a surface to support coagulation reactions. Collagen and other negatively charged surfaces activate factor XII that eventually leads to thrombin formation. The following is a schematic representation of the biochemical reactions leading to the formation of fibrin clot.
The intrinsic pathway of the clotting cascade is activated by contact of blood with the exposed subendothelial components such as collagen, or by exposure of blood to foreign surfaces such as mechanical heart valves. The extrinsic pathway of the clotting cascade, on the other hand, is activated by tissue factor (thromboplastin). Although, the two pathways are distinguishable in vitro, it is believed that the two pathways are activated simultaneously in vivo. Once the intrinsic and the extrinsic pathways are activated, they
both lead to the activation of factor X, which ultimately results in formation of a stable fibrin clot.¹

Normally, powerful antithrombotic mechanisms are present to slow coagulation and prevent extension of the clot into normal blood vessels. The presence of tissue factor, phospholipids and collagen in the wound helps to limit clot formation to the area of injury. Additionally, blood flowing past the injury site as well as antithrombotic forces closely linked to the normal endothelium play an important role in limiting the extent of coagulation. Blood flow tends to dilute activated clotting factors and thrombin that escaped the injured site. These substances can then be neutralized by clotting factor inhibitors or cleared by the liver. The normal endothelium close to the injury site also contributes to the suppression of coagulation. The normal endothelium is a good source of natural anticoagulants such as antithrombin III and protein C. Endothelial cells also release antiplatelet factors such as prostacyclin and stimulate fibrinolysis by releasing the fibrinolytic enzyme, tissue plasminogen activator (TPA).⁵²,⁵³

Antithrombin III is a direct inhibitor of thrombin. It forms a 1:1 molecular complex with the enzyme and neutralizes it. Endothelial cells in microcirculation contain large amounts of antithrombin III and neutralize any circulating thrombin that has escaped a distant injury site. Antithrombin III also inactivates factors Xa, IXa, and inhibits factor VII from binding to tissue factor.⁵² Protein C, once activated, destroys factor V and factor VIII. Protein S serves as a cofactor in this process. Both protein C and S are vitamin K dependent; therefore, vitamin K deficiency induced by oral anticoagulation produces a
fall in the circulating protein C and S levels. During the early hours of anticoagulation with warfarin, this may cause a temporary state of hyper-coagulability due to the decline of natural anticoagulation mechanisms before the onset of anticoagulation effect of warfarin. When endothelial cells are stimulated by thrombin, arachidonic acid, a 20-carbon polyunsaturated fatty acid, is liberated from membrane phospholipids and then enzymatically converted to prostacyclin. Although prostacyclin has a relatively short half-life (about 30 minutes), it helps to limit the clot formation to sites of vascular injury. Finally, the fibrinolytic system that is activated in the injury site limits the ultimate size and distribution of thrombus. The endothelial cells synthesize TPA, the enzyme that converts plasminogen to plasmin. Plasmin breaks down fibrin, which leads to dissolution of clot and formation of soluble fibrin degradation products. These products are ultimately removed by local blood flow. 1,52-54

While normal clot formation is necessary for maintaining the integrity of the vascular system, pathologic clot formation can occur in variety of clinical settings such as deep vein thrombosis, pulmonary embolism, and stroke. Three factors influence the formation of pathologic clots: abnormalities of blood flow, abnormalities of surface in contact with blood, and abnormalities of clotting components. These factors are described in a model referred to as Virchow’s Triad.

As mentioned in the previous section, several clotting factors bind directly to negatively charged phospholipids by means of specific binding sites. These binding sites are γ-carboxyglutamic acid (gla) residues that are added to clotting factors in the liver just after they are formed. In the presence of oxygen, carbon dioxide, and vitamin KH₂ (reduced
vitamin K), glutamic acid (glu) residues on precursors of clotting factors undergo γ-carboxylation to form gla residues. This process results in oxidation of vitamin KH₂ to vitamin K epoxide (KO), a biologically inactive form of vitamin K. In order to maintain an adequate supply of vitamin KH₂, a hepatic recycling mechanism is in place which converts vitamin KO to vitamin KH₂. Each molecule of vitamin K is likely recycled hundreds of times before it is converted to inactive degradation products.

Warfarin interferes with the hepatic recycling of vitamin K by blocking the vitamin K epoxide reductase enzyme. As a result, vitamin KH₂ supplies get depleted, which limits the γ-carboxylation of glu to gla residues. The result is accumulation of noncarboxylated clotting factor precursors with markedly reduced ability to contribute to thrombin generation. The following is a schematic representation of this process.

![Figure A-2: Role of vitamin K](image-url)
In the absence of vitamin K (e.g. when taking warfarin), clotting factors cannot bind to the negatively charged surfaces of phospholipids. Therefore, the blood is less likely to clot, and if warfarin is given in excessive doses, bleeding can occur.

**Historical perspectives**

The first oral anticoagulant, *dicumarol*, was identified in 1939 as a result of years of investigation and research. Beginning in the early 1900’s, scientists identified a hemorrhagic disease of cattle that was caused by consumption of spoiled sweet clover. A few years later, it was found that these cattle were deficient in prothrombin, one of the few coagulation factors known at the time. During this time, Henrik Dam described a hemorrhagic disease in chicken fed a special diet and postulated the existence of a compound (vitamin K), lack of which would lead to the hemorrhagic disorder. Later on, Dam, Almquest, and Stohstad isolated this vitamin and Doisy et al identified its structure. Doisy and Dam received a noble prize for their work in 1943. In 1939, Karl P. Link, a biochemist at the University of Wisconsin, while investigating this hemorrhagic disease (the sweet clover disease), isolated the causative compound, dicumarol.

Link synthesized this compound, and, in 1941, physicians in the Mayo clinic used it on humans as an anticoagulant for the first time. Link, however, continued his investigation in order to identify a related compound with better pharmacological properties. In the late 1940’s, he synthesized *warfarin sodium*, which emerged as an ideal rodenticide and
quickly became the mostly widespread used rodenticide in the world. In the 1950's, scientists experimented with warfarin as an anticoagulant for humans. Warfarin had better pharmacokinetic and pharmacodynamic properties than dicumarol. However, it was not until President D.D Eisenhower used it after a heart attack in mid 1950's that warfarin’s use became commonplace. Subsequently, warfarin became the major oral anticoagulant formulation throughout North America. Even though several other classes of anticoagulant are now available and in wide use in Europe and other parts of the world, warfarin remains the predominant formulation used in North America.1

Therapeutic indications

Atrial fibrillation

Atrial fibrillation is a common cardiac rhythm disorder and a risk factor for stroke. The rate of stroke is increased in patients with atrial fibrillation due to stasis of blood in the atrium. A number of placebo controlled clinical trials have demonstrated the marked efficacy of warfarin in lowering the relative and absolute risk of stroke in these patients. Since atrial fibrillation raises the risk of stroke fivefold, a complete reversal of this effect would result in a relative risk reduction of 80%. In fact, the pooled relative risk reduction has been reported to be 68% in five primary prevention clinical trials. The average absolute risk reduction was reported to be 3.1% per year in these primary prevention trials. Warfarin has also been shown in these trials to be relatively safe. Although the intensity of anticoagulation may differ in patients according to concurrent risk factors, warfarin therapy is essential in patients with atrial fibrillation.57-59
**Pulmonary embolism**

Pulmonary embolism is the third leading cause of death due to cardiovascular complications. Venous thrombosis and pulmonary embolism (venous thromboembolism) frequently develop in hospitalized patients after major trauma or surgery. However, they can also develop in healthy individuals with predisposing factors such as obesity, heart disease and immobilization. Venous thromboembolism is the most common preventable cause of death in hospitalized patients. Deep vein thrombosis (DVT) usually occurs in the deep veins of the calf muscles and proximal deep veins of the leg. If left untreated, approximately 20% of calf vein thrombi extend into the proximal venous system, where they can cause pulmonary embolism. In fact, 90% of pulmonary emboli originate from thrombi in the deep venous system of the legs. Generally, the accepted treatment for venous thromboembolism is a combination of intravenous heparin followed by three months of oral warfarin. The intensity and the duration of anticoagulation, however, can be variable and is subject to debate. Patients with continuing risk factors such as prolonged immobilization, or malignancy should take warfarin for longer duration.

**Acute myocardial infarction**

Acute myocardial infarction, in the majority of cases, is caused by rupture of occlusive thrombosis developed at a site of vessel wall injury. Many studies have shown that warfarin is effective in preventing stroke, pulmonary embolism and re-infarction in patients with acute myocardial infarction. Currently, patients with anterior Q-wave infarction, severe left ventricular dysfunction, history of systemic or pulmonary
embolism, or atrial fibrillation initially receive heparin, followed by oral warfarin. The duration of warfarin therapy depends on the persistence risk factors such as atrial fibrillation or recurrent thromboembolic events. 60

Prosthetic heart valves
Patients with prosthetic heart valves are at risk for thromboembolic events. The risk of thromboembolism is especially high in patients with mechanical valves such as caged-ball, tilting disk, and bileaflet valves. Therefore, all patients with mechanical prosthetic heart valves must receive warfarin indefinitely. Although biological prosthetic heart valves carry less risk, it is necessary to consider all risk factors for thromboembolism when considering anticoagulation therapy. Patients with biological heart valves should be treated with warfarin for at least three months after insertion. 61-63
Therapeutic drug monitoring

The efficacy of warfarin is measured by prothrombin time (PT), a test developed by Dr. A. Quick in the mid 1930's who was interested in developing a coagulation test to assess liver function. The PT evaluates the extrinsic system of the clotting pathway and is particularly useful for monitoring oral anticoagulants because it evaluates three of the four vitamin K dependant proteins: factor VII, factor X, and factor II. Moreover, the PT is also used in screening for vitamin K deficiency from other causes such as liver disease, and malabsorption. The PT is measured by adding calcium and tissue thromboplastin to a sample of plasma from which platelets have been removed by centrifugation. Automated instruments, using light scattering techniques that measure optical density, then measure the time it takes for clot formation. In non-anticoagulated subjects, the mean normal PT is approximately 12 seconds for most reagents. Unfortunately, a number of factors such as biological, pre-analytical, analytical and result reporting variables can significantly affect PT results.

Biological variables:

Since the primary source of vitamin K is dietary (mainly, green leafy vegetables), the dietary status of the patient is an important variable. Vegetarians might require higher doses of anticoagulants compared to patients who don’t eat large amounts of vitamin K containing food. Fluctuations in the dietary intake of vitamin K can also have an impact on the PT results. In addition, microorganisms in the GI system contribute some vitamin K. Disease states that alter the normal flora can change the anticoagulation state of a
patient. Many drugs (e.g. Acetaminophen, antibiotics, oral contraceptives) interact with oral anticoagulants through altering their absorption or metabolism. Alcohol also can significantly affect the metabolism of oral anticoagulants.

**Pre-analytical variables:**

It is necessary that appropriate care be taken in acquiring the blood from patient. The venipuncture also should be as atraumatic as possible. The anticoagulant of choice that is added to the blood sample is sodium citrate. The strength of the sodium citrate solution being used is important in maintaining consistency of results. Significant differences are observed between PT results obtained with 3.2% citrate concentration and 3.8% concentration. Therefore, a single citrate concentration should be used within a facility to avoid variations in PT results. The use of different concentrations of citrate solutions between facilities can result in different PT results for any given blood sample.

**Analytical variables:**

The choice of instrument, thromboplastin, as well as the expertise of the person performing the test is among the analytical variables that can affect PT. The reagent and the instrument should be compatible. The manufacturers of the instruments and reagents typically design their product such that they would perform best when used together. Using instruments and reagents from different manufacturers can lead to less than optimal results. Thromboplastins can be obtained from a variety of human and animal tissues:
Brain, lungs, and placenta are good sources of thromboplastin. Recently, recombinant human tissue factor has been introduced. The advantage of this product is the high level of homogeneity between different batches produced, especially compared to the high biological variability found in the animal products. Historically, however, animal products have been the main source of thromboplastin. In United States and Canada, rabbit brain thromboplastins have been more commonly used. The problem often encountered is the inherent biological differences between extracts obtained from different animals or in different batches from the same group of animals.

**Result reporting variables:**

PT results have been reported in different formats such as percent activity, PT ratio, index values and INR. Although not used very often, the percent activity is calculated using a reference solution such as normal saline or diluted normal plasma. The PT ratio is calculated by dividing the patient’s PT result in seconds by the mean of normal PT range. The PT index is the reciprocal of the ratio reported as percentage. Presently, the most
common way of reporting the PT result is in the form of INR, which would be discussed in the following sections.

**International Normalized Ratio (INR)**

In an attempt to reduce the variability in reporting PT, the World Health Organization developed and recommended International Normalized Ratio (INR) as the universal system for reporting PT results. In this system, all commercially available thromboplastins are compared to an international reference thromboplastin and then are assigned an International Sensitivity Index (ISI). The ISI of the international reference thromboplastin is 1.0. Manufacturers calculate the ISI of their thromboplastin using the WHO guidelines. This value is used to mathematically convert PT to INR:

\[
\text{INR} = \left( \frac{\text{patient PT}}{\text{mean of normal PT}} \right)^{\text{ISI}}
\]

The INR value is approximately equal to 1 in normal patients who are not anticoagulated. The target INR for anticoagulated patients is 2.0-3.0 with the exception of patients with mechanical heart valves. In these patients the target INR is 2.5-3.5 due to their increased risk of thrombosis. The American Heart Association recommends that INRs should be tested daily until the therapeutic range has been achieved for two consecutive days, then three times during the first subsequent week, and once every 4-6 weeks thereafter. ¹, 64, 65
Factors such as age, weight, liver function, race, renal disease, hyperthyroidism, fever, medications, GI state and alcohol consumption should be considered when initiating and monitoring warfarin therapy. In addition, there are numerous food and drug interactions with warfarin. The risk of hemorrhage from over anti-coagulation and risk of thrombosis from under coagulation is very high; therefore, it is essential to monitor patients regularly.  

III- Literature review

Several studies have evaluated the effectiveness of pharmacist-managed anticoagulation clinics. These clinics have been very successful in effectively managing anticoagulated patients. This includes higher percentage of INRs within the therapeutic range, improved patient compliance, fewer warfarin-related hospitalizations due to bleeding or rethrombosis, and improved patient satisfaction. However, these clinics are operated in hospitals and require considerable resources to establish. There have been reports of community pharmacist managed warfarin monitoring in the literature, but there is no objective research evaluating specific outcomes such as effectiveness of their service, patient satisfaction or economic benefits. The pharmacist managed anticoagulation clinics usually use warfarin-dosing nomograms that guide warfarin dose adjustments based on INR levels. Many of these nomograms have been developed and used by such clinics. Typically, they adjust the dose by 5-20% of the original dose as recommended by the “Consensus Guidelines for Coordinated Outpatient Oral Anticoagulation Therapy Management”. The use of such nomograms is accompanied
by ongoing patient assessment and education in order to optimize anticoagulation therapy.

**Experimental design**

**Study design**

This study was a prospective, randomized, parallel, controlled study. Patients were randomly assigned to their physician or the community pharmacy for anticoagulation management. Variable block randomization was employed. Block randomization was used to ensure numerical equity of the two treatment groups over time, as the number of eligible patients per practice is not very large. The blocks were of variable size to prevent centers from being able to predict what the next treatment would be, and use this information to decide whether to randomize a patient or not. Due to the fact that most physicians' offices have small number of patients, block sizes were fairly small (2-4 patients per block). Randomization was performed by the study investigators.

**Patient selection**

Interested physicians participated in the study by signing a “physician informed consent form” (Appendix 1.1). Patients of the participating North Shore physicians who had been on warfarin for at least one month were asked by their physician to participate in the study. A minimum treatment duration of one month ensured patients were beyond the stage of initial clotting factor depletion when INR results fluctuate more dramatically. The attached consent form (Appendix 1.2), were reviewed and signed by patients. Patients were included in the study if they were:
1. cared for by a North Shore physician who has agreed to participate in the study,
2. received warfarin therapy for at least one month,
3. willing to consent by signing the “informed consent form”
4. willing to go to either Northmount Pharmacy or Davies Pharmacy to get their warfarin prescription filled,
5. willing and able to have INR tests carried out by Northmount or Metro labs,
6. willing and able to complete a brief entry and exit survey.

Patients were excluded from the study if they were:

1. unable or unwilling to give consent on their own behalf,
2. had been receiving warfarin for less than one month,
3. receiving warfarin for indwelling venous catheters (as INR monitoring is not routinely used)

**Baseline evaluation**

This included a full patient history, including indication for warfarin therapy, previous adverse drug reactions caused by warfarin, previous hospitalization, concomitant drug therapies, and previous INR history. This information was recorded in a data collection sheet prepared for this study.
Conduct of study

The community pharmacy sites for this project were Northmount and Davies pharmacies that are located within one block of Lions Gate Hospital. All physicians who practice on the North Shore were asked to participate in the study either in person by a study investigator or a letter. Prior to initiation of data collection, participating physicians were given a thorough overview of the study methods, including patient recruitment. Pharmacists from both pharmacies were also given thorough training prior to initiation of the study. This training included information on study methodology, patient counseling, warfarin indications, pharmacology, monitoring and adverse effects. A package of reference information was kept in each pharmacy. Study collaborators were available by pager throughout data collection to help with questions from physicians, pharmacists, and patients regarding participation in the study.

Patients randomized to physician management followed their usual routine. They were given a warfarin prescription by their physician and followed the procedure currently used by the prescribing physician. This involved filling the prescription at a pharmacy of their choosing, then visiting a laboratory for International Normalized Ratio (INR) blood testing. INR results were phoned to the physician and the patient was contacted for dose adjustment instructions as necessary. The data was documented in the patients’ chart as per usual routine.

Patients randomized to community pharmacist management were given the appropriate warfarin nomogram order sheet, signed by the prescribing physician. This nomogram served as a prescription for the community pharmacy. Appendix 1.3 shows the
nomogram for a target INR of 2.0 to 3.0. A similar nomogram (appendix 1.4) was used for a target INR of 2.5 to 3.5. These nomograms were based on those developed and studied by Wilson and Ansell, and employed the principles outlined in the Consensus Guidelines for Coordinated Outpatient Oral Anticoagulation Therapy Management. Patients took the signed nomogram to Davies or Northmount Pharmacy to have their warfarin prescription filled, receive comprehensive warfarin counseling, and instructions for INR testing. Northmount or Metro Laboratory called INR results to the applicable pharmacy, and the pharmacist contacted the patient for appropriate dose adjustment. All data was documented in special forms prepared for this purpose. Regular periodic reports were sent to the physician regarding patient progress. The nomogram and educational material given to the pharmacists provide instruction for contacting the prescribing physician should specific complications arise (e.g. excessively high INR, bleeding). The documentation form also served as a checklist, so pharmacists asked a series of questions each time they interact with the patient. These questions were meant to be a safety measure and would also provide information for our secondary outcomes (e.g. Whether they have experienced bleeding or not).

Data was to be collected over a 12-month period, with an average follow-up of 6 months per patient assuming a steady recruitment rate throughout the data collection period. Upon completion of the trial, patients were to be given a satisfaction survey to complete (Appendix 1.5).
Management of patient care

Patients were permitted to continue or start on any medication that their physician would prescribe for them. If there were any drug interactions between warfarin and another medication, the pharmacist was required to bring that to the prescribing physician’s attention. This did not interfere with the results of the study, since pharmacists outside the study would do the same in the control arm, as it is required by law.

Patients withdrawn from the study for any reasons continued to be followed in an attempt to identify any differences between them and patients who stayed in the study. Patients were free to withdraw from the study at any time at their discretion; however, every effort was made to encourage them to continue if their safety was not being jeopardized. Patients who withdrew from the study were analyzed in the group to which they were randomized.

Biostatistical considerations and analysis

The sample size for this study was calculated using the formula appropriate for two independent groups using proportions. This calculation was based on the results of study published by Grey et al which reported 30.8% of INR values outside the target range when warfarin therapy was managed by a physician, versus 15.5% when monitored in a pharmacist-run anticoagulation clinics. A sample size of 121 patients per arm would allow detection of a 15% difference in our primary outcome based on an alpha value of 0.05 and beta of 0.2 (80% power). This sample size was calculated using a two-tailed test.

The following table was set up to give the reader some indication of sample size needed:
### Table A-2- sample size

<table>
<thead>
<tr>
<th>Proportion of outcomes in control group</th>
<th>0.2</th>
<th>0.3</th>
<th>0.35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of outcomes</td>
<td>0.1</td>
<td>191</td>
<td>59</td>
</tr>
<tr>
<td>of outcomes in study group</td>
<td>0.15</td>
<td>860</td>
<td>121</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>297</td>
<td>136</td>
</tr>
</tbody>
</table>

The randomization process was to be assessed for group comparability through a descriptive summary of diagnosis, age, weight, duration of warfarin therapy and baseline warfarin dose (for patients previously on warfarin) and concomitant medications known to interact with warfarin.

The primary outcome was to be analyzed using a chi-square test for proportions with an overall p-value of 0.05 considered significant. All other endpoints were to be analyzed using descriptive statistics. A professional statistician was consulted regarding this study design and was involved in the ongoing development of methodology and data analysis.

Data was to be analyzed based on intent-to-treat approach as outlined in *Management of patient care* section of this document. Dropouts were to be followed as already mentioned.

**Significance of the study**

This was to be the first study designed to evaluate the impact of community pharmacist-managed warfarin therapy. It has been demonstrated that warfarin management by
pharmacists in hospital and clinic settings results in improved outcomes. Unfortunately, warfarin clinic set up and operation require funding. There has been no formal analysis of warfarin management by community pharmacists, such programs have been described in the literature \(^3\). The reason that no study has been conducted may be the relative complexity of organizing the numerous disciplines involved.
determine whether warfarin management by community pharmacists can result in the same benefits.

**Study Procedures:**
If I agree to participate in this study, my patients receiving chronic warfarin therapy will receive a letter from me asking if they are interested in participating in this study. Study investigators and/or my secretary will follow-up at least one week after the patient receives the letter. If patients are interested in participating, an appointment will be set up with my secretary and/or a study investigator to review the patient informed consent form.

Patients who sign the consent form will be randomized to either physician or pharmacist warfarin management by a study investigator using random numbers. Patients randomized to the physician group will have their warfarin therapy managed as usual. For patients randomized to the pharmacist group, I will sign a prescription developed for this study which includes a warfarin dosing nomogram. The nomogram provides guidelines for warfarin dose adjustment based on INR results, and recommends the interval of INR measurement based on the current American College of Chest Physician guidelines (Chest 1998; 5(suppl):445S-469S). I will be sent each INR result from the lab, but will not participate in warfarin dose adjustment unless the INR is above 6.0, or the patient exhibits bleeding or signs of re-thrombosis (as per nomogram).

During the study (expected June/99 - June/00), a record will be kept of the following information for both physician and pharmacist-managed patients:
- the number, frequency and value of INR tests
- the number of hospital admissions due to re-thrombosis or warfarin-related bleeds
- the number of minor bleeds as reported by the patient
- the number of physician office visits related to warfarin therapy.

The primary outcome assessed will be the number of INR values outside the target range. A pharmacoeconomic analysis accounting for monitoring costs, physician office visits, dispensing costs and hospital admissions will also be carried out. Patients will also be asked to complete a brief satisfaction survey of their warfarin management.

**Eligibility:**
I understand that I can be included in this study only if I have at least one patient who complies with all the following:
- able and willing to give written informed consent
- received warfarin for at least one month
- willing and able to have warfarin prescriptions filled at Davies or Northmount Pharmacy
- willing and able to have INR tests done at Northmount or Metro Laboratories
**Physician Consent:**
I understand that participation in this study is entirely voluntary and that I may refuse to participate or I may withdraw from the study at any time without any consequences.

I have received a copy of this consent form for my own records.

I consent to participate in this study.

<table>
<thead>
<tr>
<th>Physician Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Witness Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Investigator's Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
leading to fewer complications such as bleeding and hospitalization. The purpose of this study is to determine whether warfarin management by community pharmacists can result in the same benefits.

**Study Procedures:**

If I agree to participate in this study the investigator, my physician, or my physician’s secretary will open a sealed envelope to determine whether my warfarin dose will be adjusted by my physician or a pharmacist. If I am assigned to dose adjustment by a physician, my warfarin therapy will be carried out as it normally would. If I am assigned to dose adjustment by a pharmacist, my physician will give me a signed prescription outlining what warfarin dose I should receive based on my INR blood test. I will be contacted by my pharmacist if further dose adjustments are required. The type and number of blood test measurements will not differ whether I am being followed by a pharmacist or a physician.

Whether my warfarin dose is adjusted by my physician or pharmacist, I will be contacted by phone to answer some questions regarding my satisfaction with my warfarin therapy, and whether I am experiencing any side effects. These questions will take approximately 5 to 10 minutes to answer.

**Exclusions:**

I understand that I must be excluded from participating in the study if:

a) I refuse or am unable to give written informed consent  
b) I have been taking warfarin for less than one month  
c) I am unwilling or unable to have my warfarin prescription filled at Davies or Northmount Pharmacy  
d) I am unwilling or unable to have my blood tests (INR tests) done at Northmount or Metro Laboratories

**Risks:**

There are no additional risks associated with participating in this study. Previous research has shown that trained pharmacists can manage warfarin therapy at least as effectively as physicians. There are no additional laboratory tests compared to standard therapy.

**Benefits:**

The direct benefits to me as a participant in this study, if I am selected to have my warfarin dose adjusted by my pharmacist, include more contact and warfarin counseling from my pharmacist.

**Alternative Treatments:**

I understand that if I decide not to participate or to withdraw at some later date, my warfarin therapy will be managed by my physician as usual.
APPENDIX 1.3. WARFARIN DOSING NOMOGRAM FOR TARGET INR OF 2.0 - 3.0

Date: __________________________ Date warfarin therapy initiated: __________________________

Patient Name: __________________________ Indication for warfarin therapy: __________________________

Please have the pharmacists at Davies or Northmount Pharmacy adjust your warfarin dose according to the nomogram below. Please visit Northmount Laboratories for INR testing 1 week after any dosage change.

<table>
<thead>
<tr>
<th>INR Result</th>
<th>% Change in Dose</th>
<th>Average Daily Dose</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2 mg</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>&lt;1.5</td>
<td>↑ 10-15%</td>
<td>↑ by 1mg on 2 days/wk</td>
<td>↑ by 1mg on 1 day/wk</td>
</tr>
<tr>
<td>1.5 - 1.9</td>
<td>↑ 5-10%</td>
<td>↑ by 1mg on 1 day/wk</td>
<td>↑ by 1.25 mg on 1 day/wk</td>
</tr>
<tr>
<td>2.0 - 3.0</td>
<td>no change</td>
<td>no change</td>
<td>no change</td>
</tr>
<tr>
<td>3.1 - 3.5</td>
<td>↓ 5-10%</td>
<td>↓ by 1mg on 1 day/wk</td>
<td>↓ by 1.25 mg on 1 day/wk</td>
</tr>
<tr>
<td>3.6 - 4.0</td>
<td>hold one dose and ↓10-15%</td>
<td>hold one dose and ↓ by 1mg on 2 days/wk</td>
<td>hold one dose and ↓ by 1.25 mg on 2 days/wk</td>
</tr>
<tr>
<td>4.1 - 6.0</td>
<td>hold two doses and ↓15-20%</td>
<td>hold two doses and ↓ by 1mg on 3 days/wk</td>
<td>hold two doses and ↓ by 1mg on 4 days/wk</td>
</tr>
<tr>
<td>&gt; 6.0</td>
<td>call doctor</td>
<td>call doctor</td>
<td>call doctor</td>
</tr>
</tbody>
</table>

Any prolonged bleeding, excessive bruising, blood in urine or stool or severe headache/dizziness should be reported to the prescribing physician immediately.

Physician's signature: __________________________
### APPENDIX 1.4. WARFARIN DOSING NOMOGRAM FOR TARGET INR OF 2.5 - 3.5

Please have the pharmacists at Davies or Northmount Pharmacy adjust your warfarin dose according to the nomogram below. Please visit Northmount Laboratories for INR testing 1 week after any dosage change.

<table>
<thead>
<tr>
<th>INR Result</th>
<th>% Change in Dose</th>
<th>Average Dose</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2 mg</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>&lt;2.0</td>
<td>↑ 10-15%</td>
<td>↑ by 1mg on 2 days/wk</td>
<td>↑ by 1.25mg on 2 days/wk</td>
</tr>
<tr>
<td>2.0-2.4</td>
<td>↑ 5-10%</td>
<td>↑ by 1mg on 1 day/wk</td>
<td>↑ by 1.25mg on 1 day/wk</td>
</tr>
<tr>
<td>2.5 - 3.5</td>
<td>no change</td>
<td>no change</td>
<td>no change</td>
</tr>
<tr>
<td>3.6 – 4.0</td>
<td>↓ 5-10%</td>
<td>↓ by 1mg on 1 day/wk</td>
<td>↓ by 1.25mg on 1 day/wk</td>
</tr>
<tr>
<td>4.1 - 4.5</td>
<td>hold one dose and ↓ 10-15%</td>
<td>hold one dose and ↓ by 1mg on 2 days/wk</td>
<td>hold one dose and ↓ by 1.25mg on 2 days/wk</td>
</tr>
<tr>
<td>4.6 - 6.0</td>
<td>hold two doses and ↓ 15-20%</td>
<td>hold two doses and ↓ by 2mg/day</td>
<td>hold two doses and ↓ by 1mg on 4 days/wk</td>
</tr>
<tr>
<td>&gt; 6.0</td>
<td>call doctor</td>
<td>call doctor</td>
<td>call doctor</td>
</tr>
</tbody>
</table>

*Any prolonged bleeding, excessive bruising, blood in urine or stool or severe headache/dizziness should be reported to the prescribing physician immediately.*

physician’s signature: __________________________
Appendix 1.5. PATIENT SATISFACTION SURVEY*

A Prospective, Randomized Comparison Of
Outpatient Warfarin Management By Community Pharmacists Versus Physicians

Patient Study Number: ______________________________

Completed (check one):

_________ on initial recruitment

_________ after at least 3 months of study follow-up

1. The quality of information that I received from my physician/pharmacist regarding my warfarin therapy was:

   poor        fair        good        very good        excellent

2. The skill and competence of the physician/pharmacist in the management of my warfarin therapy was:

   poor        fair        good        very good        excellent

3. The willingness of my physician/pharmacists to listen to my concerns regarding my warfarin therapy was:

   poor        fair        good        very good        excellent

4. The level of concern displayed by my physician/pharmacist when dealing with my warfarin management was:

   poor        fair        good        very good        excellent

*Based on a previously published, validated survey:
Appendix 2- summary of telephone poll conducted in order to assess feasibility of offering financial compensation for physicians’ time involvement in the original study (S=Secretary)

<table>
<thead>
<tr>
<th>Date</th>
<th>Date spoke</th>
<th>Date who spoke</th>
<th>Date who called</th>
<th>Date who answer</th>
<th>Why</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 14-Jan</td>
<td>S</td>
<td>No</td>
<td>S asked Dr.: not interested to participate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>S</td>
<td>No</td>
<td>S: letter has phone# on it, if he was interested he would have called. Not interested-hung up phone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 10-Jan</td>
<td>S</td>
<td>No</td>
<td>S: they aren't interested. Got the letter &amp; put them on their desk: not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 14-Jan</td>
<td>S</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>S</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 10-Jan</td>
<td>12-Jan</td>
<td>No</td>
<td>S: called back: Dr. says not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 10-Jan</td>
<td>10-Jan</td>
<td>No</td>
<td>S: called back: Dr. says not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 10-Jan</td>
<td>10-Jan</td>
<td>No</td>
<td>S: called back: Dr. says not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 10-Jan</td>
<td>11-Jan</td>
<td>No</td>
<td>S: Dr. saw the letter, has 3 pts elderly Chinese who will not be interested Can't see any advantage from the study. Perfectly happy following my own patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 12-Jan</td>
<td>Dr.</td>
<td>No</td>
<td>Assumed same as Martin (same office) Had said ok in summer, then never cooperated. Same office as Martin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 12-Jan</td>
<td>A/M</td>
<td>No</td>
<td>S: called back: Dr. says not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 13-Jan</td>
<td>S</td>
<td>No</td>
<td>S: none of our Drs do that (study/money)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 13-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: called back: Dr. says not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 13-Jan</td>
<td>S</td>
<td>No</td>
<td>S: Dr. doesn't participate in studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: called back: Dr. says not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>Dr: I am involved w/3 studies already-feel overloaded &amp; don't think I can do this</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22 14-Jan</td>
<td>S</td>
<td>No</td>
<td>S: Dr. on mat leave till March Dr. called Zahra @LGH-not convenient for his patients to go to Northmount/Davies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: No they are not interested (hung up phone)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S asked Dr.: not interested to participate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: Dr. doesn't participate in studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: he never does studies: No thank you!</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>Dr: I prefer to monitor my patients myself-no thank you!</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: called back: Dr. says not interested</td>
<td></td>
<td></td>
</tr>
<tr>
<td>32 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S asked Dr.: not interested to participate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S asked Dr.: not interested to participate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>34</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: no thanks!!</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S asked: he follows his pts quite diligently &amp; will feel more comfortable continuing on himself</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37 14-Jan</td>
<td>14-Jan</td>
<td>No</td>
<td>S: didn't know about it: usually they leave a message if they are interested. Ask &amp;callback if int. only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38 10-Jan</td>
<td>S</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>39</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41</td>
<td></td>
<td>No</td>
<td>Bita's family Dr: previously said don't wish to participate</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
42 No

43 10-Jan A/M
44 14-Jan S
45 "
46 10-Jan A/M
47 "
48 14-Jan A/M
49 "
50 10-Jan S
51 10-Jan A/M
52 10-Jan S
53 10-Jan A/M
54 10-Jan S
55 10-Jan S
56 10-Jan S
57 10-Jan S
58 " "
59 10-Jan S
60 10-Jan S
61 10-Jan S
62 10-Jan S
63 10-Jan A/M
64 12-Jan S
65 " "
66 " "
67 12-Jan S
68 12-Jan A/M
69 12-Jan S
70 14-Jan S
71 " "
72 13-Jan A/M
73 13-Jan A/M
74 " "
75 14-Jan A/M
76 " "
77 14-Jan S
78 " "
79 " "
80 14-Jan S
81 " "
82 " "
83 14-Jan S
84 14-Jan S
85 14-Jan S
86 14-Jan S
87 14-Jan S
88 14-Jan S

(conflict of interest)

have not heard of it, will call if interested

S: didn't recall seeing the letter, will call if interested

S: didn't see a letter come in, will call if interested

S: no idea whether she is interested. Will ask & call if she is

S: Didn't know anything about this. Will call back if interested
S: Dr. didn't say anything to me, therefore, she must not be
interested-will ask & call if she is

S: they would have called if they were interested- will ask &
call if we are

S: don't know-will call if interested

S: didn't mention anything to me-will call if interested

S: the letter is on his desk- will call you if he is interested

S: I don't have a clue!! Will call if interested

S: haven't heard anything at all-I am sure they would have
called if they were interested

S: will call back tomorrow if interested

S: don't know-will call if interested

S: asked: Dr. already sent the letter back to me

S: Lynn Valley clinic: Drs come & go-but I will ask &post
something in the staff room

S: no one said anything to me. Will call you if interested

S: don't think he is interested. But will ask & call if he is

S: not heard of it. Will call if interested

S: will ask him and call you back

S: will call back if interested

S: will put a note on his desk-will call back if interested

S: will let them know & call you if interested
<table>
<thead>
<tr>
<th>Date</th>
<th>Name</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-JanS</td>
<td>S: will ask him &amp; get back to you</td>
<td></td>
</tr>
<tr>
<td>14-JanS</td>
<td>S: never heard of it-will call if interested</td>
<td></td>
</tr>
<tr>
<td>14-JanA/M</td>
<td>S: will ask &amp; get back to you if interested</td>
<td></td>
</tr>
<tr>
<td>14-JanS</td>
<td>S: don't know, will call if interested</td>
<td></td>
</tr>
<tr>
<td>10-JanS</td>
<td>S: she will ask and will call back only if interested</td>
<td></td>
</tr>
<tr>
<td>13-JanS</td>
<td>S: will leave a message for Drs, will call if interested</td>
<td></td>
</tr>
<tr>
<td>10-JanDr.</td>
<td>Dr. Yes</td>
<td>Dr. Boileau called: interested, tell me what I should do</td>
</tr>
<tr>
<td>12-JanS</td>
<td>12-JanDr. Yes</td>
<td>Dr. wanted me to explain the study to her-then she said yes</td>
</tr>
<tr>
<td>12-JanA/M</td>
<td>13-JanDr. Yes</td>
<td>you do my INRs and pay me for it-Sure I'll do it</td>
</tr>
<tr>
<td>14-JanS</td>
<td>14-JanS Yes</td>
<td>Dr. says he likes to participate</td>
</tr>
<tr>
<td>14-JanS</td>
<td>14-JanS Yes</td>
<td>Dr. left a message with me-would like to participate</td>
</tr>
<tr>
<td>14-JanS</td>
<td>14-JanS No</td>
<td>Dr. not interested</td>
</tr>
<tr>
<td>14-JanDr.</td>
<td>14-JanDr. maybe</td>
<td>talked with him about study at length-says if we had a pharmacy in West Van, he will consider it</td>
</tr>
<tr>
<td>13-JanDr.</td>
<td>13-JanDr. maybe</td>
<td>she thinks it is a good idea-but if SDM/Safeway in deep cove were involved, then she will consider</td>
</tr>
<tr>
<td>14-JanS</td>
<td>14-JanS maybe Dr. says he will only do it IF he has to do no work for it!!!</td>
<td></td>
</tr>
<tr>
<td>13-JanS</td>
<td>14-JanDr. maybe He thought it was $2000/patient-sounded discouraged when f</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 3-A Survey of Physicians’ Reasons For Not Participating In A Randomized Clinical Trial Comparing Outpatient Anticoagulation Management By General Practitioners And Community Pharmacists

We have listed below some questions that we feel may help us determine reasons for non-enrollment in the study titled “A Randomized Controlled Trial Comparing Outpatient Anticoagulation Management By General Practitioners And Community Pharmacists”. The answers to these questions are important, as they can help shape future trials and patient programs that may be proposed for this area. We would greatly appreciate your participation.

Please do not write your name or any identifying information on the survey. We ask that if you choose to complete and return the questionnaire, complete and return the enclosed postcard separately. Please use the pre-addressed, stamped envelope provided for the survey only. Detailed instructions are provided on the last page of this survey.

Please circle the appropriate response:

Question 1- How did you first hear about this study?

1- from other physicians
2- from letters sent out to your mail box
3- from study investigators (e.g. in the GP meeting, or telephone calls)
4- never heard of this study before

Question 2- At the present, how many of your patients are on warfarin therapy?

1- more than 10
2- 5-10
3- 1-5
4- none

Question 3- I have discussed the study with my patients:

1- Yes
2- No (please proceed to question 4)
Question 3a- If you said yes to question 3, please indicate what fraction of your patients were not able to participate in the study (for example, couldn’t speak English, or had difficulty getting around):

1- none
2- less than half
3- half
4- more than half
5- all

Question 3b- If you said yes to question 3, please indicate what fraction of your patients were not willing to participate in the study:

1- none
2- less than half
3- half
4- more than half
5- all

Question 4- In the past, how many clinical trials have you participated in?

1- more than 10
2- 5-10
3- 1-5
4- none

A range of opinions exist about the reasons physicians were not interested in participating in this study. Please indicate the extent to which you agree or disagree with each of the following statements:

Question 5- The relationship I have with my patients is very important to me, and I do not want to undermine this relationship by enrolling them in a study.

1- Strongly agree
2- Mildly agree
3- Undecided or unsure
4- Mildly disagree
5- Strongly disagree
Question 6- I am concerned about the scientific benefits of the study. I believe there are no possible benefits from this study.

1- Strongly agree  
2- Mildly agree  
3- Undecided or unsure  
4- Mildly disagree  
5- Strongly disagree  

Question 7- I am concerned about the scientific design of the study.

1- Strongly agree  
2- Mildly agree  
3- Undecided or unsure  
4- Mildly disagree  
5- Strongly disagree  

Question 8- I am concerned about the long-term economic impact of the study:

1- Strongly agree  
2- Mildly agree  
3- Undecided or unsure  
4- Mildly disagree  
5- Strongly disagree  

Question 9- I am concerned about the short-term economic impact of the study (i.e. during the study period):

1- Strongly agree  
2- Mildly agree  
3- Undecided or unsure  
4- Mildly disagree  
5- Strongly disagree  

Question 10- I don't believe that a pharmacist can efficiently and safely manage patients on warfarin:

1- Strongly agree  
2- Mildly agree  
3- Undecided or unsure  
4- Mildly disagree  
5- Strongly disagree
Question 11- I have problems with random assignment of my patients to the study arm (i.e. anticoagulation management by pharmacists) or the control arm (i.e. anticoagulation management by myself).

1- Strongly agree
2- Mildly agree
3- Undecided or unsure
4- Mildly disagree
5- Strongly disagree

Question 12- I would have had difficulty following the procedures involved in the study. For example, they were too time consuming or too restrictive.

1- Strongly agree
2- Mildly agree
3- Undecided or unsure
4- Mildly disagree
5- Strongly disagree

Question 13- I am concerned about the issue of responsibility. I would like to continue to be responsible for my patients.

1- Strongly agree
2- Mildly agree
3- Undecided or unsure
4- Mildly disagree
5- Strongly disagree

Question 14- I believe that the pharmacists should accept legal liability for the patients if they are managing warfarin therapy.

1- Strongly agree
2- Mildly agree
3- Undecided or unsure
4- Mildly disagree
5- Strongly disagree
Question 15- I would feel personally responsible to my patients if one treatment group (i.e. warfarin management by myself or by pharmacist) resulted in a significantly different outcome:

1- Strongly agree
2- Mildly agree
3- Undecided or unsure
4- Mildly disagree
5- Strongly disagree

Question 16- I am concerned about other health care professionals doing the job of a physician.

1- Strongly agree
2- Mildly agree
3- Undecided or unsure
4- Mildly disagree
5- Strongly disagree

Many North Shore physicians have expressed concern of possible links between this study and regionalization. This study was carried out independently by the UBC Faculty of Pharmacy. Although there was no connection between the North Shore Health Region administration and this study, we feel it is valid to ask the following question given the frequent concern expressed by physicians:

Question 17- I would have been more likely to participate if I was confident that the North Shore Health Region was not involved in any way and would not be informed of the results.

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree
Question 18- From the following list summarizing the questions above, please rank the most 3 important reasons for you not participating in the study by placing the appropriate letter in the boxes (left column) from the choices in the right column:

<table>
<thead>
<tr>
<th>Most important</th>
<th>2nd most important</th>
<th>3rd most important</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) concern about the physician-patient relationship</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) concern about the short term economic implication of the study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) concern about the long term economic implications of the study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) concern about scientific benefit of the study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) concern about the scientific design of the study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) concern about the random assignment of my patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) concern about the issue of responsibility to my patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>h) feeling of personal responsibility if treatments are unequal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>i) concern about pharmacists' ability to manage warfarin therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>j) concern about the Region taking over the control of health care on the North Shore</td>
<td></td>
<td></td>
</tr>
<tr>
<td>k) no patients in my practice take warfarin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>l) concern about my patients' willingness to participate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>m) concern about patients' ability to participate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n) concern about other health care professionals taking over physicians' responsibilities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>o) pharmacists should accept legal liability for the patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p) never heard of the study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>q) don't like to participate in studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>r) difficulty following procedures in this study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>s) others, please</td>
<td></td>
<td></td>
</tr>
<tr>
<td>specify: ___________________________________________</td>
<td></td>
<td></td>
</tr>
<tr>
<td>__________________________________________________</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

112
Question 19- In your opinion, what is the most influential reason why we were unable to recruit enough physicians to participate in this study?

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

Question 20- If you have a general policy of not participating in studies, please list the reasons why:

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

Question 21- If you are concerned about the scientific design of the study, please indicate what those concerns are:

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________
We would like to thank you for taking the time to complete this questionnaire.

✓ Please do not write your name or any identifying information on the survey.
✓ To ensure anonymity and also to make sure you will not be sent subsequent follow up letters once we have received your completed survey, we have attached a separate postcard with the questionnaire.
✓ Please complete and return the postcard separately.
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Please return your questionnaire in the enclosed envelope to:

Bita Bateni/ Steve Shalansky  
Pharmacy Department  
Lions Gate Hospital  
231 E. 15th St.  
North Vancouver, B.C. V7L 2L7
Appendix 4: A Survey of Physicians' Reasons For Not Participating In A Randomized Clinical Trial Comparing Outpatient Anticoagulation Management By General Practitioners And Community Pharmacists:

We have listed below some questions that we feel may help us determine reasons for non-enrollment in the study titled “A Randomized Controlled Trial Comparing Outpatient Anticoagulation Management By General Practitioners And Community Pharmacists”. Even though you agreed to participate in this study, a large number of physicians did not agree to participate. The answers to these questions are important, as they can help shape future trials and patient programs that may be proposed for this area. We would greatly appreciate your participation.

Please do not write your name or any identifying information on the survey. We ask that if you choose to complete and return the questionnaire, return the enclosed postcard separately. Please use the pre-addressed, stamped envelope provided for the survey only. Detailed instructions are provided on the last page of this survey.

Please circle the appropriate response:

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1- from other physicians
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3- from study investigators (e.g. in the GP meeting, or telephone calls)
4- never heard of this study before

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1- more than 10
2- 5-10
3- 1-5
4- none

Question 3- I have discussed the study with my patients:

1. Yes
2. No (please proceed to question 4)
Question 3a- If you said yes to question 3, please indicate what fraction of your patients were not able to participate in the study (for example, couldn't speak English, or had difficulty getting around):

1. none
2. less than half
3. half
4. more than half
5. all

Question 3b- If you said yes to question 3, please indicate what fraction of your patients were not willing to participate in the study:

1. none
2. less than half
3. half
4. more than half
5. all

Question 4- In the past, how many clinical trials have you participated in?

1- more than 10
2- 5-10
3- 1-5
4- none
5-

A range of opinions exist about the reasons physicians were not interested in participating in this study. Although you agreed to participate, we would like to know if you had any concerns about this study. We have listed below some of the common concerns that we have heard about and would like to know if you also had some of these concerns. Please indicate the extent to which you agree or disagree with each of the following statements:

Question 5- The relationship I have with my patients is very important to me, and I do not want to undermine this relationship by enrolling them in a study.

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree
Question 6- I am concerned about the scientific benefits of the study. I believe there are no possible benefits from this study.

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree

Question 7- I am concerned about the scientific design of the study.

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree

Question 8- I am concerned about the long-term economic impact of the study:

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree

Question 9- I am concerned about the short-term economic impact of the study (i.e. during the study period):

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree

Question 10- I don’t believe that a pharmacist can efficiently and safely manage patients on warfarin:

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree
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4. Mildly disagree
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1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree

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1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree
Question 15- I would feel personally responsible to my patients if one treatment group (i.e. warfarin management by myself or by pharmacist) resulted in a significantly different outcome:

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree

Question 16- I am concerned about other health care professionals doing the job of a physician.

1. Strongly agree
2. Mildly agree
3. Undecided or unsure
4. Mildly disagree
5. Strongly disagree
Question 17- From the following list, please rank the most 3 important reasons for you agreeing to participate in the study by placing the appropriate letter in the boxes (left column) from the choices in the right column:

<table>
<thead>
<tr>
<th></th>
<th>a) I would save time if a pharmacist followed my warfarin patients during the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b) I felt this study might help establish a permanent community pharmacy warfarin program, and I feel this would be beneficial to myself and my patients.</td>
</tr>
<tr>
<td></td>
<td>c) I think MSP doesn’t pay enough for each warfarin dosage adjustment based on the INR results.</td>
</tr>
<tr>
<td></td>
<td>d) I think pharmacies might provide better warfarin management.</td>
</tr>
<tr>
<td></td>
<td>e) I was interested in the financial compensation offered by this study.</td>
</tr>
<tr>
<td></td>
<td>f) I think participating in research advances the profession.</td>
</tr>
<tr>
<td></td>
<td>g) I wanted to help this student with her Masters thesis</td>
</tr>
<tr>
<td></td>
<td>h) Others, please specify:</td>
</tr>
<tr>
<td>Most important</td>
<td></td>
</tr>
<tr>
<td>2nd most important</td>
<td></td>
</tr>
<tr>
<td>3rd most important</td>
<td></td>
</tr>
</tbody>
</table>

Question 18- What was the main reason for you volunteering to participate in the study?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
Question 19- In your opinion, what is the most influential reason why we were unable to recruit enough physicians to participate in this study?

__________________________________________________________________________

__________________________________________________________________________

Question 20- Please use the space below to provide further comments.

__________________________________________________________________________

__________________________________________________________________________

We would like to thank you for taking the time to complete this questionnaire.

✓ Please do not write your name or any identifying information on the survey.
✓ To ensure anonymity and also to make sure you will not be sent subsequent follow up letters once we have received your completed survey, we have attached a separate postcard with the questionnaire.
✓ Please return the postcard separately.
✓ Please use the pre-addressed, stamped envelope provided for the survey only.

Once we receive the post card, your name will be taken off the list and you will not be sent follow up letters.

Please return your questionnaire in the enclosed envelope to:

Bita Bateni/ Steve Shalansky
Pharmacy Department
Lions Gate Hospital
231 E. 15th St.
North Vancouver, B.C. V7L 2L7
Appendix 6- Survey postcard

Dr. Error! Bookmark not defined.
If you completed and returned the survey, please return this postcard separately. This will ensure that we don’t send you follow-up letters.
If you didn’t complete the survey, please discard this post card.

Thank you