

ESTIMATING THE PREVENTABLE PORTION OF LIFESTYLE-RELATED
REPRODUCTIVE CASUALTIES

By

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ABSTRACT

The purpose of this study was to review the evidence linking maternal and paternal lifestyle habits in the preconception and prenatal period to adverse reproductive outcomes; to determine either the proportion of reproductive casualties which could be attributed to lifestyle risk, thus be amenable to prevention, or the information required to estimate the preventable portion of lifestyle-related reproductive casualties; and to examine a method for surveillance of reproductive health in the community which would provide the basis for a comprehensive information system suited to the needs of the research, planning, preventive medicine and health promotion communities.

As a means of managing the size of the study report, only a representative set of lifestyles (smoking, alcohol consumption and nutrition) and research literature (major cohort and case-control studies in human populations) was reported in detail. A method was developed to review and describe the degree to which the evidence meets established criteria for causal association. The most recently available prevalence data for determining smoking, alcohol and nutritional risk, and incidence data for seven reproductive outcomes (infertility, spontaneous abortion, stillbirth, infant mortality, congenital anomalies, fetal growth and morbidity) in the British Columbia population were used to calculate the preventable portion of reproductive casualties in this community. A review of the variables required, compared with the data available, provided the

basis for recommendations regarding a reproductive health information system to support community surveillance, evaluation and research.

The study supports the conclusion that there is evidence of a causal link between exposure to lifestyle risks and the majority of adverse reproductive outcomes selected as indicators of reproductive health. The calculation of the preventable portion (etiologic fraction) of lifestyle-related reproductive casualties in British Columbia suggests the preventable portion associated with single lifestyle risk variables may be in the range of 10-50 percent. A more extensive and up-to-date set of population data for British Columbia is required to determine an accurate estimate. The benefits to be derived from an improved information system were detailed in the study. Reproductive health data collected for British Columbia is primarily outcome oriented with very little input data on which to base rational planning decisions for the improvement of reproductive health outcomes.

The study recommends that a more comprehensive reproductive health information system, with an integrated, linked data base, be considered a high priority by government and all institutions, agencies and individuals working to improve reproductive health outcomes in British Columbia. The potential to improve reproductive health is significant enough to warrant action at the clinical and community level, but additional data are required to plan cost-effective intervention strategies, to monitor improvements in reproductive health, and to support applied research initiatives.

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CHAPTER I: INTRODUCTION TO THE STUDY

Introduction

Over the past ten years, considerable attention has been given to the role that a positive change in lifestyle habits could play in improving the health status of the North American population. In Canada, a working document published by the national government in 1974, entitled "A New Perspective on the Health of Canadians" (Canada, Department of National Health & Welfare, 1974), introduced "the health field concept" which proposed a balance of attention be paid to each of four elements—human biology, environment, lifestyle, and health care organization—affecting the population's health. The concept was designed to be comprehensive, in that any health problem could be traced to one or a combination of the four elements, and to permit a system of analysis by which the relationship and relative significance of each of the four elements to a health problem could be assessed. This analysis, it was stated, would permit program planners to focus their attention on the most important contributing factors. Such analyses also, the report recognizes, requires information not yet at hand, places a heavy burden on research in each of the four areas, and calls for unity of purpose in all fields of research towards improving health status.

In 1979, the US Government published the Surgeon General's report on health promotion and disease prevention entitled "Healthy People" (US, Department of Health, Education, & Welfare, 1979), which also indicated the government's readiness to make unequivocal statements

regarding the link between certain lifestyle or environmental factors and poor health. Analysis of the relative contributions of the four health field concept elements to the ten leading causes of death in the United States in 1976 suggested that as much as half the mortality was due to unhealthy behavior and lifestyle; 20 percent to environmental factors; 20 percent to human biology; and 10 percent to inadequacies in health care. The significance of the document is its reflection of the growing consensus in the United States about the need for, and value of, disease prevention and health promotion. The Department of Health and Human Services is now required to submit a national disease prevention profile to the US Congress every three years.

A chapter of the Canadian working paper entitled "Science versus Health Promotion" declares that the government is prepared to take health promotion action in some areas of the environment and lifestyle in advance of scientific proof—given that a hypothesis appears "sufficiently valid to warrant taking positive action" (p. 58). This is based on the rationale that "messages designed to influence the public must be loud, clear and unequivocal" (p. 57) while science is full of "ifs" and "maybe's." It is expected, however, that the gathering of reliable evidence will remain a focus of the scientific community and that "in due course the validity of the . . . hypothesis will likely be resolved in a scientific way, precise cause-and-effect relationships will be ascertained and measured, and the exact significance of each factor determined" (p. 58).

The first national disease prevention profile submitted to the US Congress also made reference to the limits of knowledge in the field of prevention. The approach taken was to establish a continuum for preventability and determine where diseases or conditions fit within the continuum extremes of absolutely preventable and no known prevention. This type of assessment was to allow for more realistic expectations of the varying degrees of impact that might be gained from preventive measures given that risk factors associated with the target outcome, as well as intervention strategies, are understood in varying degrees. "In short," the report states, "the potential scope of disease prevention and health promotion is vast, the types of possible interventions extraordinarily varied, and the knowledge base uneven. . . . Fortunately, the data . . . indicate that many of the diseases and conditions that constitute the Nation's most pressing health problems are ones where knowledge of risks and effective risk reduction approaches are present and growing" (US, Department of Health & Human Services, 1980, p. 270).

The deliberate decision to support or encourage health promotion and prevention strategies despite limited knowledge places the health planner, as well as the clinician, in an intercept position between the scientific community which is required to be skeptical and the health education community which is required to provide clear, practical health guidelines for the public. Once consensus to promote a particular health behavior or to regulate a particular element in the environment has been reached, there is implicit need for a shared plan which

determines the complimentary role of each area of the health-oriented community in confirming or rejecting the validity of the approach, and the best approach to reaching specific goals for health status improvement.

One of the five national goals established by the US Government for health promotion and disease prevention, was to continue to improve infant health, and, by 1990, to reduce infant mortality by at least 35 percent, to fewer than nine deaths per 1,000 live births. In recognition of the two factors most associated with infant mortality, subgoals of reducing the number of low birth weight infants and reducing the number of birth defects have also been established along with measurable objectives aimed at specific outcome areas where the rates of infant death are in excess of the current national average or the prevention of birth defects and severe mental retardation does not match expectation. The type of preventive services to be made available to pregnant women as a means of achieving the goal and objectives have been identified as a balance of prenatal medical, risk assessment and referral services; lifestyle counselling prior to and during pregnancy; and adequate services for labor, delivery and postpartum period.

Unlike the United States, Canadian governments have not made a public commitment to a specific reduction in infant mortality, low birthweight, or birth defects. Despite this, there are implicitly recognized goals of perinatal health care across the country with careful monitoring of these outcomes via analysis of vital statistics

records at the provincial and national level, and by compiling area statistics within public health administrations and hospitals. Health promotion has been a component of public health prenatal education in all areas of Canada since the 1970s. The most recent focus has been in the area of nutrition, with the distribution of the "Five-Year Federal-Provincial Plan on Nutrition in Health Promotion for Pregnant Women" (Ottawa, Canada, 1984) to be implemented over the period 1984-1989. At the same time, the British Columbia [BC] government has published the first provincial health promotion guidelines to focus on the need to improve nutrition and other lifestyle habits prior to conception as well as during pregnancy (BC, Ministry of Health, 1984).

This thesis is concerned with the role of the health planner in facilitating improvement in reproductive and infant health status in the community given the reality of a limited knowledge base on which to act and the consensus (as implied by government reports and actions) that health promotion and prevention strategies should be undertaken. The primary focus will be on the lifestyle element.

The health promotion message for pregnant women is multifaceted, but clear: it is important to eat a well balanced diet; to be physically fit; not to smoke; not to take drugs unless prescribed and necessary; to drink very little alcohol, if any at all; to avoid environmental hazards; to avoid undue stress; to seek medical care early; to participate in prenatal education; to gain weight during pregnancy; to take all precautions to prevent having their baby born too soon or too small;

and to breastfeed. The general level of awareness in the community suggests the message has been received and acted upon by the majority of women and their partners in their childbearing years (BC, Ministry of Health, 1984; Ottawa, Canada, 1984; US, Department of Health, Education, & Welfare, 1979; US, Department of Health & Human Services, 1980).

Given public acceptance, the likelihood that the message is also believed to be true by those who promote it, and the probability that the underlying hypotheses will be used by many who plan and implement preventive and intervention strategies, what degree of impact can be expected when an appropriately planned and implemented lifestyle modification program is undertaken in an effort to prevent low birthweight, infant mortality, or birth defects? Moreover, given that there is considerable disagreement in the scientific community about the degree to which any of the lifestyle factors contribute to adverse infant health outcomes, based on an assessment of the evidence at hand, what types of information are required to help clarify these issues? What outcomes are affected, in what way, for whom, with what consequences? What plan of action directed toward both the goal of improving infant health and the goal of improving our knowledge base would elicit the support of both the scientific and the health promotion communities?

Objectives

The objectives of this thesis are:

1. To review the evidence linking maternal or paternal lifestyle habits around the time of conception, and maternal lifestyle habits

during pregnancy to adverse reproductive and pregnancy outcomes.

2. To determine what proportion of reproductive casualties can be attributed to lifestyle and, therefore, are amenable to prevention, or what information is required to determine if there is a preventable portion attributable to lifestyle factors.

3. To examine a method for surveillance of lifestyle-related reproductive health outcomes in British Columbia.

Rationale and Background

The desire to understand the reproductive process, its pathologies, the etiologic factors related to these pathologies and the manner in which they can be treated or prevented is shared by many. This is demonstrated by the extraordinary number of publications on the subject and the diversity of approach that stems from multi-disciplinary involvement. There is a real need to draw this information together so that all the options for improving reproductive outcome can be considered. This is especially true for the literature relating lifestyle factors to reproductive health and for literature examining the underlying mechanisms associated with the reproductive casualties.

Within this volume of literature, there are purported links between each of the lifestyle factors (nutrition, smoking, alcohol, drugs, stress, etc.) and many of the general outcomes associated with reproductive health (infertility, intrauterine death, birth defects, low birthweight, prematurity, infant death, etc.). This would suggest that a proportion of each type of reproductive casualty is, at least in part, preventable

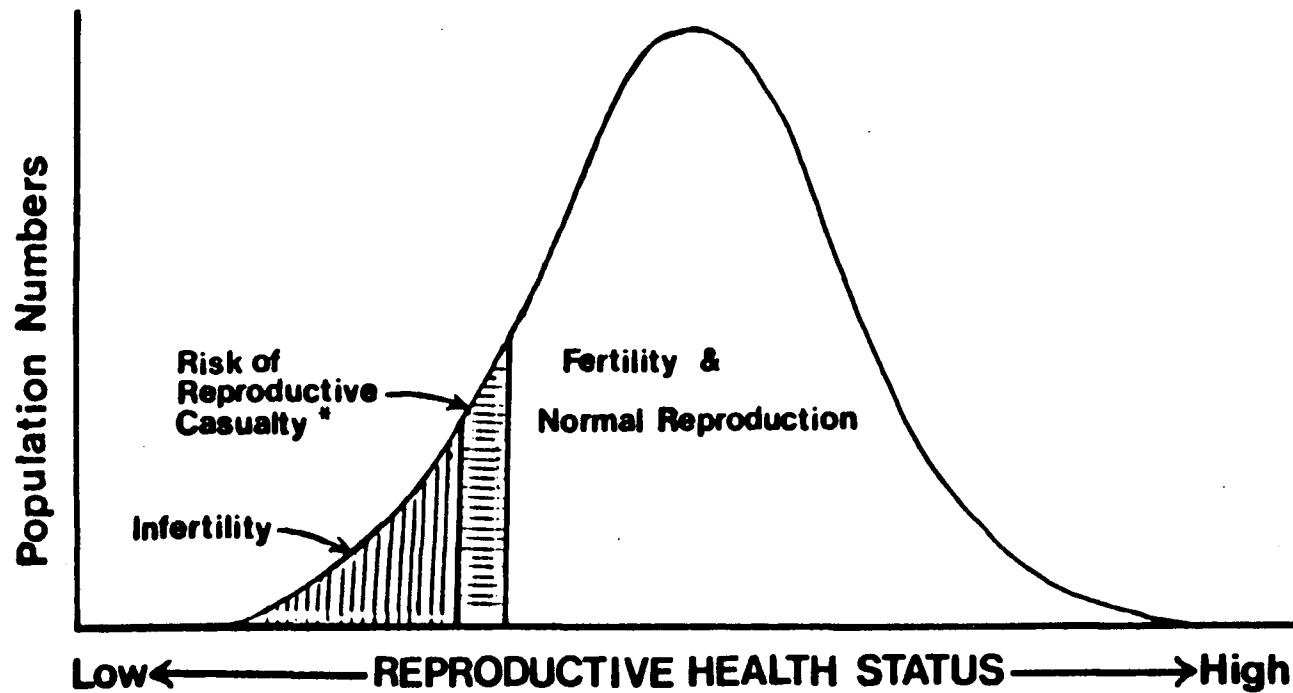
through lifestyle modification. Is this a valid suggestion? The fact that each study can only focus on a portion of the question produces a situation where there are many "pieces of the puzzle" but no completed picture.

A working hypothesis of the overall manner in which lifestyle factors may adversely affect reproductive outcome has been proposed by Wynn and Wynn (1981). This represents a comprehensive attempt to rationalize the reproductive health and lifestyle literature and for this reason, is used in this thesis as a guideline for determining the selection of the reproductive outcome measures and the boundaries for investigating evidence of the impact of lifestyle factors on these measures.

The hypothesis proposed by Wynn and Wynn (1979, 1981) can be summarized as follows: The health of parents around the time of conception is critical to the health of their infant. Poor health prior to conception and during the first weeks of pregnancy is associated with a continuum of reproductive casualties which include impaired fecundity, spontaneous abortion, stillbirth, preterm birth, fetal growth, retardation, malformations, and infant death. A reduced rate of cell replication and/or faulty cell replication are common attributes of many of these reproductive casualties. The cause of the resulting reproductive casualties is multifactorial, but some of the factors are shared by all and some of these shared factors are exogenous in nature and amenable to modification prior to conception. This suggests a proportion of each type of reproductive casualty is preventable.

Wynn and Wynn conceptualize this hypothesis by means of a "threshold of infertility" (see Figure 1) which is described as a level of marginal reproductive health, determined in part by lifestyle factors, at which conception is possible, but the risk of poor reproductive outcome is high. Based on this interpretation, the aim of any intervention would be to ensure a level of reproductive health for men and women that is above this threshold and the predeterminant of successful intervention would be the ability to identify the population within the high risk threshold and to ascertain the significant differences between those below and above the threshold level.

Given the above parameters, a number of steps must be taken to fulfill the objectives of the thesis. First, a review of the broad base of relevant literature must be completed: a review of the current literature by lifestyle factor and reproductive outcome topic area; a critical review of studies which demonstrate a quantifiable link between a lifestyle factor and adverse outcome; a review of the outcome measures which would provide the best means of measuring impact, the public health significance of the effect of lifestyle factors on reproductive health; and a review of the methods for quantifying this effect. Second, a comprehensive scheme to describe, assess, and/or monitor the impact of the lifestyle element on reproductive health in a community must be determined. Third, an attempt must be made to determine how feasible such an approach would be, given the resources of a representative community, and to judge the direct and indirect benefits of the proposal



(* The threshold of infertility)

Based on Wynn & Wynn, 1981 p14.

FIGURE 1

A Model of the Threshold of Infertility Concept

to the public, and the scientific, planning and health promotion communities.

Limitations

Many factors are involved in realizing the successful birth of a healthy infant to a healthy mother and father. The quality of maternal health and health care prior to and throughout the prenatal period; the presence or absence of maternal disease or trauma; the quality and use of health facilities and manpower resources for labour, birth and the post partum period; the quality of the environment; and family history and genetic propensity are all known to play a role in the final determination of maternal and infant health. These factors, with the inclusion of lifestyle, cover all four of the elements of the health field model. The ability to discriminate between effects of any of these four elements, or the effects of specific components within an element is clearly dependent on the information available and the interpretive ability of the interviewer. Where possible, reviews of the literature by specialists in a particular field or topic area will be accepted as a reliable critique of the relevant research in that field. Studies selected as evidence from this literature will be reviewed according to established research criteria (Andersen et al., 1979; Gehlbach, 1982; Hill, 1971; McMasters Series, 1981; Schlesselman, 1982; Susser, 1973). Some animal and tissue or cell culture studies will be referenced, since they provide much of the basis for speculation in human studies, but research selected for discussion of issues will pertain to human population only.

Thesis Format

The chapters which follow have been organized in the following manner. Chapter two provides a definition of the reproductive outcome measures included in the study, a review of the extent to which adverse outcomes are perceived to occur generally in the population, the most recent British Columbia outcome data where available, and the problems associated with determining accurate incidence or prevalence rates for these outcomes. Chapter three reviews the evidence that lifestyle factors contribute to the occurrence of reproductive casualties and reports on the prevalence of adverse lifestyle habits in the community where available. Chapter four examines an appropriate method for measuring the impact of the lifestyle element and provides estimates of the preventable portion of lifestyle-related reproductive casualties from the study and British Columbia data. Chapter five examines the rationale and design of the Reproductive Health Index, a measure to describe and monitor the reproductive health status of a community, and the change in reproductive outcomes that might be attributed to the lifestyle element. Disparities between the type of data routinely collected in the community and the type of data seen to be important for evaluation and surveillance will be identified and discussed in terms of their feasibility and potential benefits. Chapter five concludes with an overall evaluation of the extent to which study objectives are met, and the implication of the study results for the scientific, health promotion and prevention, and planning communities in improving reproductive health outcomes.

CHAPTER II: MEASURING REPRODUCTIVE HEALTH IN A COMMUNITY

The extent to which a population encounters problems in producing healthy, living infants is influenced to varying degrees by each of the four elements which comprise the health field concept—human biology, environment, health care organization, and lifestyle. The extent to which the impact of any one of these elements on reproductive outcome can be assessed, and potentially influenced, is dependent on (a) the ability to adequately describe and accurately document the type and number of reproductive impairments or casualties occurring in the population of childbearing years, and (b) on the ability to adequately describe the population in which reproductive casualties do and do not occur.

The purpose of this chapter is to review the manner in which each type of reproductive problem is described and quantified, and the problems associated with determining accurate incidence or prevalence rates. The reproductive problems to be considered are: lack of fertility and impaired fecundity; spontaneous abortion; stillbirth; neonatal mortality; birth defects and malformations; fetal growth retardation and infant morbidity associated with impaired growth and development.

The ultimate aim in this approach is to develop a reproductive health index which will adequately describe all the reproductive problems occurring in a community, and help to identify relationships between the types of problems. This aim is based on the premise that there

are common causal or mediating factors that affect reproductive capacity per se, and where these factors are amenable to modification and are altered, benefits to reproductive health should be evident across the continuum of reproductive outcome measures.

A comprehensive index of reproductive health could provide a means of examining the community-specific relationship between the occurrence of different types of reproductive problems as well as a means of assessing the impact of deliberate change in environmental, health care, lifestyle, or biological factors important to reproductive outcome. However, the information needed to carry out this type of analysis is not currently available, for understandable reasons—given that our health care system is extremely compartmentalized. Specialists who are involved in treatment of infertility, for example, end their involvement when pregnancy occurs; obstetricians, when a birth occurs; geneticists may begin their involvement around the period of conception and early pregnancy or after birth; paediatricians do not become involved until a birth occurs. Medical and hospital care is primarily oriented to cases and individual clientele; public health, to populations; occupational health to worksites and the environment, etc. Reproductive health care is the end result of many distinctly independent activities and areas of focus, and the corresponding reporting and data collection system reflects this independent approach.

If, for example, an excess of pregnancies resulting from successful treatment of infertility subsequently end in spontaneous abortion,

stillbirth and/or fetal growth retardation, this association (unless extreme) would go unnoticed at the community level for lack of access to linked records. And, if these pregnancies were associated with a high proportion of women who smoked or were inadequately nourished, this would also go unnoticed since (a) record linkage is not established and, more importantly, (b) lifestyle habits are not consistently assessed or recorded.

It is apparent that the development of a comprehensive index of reproductive health would require some changes be made to the present reporting system. In order to assess the feasibility of establishing an index, incidence or prevalence data available from the BC community (or a representative community) will be reported along with a discussion of the type of data needed to assess the impact of the various factors important to reproductive outcome. Since the focus of the study is on the potential impact of lifestyle factors, discussion will be limited to lifestyle—but the process of review for this chapter is equally applicable to environmental, health care, and biological factors.

Fertility and Impaired Fecundity

The manner in which variables concerned with the fertility or fecundity status of the population are classified and defined is generally determined by the way the information is to be used (i.e., for family planning and demography studies, for clinical research on infertility treatment, etc.). Apart from reporting on annual general fertility rate, one which relates the total number of live births for

the year to an approximation of the population exposed to the risk of pregnancy (midyear population of women 15-44 years)—or specific fertility rates for selected subgroups of the population (e.g., age-specific rates)—which can be readily calculated from vital statistics data, information about fertility and impaired fecundity is not regularly collected nor reported for any community. Available information is most likely to be generated as a function of population growth studies, demographic surveys associated with family planning issues, and clinical investigations of the diagnosis and treatment of infertility.

Questions of primary interest to this study are: what proportion of the population who try to conceive do not become pregnant? How is this proportion calculated? What types of problems are associated with infertility, how is this assessed, and how many are affected? Are reproductive outcomes of individuals with a history of infertility or impaired fecundity who become pregnant different from those who have no history of infertility? In particular, is there a relationship between infant health and a history of impaired fecundity? Are the lifestyle characteristics associated with individuals who have difficulty conceiving any different from those who do not?

A variety of reproductive models (i.e., macrosimulation and microsimulation) (Menken, 1975; Sheps, 1971) have been developed as a means to study the relationship between measures of fertility and determinants of fertility. Fertility is influenced by seven key variables: fecundability (the physiological capacity to produce a

live child), exposure (marriage/cohabitation and marriage disruption), the period of postpartum infecundability, contraception, onset of permanent sterility, spontaneous intrauterine mortality and induced abortion. Bongaarts and Jones (1982) refer to these variables as proximate determinants—the biological and behavioral factors through which social, economic, psychological, and environmental variables affect fertility.

Reproductive models are important tools for those involved in population studies (Menken, Stein, & Susser, 1982) and they also help to clarify limitations in the study of health effects on fertility. For example, while there is evidence of an interaction of specific health factors, such as nutrition, with both fecundity and fertility (Stein & Susser, 1982), population models indicate that the effect of health factors on fecundity, except in the extremes, is far less powerful than the effect of the social variables such as marriage, and behavioral variables such as contraceptive use, which promote or inhibit fertility. Fertility differentials cannot be attributed conclusively to these health factors because the confounding behavioral variables are difficult, if not impossible, to control adequately in the analysis. These models may not be sufficiently sensitive, therefore, to assess health effects (as compared to social effects) at the community level. In smaller populations the weight of factors associated with fertility are likely to shift.

A similar conclusion was reached by Bonham and Placek (1978) in

their attempt to examine the relationship of maternal health, infant health and sociodemographic factors to fertility by means of cross-sectional data from the 1973 US National Survey of Family Growth and the 1972 National Natality Survey.

Data have been reported on each of the proximal determinants of fertility by the US National Center for Health Statistics as collected in seven national, cross-sectional surveys of fertility and family planning carried out between 1955 and 1976 (Mosher, 1982). Results from 1982 data collected during interviews with a nationally representative sample of 7,600 US women between 15-44 years in 1982 have yet to be reported. These surveys represent the only substantive North American data on fecundity status of the population. The data are informative to the extent they describe the prevalence of impaired fecundity reported by married women of different age groups, parity, racial origin, region, religion, educational attainment, and household occupation—they are not appropriate for examining cause and effect relationships, but may identify trends or variations which deserve further study. The sample available for interview may underrepresent some groups of women (for example, those without children may be more likely to be away from home) and the information reported is subject to recall bias—either situation could result in conservative estimates. For these reasons, the value of carrying out these surveys has been debated (Ryder, 1973, 1975; Westoff, 1975).

Of interest to this study is the report of reproductive impairments

among 6,482 married couples who were interviewed for the 1976 National Survey of Family Growth [NSFG] (Mosher & Pratt, 1982) which describes fecundity and fertility status, and reproductive history variables for this population.

Fecundity was defined in the NSFG survey as the physiological capacity of a couple to produce a live child and information was collected according to six mutually exclusive categories: the surgically sterile for contraceptive reasons comprising 19 percent of the sample population; the surgically sterile for noncontraceptive reasons which described 10 percent; the nonsurgically sterile, one percent; the subfecund, 10 percent; those with long interval infertility, 4 percent; and those who were fecund, the remaining 56 percent of the survey population.

The term "impaired fecundity" was used to describe all couples for whom it was physically difficult or impossible to conceive or carry a baby (or another baby) to term. This group consisted of the nonsurgically sterile couples (i.e., sterile for reasons such as accident or illness), the subfecund couples (for whom it is difficult but may be possible to conceive and carry a pregnancy to term), and those who did not achieve a pregnancy after three continuous years of unprotected exposure (long interval infertility, presumed sterile). Couples with impaired fecundity represented 16 percent of the survey population. Of this group, the subfecund couples (14 percent) represent the group to be identified in a reproductive health index on the assumption that their infertility

is not permanent and their reproductive health could be improved with treatment.

About 47 percent of all couples with impaired fecundity wanted to have a baby, with the majority of childless couples (75 percent) and couples with only one child (57 percent) wanting a child. This suggests that the proportion of married couples in the 15-44 year old age group who try to conceive but are unable to become pregnant is around 7 percent of this population. In the United States a 7 percent estimate represents close to 2 million couples in 1976 terms.

In general, prevalence data can help to establish estimates of the "at risk" population likely to seek medical treatment for infertility or other reproductive problems, such as spontaneous intrauterine loss, or can be used to derive estimates of norms, such as age of natural menopause, for evaluating research on health factors and reproductive performance (Krailo & Pike, 1983). Menken and Sheps (1970), however, have demonstrated that prevalence cases are a biased sample without full knowledge of duration—in cross-sectional studies, the cases with longer duration are more likely to be included while in a cohort study, the bias is in the opposite direction unless all cases are followed to their conclusion. For a recurring condition, the effect of time of measurement is even greater. In the case of impaired fecundity, the duration of the problem can range from one year (by definition) to a lifetime, and it may also occur more than once for the same or different reasons (i.e., infection, severe weight loss). These problems of

measurement make accurate estimates of community prevalence difficult, and this difficulty carries over to attempts to measure the risk of occurrence of impaired fecundity related to lifestyle factors.

Infertility, the largest component of impaired fecundity, is more commonly reported in the medical literature. Infertility is defined as "the inability to conceive after one year of unprotected intercourse" and infers a condition which warrants clinical investigation. By this definition, 10 percent of the 1976 NSFG survey couples were infertile. Incidence data for infertility could be established if physicians were to report all first consultations for treatment of infertility to the Health Ministry, and would be preferable to prevalence data for impaired fecundity as a component of the reproductive health index. The common use of contraception means that presentation for medical treatment may coincide with a couple's awareness of the problem, but not necessarily with the onset or occurrence of infertility; however, the same situation occurs in many diseases (e.g., cancer) for which incidence data are reported. The potential delay between onset and recognition of infertility is again likely to be a confounding factor in assessing the impact of lifestyle.

The assumption that one year's failure to conceive is evidence of infertility is based on studies of healthy women (Cooke et al., 1981; Cramer, Walker, & Schiff, 1979; Vessey et al., 1978) where 90 percent report a pregnancy within the first year of exposure: 95-99 percent achieve a pregnancy after 2 years of exposure and the monthly probability of conception is estimated at 12-20 percent.

Such estimates of the fecundity of the normal population do provide a basis for defining an abnormality and assessing the effectiveness of specific treatment (Cooke et al., 1981). Life-table analysis can be used to further refine expected rates according to variables of interest such as age, duration of infertility, or the type and severity of condition (Katayama et al., 1979; Lamb & Cruz, 1972).

In the medical literature, infertility data are generally reviewed in terms of diagnostic and treatment techniques rather than etiologic factors. With standardized methods, specific male disorders (e.g., azoospermis, oligospermia, disorders of motility or morphology) and/or specific female disorders (e.g., tubal damage, ovulation disorders, endometriosis, infections) are likely to be detected in 3 out of 4 couples (Cooke et al., 1981). However, for approximately 15-24 percent of couples, no definite "cause" or condition can be detected and their infertility is described as "unexplained" (Moghissi & Wallach, 1983; Templeton & Penny, 1982). The expected incidence of specific conditions related to infertility is difficult to determine because clinic-specific reports show a wide range of rates. This may reflect the lack of major centres with large enough populations to provide a representative sample, or disparity in methods of investigation and diagnosis, or referral bias. A study of infertility treatment in Canada is currently being carried out by the federal Ministry of Health and Welfare Canada. It is hoped that these data will help to provide suitable incidence rates for conditions associated with infertility treatment: unfortunately,

lifestyle characteristics of the infertile population are seldom reported and are not being collected for the Canadian study.

There is obviously insufficient data to describe the population affected by/or treated for impaired fecundity or infertility in BC, or to ascertain the determinants and consequences of the problem. It may be acceptable in the absence of any information to assume an infertility or impaired fecundity rate approximating those determined for the US population—in this case, a rate of 10 percent of married couples would represent 41,117 couples in BC based on Statistics Canada data for mid-June, 1983.

If physicians were to report the number of women and men treated for infertility/impaired fecundity as one measure of the reproductive health in the community, would this be sufficient? Could the type of problem be estimated from smaller clinic samples? The following study suggests not.

Petterson, Fries, and Nillius (1973) reported on the incidence and prevalence of secondary amenorrhea in Uppsala County, Sweden as derived from a cross-sectional retrospective study (mailed questionnaire survey) of 2,000 women—previous to this, only estimates from very select groups of women had been reported with a range of 1.9–100 percent (Drew, 1961). Sampling from the county population registry consisted of all women between the ages of 18–45 years born on the 10th and 20th days of each month, and represented one in fifteen of the female population. A response rate of 93 percent was reported. Non-respondents (n = 138) were more likely than respondents to be unmarried

or in social class III, but were similar in age distribution (the most significant factor) and place of residence. A history of amenorrhea for more than 3 months during the previous year was given by 258 women (13.8 percent) of the 1,862 respondents—183 (9.8 percent) were due to pregnancy, 13 (0.7 percent) were secondary to surgical treatment and 62 (3.3 percent) were judged to have secondary amenorrhea. No primary amenorrhea was reported.

The one year incidence rate of secondary amenorrhea of more than 3 months duration was 3.3 percent; the one year prevalence rate was 4.4 percent and the point prevalence rate at the time of the interview was 1.8 percent based on the population at risk who were not pregnant or on contraceptive pills. If these rates were to apply to the BC population, some 18,000 women (Statistics Canada, mid-June, 1983) would be affected.

Prevalence rates were lowest in women aged 25-39 years, in married women, in those living in rural areas rather than cities, in nonsmokers, in those who had had children, and in those who had experienced early rather than late menarche. In multiple regression analysis only the age factor was found to be significant, but it is possible that other factors may be shown to be significant given a larger sample size. The extreme variation among select groups from clinical studies illustrates the importance of establishing incidence and prevalence rates for types of reproductive problems from a representative sample of the total population. If enough women were affected by secondary

amenorrhea to enable measurement of the impact of various lifestyle factors, this would be a suitable outcome measure of impaired fecundity.

The value of documenting the levels and trends of various types of fecundity impairment is generally discussed in the context of demographic and social planning or medical treatment. How pertinent are these data to planning for improved neonatal health? While there is evidence, for example, that secondary amenorrhea occurs in conditions of inadequate nutrition, severe weight loss, and extremes of activity and stress; that endocrine function is altered by lifestyle factors and that an increased incidence of spontaneous abortion is associated with infertility treatment; it is not possible to relate these results from select populations to occurrences in the community unless data are collected on the total population or a representative sample. Thus, data for the infertility/impaired fecundity component of the reproductive health index should include: (a) the incidence of infertility-related reproductive disorders of males and females of childbearing years, determined as the initial contact for treatment of each separate occurrence; (b) the diagnosis given for the disorder; and (c) other variables consistent with the use of the index to measure the effect of factors such as lifestyle.

Spontaneous Abortion

Abortion refers to the spontaneous or therapeutic termination of pregnancy before the fetus has attained viability. The current determination of viability—the time at which a fetus is capable of independent extra-uterine life—is a fetal age of 20 weeks corresponding

to a fetal weight of approximately 400-500 grams. Beyond 20 weeks of gestation, spontaneous intrauterine mortality is defined as stillbirth in most jurisdictions.

An annual general abortion rate or ratio may be calculated relating the number of abortions (or spontaneous abortions, if data are available) to an approximation of the population exposed to the risk (midyear population of women 15-44 years), to total live births, deliveries, or known pregnancies. Specific abortion ratios can also be calculated for selected subgroups of the population over varying time periods. For age-specific abortion rates it is important to use maternal age at time of conception in order to prevent the distortion which can occur when age at time of abortion is compared to age at time of live birth—this is specifically relevant to the teenage population where large numbers are involved or where age at conception occurs at the upper limit of an age group category (World Health Organization [WHO], 1970). With adequate data, weekly or monthly abortion ratios for successive periods of gestation can be calculated using life-table procedures. In this case, the sum of the net rates for spontaneous abortions at each time period would equal the spontaneous abortion rate per 1,000 pregnancies for the aggregate of all spontaneous abortions or time periods.

Information about the occurrence of spontaneous abortion in a community is not, however, readily available. No country reports a complete registration of abortions as part of vital statistics—although some, including Canada, mandate reporting of all induced abortions. An

accurate estimate of spontaneous abortion is difficult since early spontaneous abortions are often not recognized by women, or if detected, may not require medical treatment and, thus, would not be reported. Hospital discharge data can provide some incidence data but because the proportion of all cases of spontaneous abortion that are admitted to hospital varies between institutions and communities and the cases are not always clearly identified, this is not an accurate means of estimating the occurrence of spontaneous abortions in the population.

Estimates of the incidence of spontaneous abortion in the population are primarily derived from retrospective surveys although some prospective studies have been carried out. Confounding variables that affect these estimates include: previous history of spontaneous abortion and maternal age; problems of delayed observation/recording, such as subclinical abortion, induced abortion or delayed menses; and artificial variables such as recall bias in retrospective studies, selection bias, compensation for pregnancy loss, definitional problems and possibly a recurrence artifact (Jansen, 1982; Leridon, 1976).

Specific problems associated with studies of spontaneous abortion are as follows: problems of observation are a factor in all studies; memory artifact is a factor in all retrospective studies; selection bias is a factor in studies of pregnant women but not in studies of non-pregnant women. In retrospective studies where pregnancy is a method of recruitment, bias is minimized by excluding the current pregnancy from analysis (Naylor, 1974; Naylor & Warburton, 1979).

Prospective studies of pregnant women are often biased by the exclusion of early spontaneous abortions not requiring medical care and can be corrected by using life-table methodology and excluding spontaneous abortions which occur within the first week of entry to a study (Shapiro, Levine, & Abramowicz, 1971). Abortion-only sequences will be missed when a pregnant sample is selected, resulting in some degree of under reporting. The clinic setting associated with case selection may lead to over or under reporting of spontaneous abortion (WHO, 1970).

According to embryological (Hertig, 1967; Hertig et al., 1959; Shepard & Fantal, 1979; Short, 1979) and endocrinological (Bloch, 1978; Braunstein et al., 1977; Chartier et al., 1979; Rosal, Saxena, & Landesman, 1975) studies, the greatest loss of fertilized ova occurs prior to implantation and during the week following implantation. Subclinical spontaneous abortion is not included in abortion statistics but the incidence of subclinical and clinical spontaneous abortion combined (less than 20 weeks gestation) is estimated at 20-24 percent for all pregnancies and at 10 percent for primigravid women 20-29 years of age (i.e., optimal reproductive conditions). The application of life-table methods to prospective studies of spontaneous abortion (French & Bierman, 1962; Shapiro, Levine, & Abramowicz, 1971) produces a similar range of estimates.

Studies reporting the effect of a previous spontaneous abortion on subsequent abortion incidence show that results vary with sampling methods. Where sampling methods selected against the inclusion of abortion-only sequences, the incidence of abortion after one, two and

three previous abortions was 22.7-23.7 percent, 26.2-28.4 percent, and 32.2-33.3 percent, respectively. (Naylor & Warburton, 1979; Warburton & Fraser, 1964). In a study of women with a prior history of spontaneous abortion, the incidence was reported to be 20.3 percent after one abortion, 44.4 percent after two, and 58.0 percent after three (Macnaughton, 1964).

Jansen (1982) has critically reviewed the fourteen major abortion studies; classified the sample populations in terms of their being pregnant or non-pregnant, with or without known reproductive problems (i.e., infertile, "habitual" aborters), whether they were studied retrospectively or prospectively; has identified the inherent biases of the studies and suggested ways to correct for these biases. Close agreement exists on empirically derived incidences of spontaneous abortion in North American populations, irrespective of the method of data collection, provided that age, previous abortion history, and gravidity are controlled (Jansen, 1982). The normal incidence of clinically apparent abortion among first pregnancies in women under 30 years is determined to be in the range of 8.3-11.0 percent. The overall spontaneous abortion incidence for all ages was found to be between 12-15 percent. The cumulative percentage for married women with one or more completed pregnancies is reported to be 25.9 percent (Mosher & Pratt, 1982). Table 1 reports incidence data derived from the North American studies of spontaneous abortion for different age groups and reproductive histories.

TABLE 1

Number of Currently Married White Women 15-44 Years of Age and Percent Distribution by Number of Reported Spontaneous Pregnancy Losses, According to Age, Parity, and Fecundity Status: United States, 1976

Age, parity, and fecundity status	Number of women in thousands	Total	No reported spontaneous pregnancy loss	1 or more reported spontaneous pregnancy losses			
				All losses	1	2	3 or more
Percent distribution							
All women	24,795	100.0	78.4	21.6	15.0	4.1	2.5
<u>Age</u>							
15-24 years.....	5,412	100.0	89.0	11.0	9.3	0.9	0.8
15-19 years.....	918	100.0	88.9	11.1	9.0	0.1	1.9
20-24 years.....	4,493	100.0	89.0	11.0	9.4	1.0	0.6
25-34 years.....	10,993	100.0	80.4	19.6	14.1	3.8	1.7
25-29 years.....	5,806	100.0	85.0	15.0	11.9	2.2	0.9
30-34 years.....	5,187	100.0	75.2	24.8	16.6	5.5	2.6
35-44 years.....	8,390	100.0	69.0	31.0	19.8	6.7	4.6
35-39 years.....	4,339	100.0	71.2	28.8	19.4	5.2	4.1
40-44 years.....	4,051	100.0	66.5	33.5	20.2	8.2	5.0
<u>Parity</u>							
0.....	4,874	100.0	89.9	10.1	7.0	1.9	1.2
1.....	4,923	100.0	82.5	17.5	12.3	3.0	2.2
2.....	6,939	100.0	79.2	20.8	15.5	3.1	2.2
3 or more.....	8,059	100.0	68.2	31.8	21.1	7.0	3.7
<u>Fecundity Status</u>							
Surgically sterile:							
Contraceptive.....	4,781	100.0	75.2	24.8	16.4	5.3	3.1
Noncontraceptive..	2,404	100.0	61.7	38.3	21.8	10.1	6.4
Impaired fecundity..	3,701	100.0	67.6	32.4	18.4	7.6	6.5
Fecund.....	13,909	100.0	85.2	14.8	12.4	1.8	0.5

Source: Mosher, W. D. & Pratt, W. F. (1982).

Abortion incidence is proposed to be a sensitive and objective parameter with which to assess distortions in human reproductive physiology. Abortion incidence accompanying all but three modes of infertility treatment are higher than those found in the baseline population, and are not explained simply by heightened clinical awareness. The increased risk may result from a residue of incompletely treated reproductive abnormality, may be introduced by therapy, or may be both. This proposed use of spontaneous abortion as an indicator of reproductive health problems may be equally applicable to assessing the impact of the lifestyle element on reproductive health, as long as data are derived from the general rather than the clinical population. The methodology used in determining treatment effect is reported and evaluated by Jansen (1982). Methodology specifically used to examine lifestyle influences on spontaneous abortion is reported by Kline and colleagues (Kline et al., 1980; Strobino et al., 1980; Warburton et al., 1980).

In attempting to determine the data that are important to an index of reproductive health and to the assessment of lifestyle effect, the following issues are considered: Studies which include morphological examinations of abortuses report an incidence of abnormalities ranging from 30-60 percent (Poland et al., 1981; Warburton et al., 1980). Abnormalities which lead to inevitable abortion (usually cytogenetic) are more likely to occur in the early weeks of a pregnancy and can represent 80-90 percent of very early abortions. On the other hand, the proportion of abortuses without abnormalities seem to be higher in the 12th-18th week of gestation and an excess of normal karyotype

fetal abortions are purportedly associated with some lifestyle factors. Could a rough estimate of cytogenetic involvement be deduced from reports of spontaneous abortion by gestational age? Abnormalities can also result from non-cytogenetic factors affecting development at the time of the insult. Is it possible to identify these and the factors associated with them?

A descriptive study of a selected BC population designed to identify the embryos and fetuses that spontaneously abort as normal or abnormal; to document the abnormalities; and to correlate these findings with factors in the parental reproductive, contraceptive, medical and genetic history has been reported by Poland and colleagues (1981). Although the sample may be biased in favor of high risk patients who were admitted to hospital in the early stages of threatened abortion, and is a selected rather than representative population, the study provides the most comprehensive data available for BC.

The sample included all conceptuses spontaneously aborted before 20 weeks of pregnancy at the Vancouver General Hospital from 1966-1976 and totalled 2,020 abortuses from 1,961 women. Of these, 1,126 (56 percent) were embryos (defined as a crown-heel length of <30 mm); 813 (40 percent) were fetuses (defined as 30-180 mm in length); 31 (2 percent) were hydatiform moles and the remaining 50 could not be categorized. Retrospective data related to parental history and drug use, infections, disease or trauma during the study pregnancy were obtained from personal interview of the mother during the hospital period or medical records.

Of the 1,939 embryos and fetuses, 1,153 (59 percent) were abnormal. The frequency of abnormalities in embryos was 84 percent and in fetuses was 26 percent. A comparison by the authors of the frequencies of defects in the study fetuses (1966-1976) with those in terms births (livebirths and stillbirths, 1966-1973) recorded in the Registry of Handicapped Children and Adults, BC Department of Health, showed that defects occurred in any given system at least 10 times more frequently in the fetus.

Tissue culture and chromosome analysis became available toward the end of the study and was completed for 228 embryos and 59 fetuses. In this sample abnormal chromosomes were associated with 58 percent (109/188) of embryos with growth disorganization and 67 percent (16/24) of other abnormal embryos; with a smaller proportion of normal embryos (25 percent, 4/16) and abnormal fetuses (22 percent, 4/18) and with only 2 percent (1/41) of normal fetuses. Associated chromosomal anomalies appear to present an adequate explanation for defective development. Ready explanations were not apparent in cases of normal karyotype despite the fact that embryos with growth disorganization have obviously received a severe insult at a very early stage of development.

The authors review the difficulty of establishing or interpreting associations between maternal factors and morphology of the abortus given (a) recall bias, (b) the multiplicity of factors involved, and (c) the common experience of multiple events occurring during the critical period. Determining causal associations under these conditions requires large numbers complete with detailed maternal history and

Careful morphological examination, even with supporting evidence from animal or case-control studies.

To examine the association between selected maternal factors and conceptus outcome, abortuses were classified into 5 groups (normal and abnormal embryo, embryo with growth disorganization, normal and abnormal fetus) and temporarily classified as early (embryos) versus late (fetuses) abortions. Lifestyle factors with the exception of drug use and alcoholism were not examined.

Results suggest it is possible to identify (in a general fashion) factors of importance to spontaneous abortion through within-group differences in the proportion of late to early abortions (i.e., ethnic groups, blood groups-RH factor, obstetric history classifications). For example, results reported for obstetric history show that women who had had no previous pregnancy or no previous successful pregnancy had a significantly increased proportion of early abortions (specifically of embryos with growth disorganization), and women who had had live births and pregnancy loss (either spontaneous abortion or stillbirth) had a significantly increased proportion of late abortions of normal fetuses. Ethnic group variation in incidence of both late and early, and normal and abnormal abortus, appear similar to the social class variations reported by Alberman and colleagues (1976). It is not clear whether these variations are real or due to sample selection.

The following is concluded from this review: Data for the spontaneous abortion component of an index of reproductive health should include (a) the incidence of clinically recognized spontaneous

abortions by gestational age, categorized as embryos (crown-heel length <30 mm) or fetuses (crown-heel length of 30–180 mm); (b) data describing prior obstetric/reproductive history; and (c) other variables consistent with the use of the index as a tool for measuring effect of factors, such as lifestyle, on outcome.

Stillbirth

Stillbirth refers to an infant born without any sign of life at delivery and is distinguished from other intrauterine mortality, such as late fetal abortion, by gestational age or in some cases, birthweight. Variations in the definition of stillbirths for vital statistics reporting include restricting the definition to infants of 20 weeks gestation or more, to infants of 28 weeks gestation or more; to infants of 500 g or more, or to infants of 1,000 g or more.

In the 1960s, Statistics Canada revised its definition to conform to recommendations by the World Health Organization that stillbirth refer to intrauterine death "after at least 20 weeks" gestation—prior to this, the definition in use made reference to the 28th week of pregnancy. To allow for international comparison and "change over time" trend analyses, stillbirths are reported for both 20 and 28 weeks gestation or more.

Registration of stillbirths is mandatory in all developed countries and the resulting vital statistics are the primary data source. Supplementary data, such as clinico-pathology series comparing characteristics of stillborn infants to those of infants dying in the early neonatal period, are occasionally reported in the literature.

Stillbirth registration data provide a composite of the information required for livebirth and for infant death registration. Problems of measurement concerning criteria for cause of death are similar to those encountered with all infant death reports and are discussed in the following section on neonatal mortality.

A stillbirth rate can be determined by relating the annual number of fetal deaths of a specific period of gestation to the number of live births plus fetal deaths as follows:

$$\text{Annual Stillbirth Rate} = \frac{\begin{array}{l} \text{annual number of fetal deaths} \\ \text{of specific period of gestation} \end{array}}{\begin{array}{l} \text{annual number of live births plus} \\ \text{annual number of fetal deaths of} \\ \text{specific period of gestation} \end{array}} \times 1,000$$

Both the numerator and denominator are affected if fetal deaths are inadequately reported and if fetal age is misjudged at the 20 week boundary between late abortion (which are not required to be registered) and stillbirth. A stillbirth or fetal mortality ratio can be used to relate fetal deaths of a stated gestational period to live births alone.

Questions of interest to this study include: What proportion of clinically recognized pregnancies are reported as stillbirths? At what gestational age and birthweight do stillbirths occur? What factors are associated with stillbirths and do these vary with gestational age? What proportion of stillbirths are associated with fetal growth retardation, birth defects, or placental pathologies? Are the reproductive outcomes of individuals with a history of a stillbirth

different from those who have no history of reproductive problems, or from those who have a history of late spontaneous abortion or early neonatal mortality? Are the lifestyle characteristics associated with individuals who have experienced a stillbirth different from those who have no history of reproductive problems, or from those who have a history of spontaneous abortions or of neonatal mortality?

A number of these questions can be answered by available data. In BC the average stillbirth rate for the period 1978-1983 was 7.8 with an annual rate ranging from 7.1-8.8 as seen in Table 2 below.

TABLE 2

Total Number of Stillbirths* and Rate per 1,000 Live
and Stillbirths for British Columbia, 1978-1983

Year	Stillbirths	Livebirths	Live & Stillbirths
	No.	No.	Rate/1,000
1978	330	37,231	8.8
1979	298	38,432	7.8
1980	297	40,104	7.4
1981	368	41,679	8.8
1982	309	42,942	7.1
1983	312	43,047	7.3

Source: Province of British Columbia, Division of Vital Statistics.

* Twenty weeks gestation and over.

Table 3 reports percentage of total stillbirths for each of nine birthweight categories for 1979-1983. On average over the five-year period, 70 percent of stillborn infants weighed less than 2,500 g and half of these infants weighed 1,500 g or less.

TABLE 3

Total Number of Stillbirths* and Percent Distribution by Birthweight Category for British Columbia, 1979-1983

Birthweight Categories in Grams	Distribution of Stillbirths by Weight				
	1979	1980	1981	1982	1983
	%	%	%	%	%
≤500	15.0	17.2	17.6	17.3	23.0
501-1,000	20.1	21.8	16.5	17.0	20.4
1,001-1,500	11.8	11.9	12.8	12.5	10.1
1,501-2,000	6.7	8.6	9.2	11.5	11.7
2,001-2,500	10.2	6.6	9.2	6.7	6.3
2,501-3,000	7.7	11.9	8.9	11.5	11.6
3,001-3,500	11.2	8.2	12.6	10.3	9.1
3,501-4,000	7.4	6.6	4.5	7.4	2.5
>4,001	3.8	2.3	3.3	3.2	2.2
Unknown	6.1	4.9	5.3	2.6	3.1
Stillbirths %	100.0	100.0	99.9	100.0	100.0
N	313	303	358	312	318

Source: Province of British Columbia, Division of Vital Statistics.

* Defined as 20 weeks gestation or more.

Table 4 represents percentage of total stillbirths born by category of gestational age, for 1979-1983. Two peaks consistently occurred around 20-25 weeks gestation and around term (38 weeks and over), each representing approximately 30 percent of the total stillbirths. One-half to two-thirds of the fetal deaths after 37 weeks were to infants weighing 3,500 g and above, which suggests a different pathology than in fetal death of these very small infants. A possible reporting bias was observed in the choice of even- over odd-numbered weeks of gestation and in numbers reported for the 20th and 40th week of gestation.

TABLE 4

Total Number of Stillbirths* and Percent Distribution
by Gestational Age for British Columbia, 1979-1983

Gestational Age Groups in Weeks	Distribution of Stillbirths by Weight				
	1979	1980	1981	1982	1983
	%	%	%	%	%
20-25	26.2	33.0	27.4	25.6	33.6
26-28	12.1	7.6	9.5	10.3	11.0
29-31	5.8	7.6	7.8	6.4	7.6
32-34	9.9	8.3	10.9	10.9	9.4
35-37	11.8	16.5	15.1	11.9	10.4
38-41	27.5	23.1	25.6	29.8	24.8
42-	4.8	3.6	3.4	5.1	3.1
Unknown	1.9	0.3	0.3	-	-
Stillbirths %	100.00	100.0	100.0	100.0	99.9
N	313	303	358	312	318

Source: Province of British Columbia, Division of Vital Statistics

* Defined as 20 weeks gestation or more.

Of the 224 stillborn infants born later than 24 weeks gestation in BC in 1983, 72 (32 percent) were growth retarded (defined as $-2SD$ or less) when compared to the fetal growth standard developed by Usher and McLean (1969).

Review of the stillbirth literature suggests the following information would be appropriate to the stillbirth component of a reproductive health index: (a) numbers and rate of stillbirths; (b) birthweight by gestational age; (c) the proportion of stillborn infants affected by growth retardation (defined by weight for gestational age at $-2SD$ or below a designated growth standard, or by weight and crown-heel length below the 5th or 10th percentile for gestational age; (d) the proportion of stillborn infants with birth defects, and the type of defect; (e) the proportion and type of major placental pathologies associated with stillbirths; (f) data describing prior obstetric/reproductive history; and (g) other variables consistent with the use of the index as a tool for measuring effect of factors, such as lifestyle, on outcome. With only minor change to the current manner of reporting or analyzing stillbirth data, information for all categories except the last, could be available for the BC community.

Infant Mortality

The established vital statistics system in developed countries provides information on the absolute frequency of deaths within the first year of life and provides the appropriate numerators and denominators for comparison of deaths within or between a particular population, area or time period.

The simplest method of making comparisons is to compute rates. The most direct relationship is expressed by relating deaths associated with pregnancy and births to the population exposed to the risk of death.

Since infant deaths account for most of the deaths occurring in childhood, mortality rates are also reported for age-specific periods within this first year after birth. Four mutually exclusive rates are routinely reported: fetal deaths (stillbirths, as described previously); early neonatal; late neonatal; and post-neonatal deaths.

The early neonatal death rate measures the rate of death during the first 7 days of life and is computed by relating deaths at ages under 7 days to live births as follows:

$$\text{Annual early neonatal mortality rate} = \frac{\text{annual number of deaths under 7 days of age}}{\text{annual number of live births}} \times 1,000$$

Fetal and early neonatal deaths are often grouped together and the resulting perinatal mortality rate measures the risk of death from the 20th week of gestation to 7 days after birth and is computed as follows:

$$\text{Annual perinatal mortality rate} = \frac{\text{Annual number of fetal deaths of specific period of gestation plus annual number of deaths under 7 days of age}}{\text{Annual number of live births plus annual number of fetal deaths of specific period of gestation}} \times 1,000$$

Beyond the perinatal period, the late neonatal mortality rate measures the risk of death between the age of 7 and 27 days of life and the postneonatal mortality rate measures this risk from 28 days of life to one year of age. Both these rates use the annual number of live births as a denominator.

Figure 2 summarizes the age-specific divisions commonly used to analyze infant death trends.

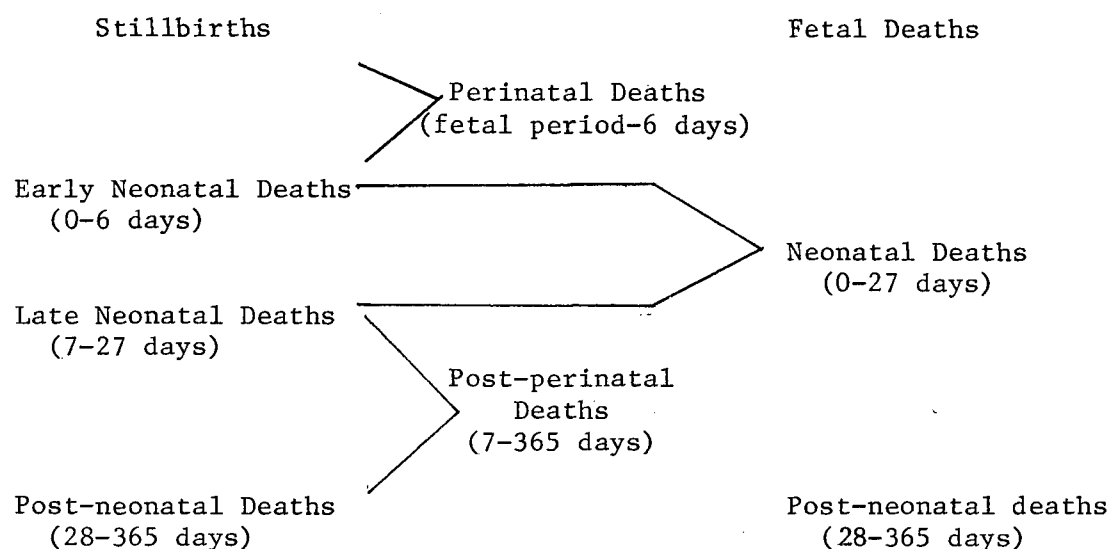


FIGURE 2

Age-Specific Classifications for Fetal and Infant Mortality

Specific rates, defined in terms of one or more characteristics of the population (i.e., cause-of-death), and adjusted (i.e., age-adjusted) rates are frequently used in detailed analysis of infant deaths.

The maternal mortality rate measures the risk of death from deliveries and complications of pregnancy, childbirth and puerperium in the group exposed to risk, which should consist of all women who have been pregnant at some time during the period. However, for lack of accurate data, this rate (more accurately termed a ratio) is usually based on the total number of live births and does not account for multiple births or fetal deaths. The ratio, commonly expressed as per 100,000 births, is computed as follows:

$$\text{Annual maternal mortality rate} = \frac{\text{Annual number of deaths attributed to maternal conditions}}{\text{Annual number of live births}} \times 100,000$$

The maternal mortality rate for BC has been reported at the level of 0.1 per 1,000 live births each year since 1972. A recent study which examined the extent to which variations in the definition of maternal death affect the number of deaths reported in the US national statistics (Smith et al., 1984) found the actual incidence of maternal mortality in the US for 1974-1978 to be 20-30 percent higher than published statistics. For 1978, the incidence rate based on study results was 12.1 per 100,000 births compared to the official report of 9.6 per 100,000 birth. The accuracy of the number of maternal deaths reported was seen to be affected by (a) whether reporting of pregnancy status was required for a death certificate; (b) the coding criteria used to assign the underlying cause of death; and (c) definitions regarding which underlying causes of death are considered maternal causes. Coding according to ICD-9-CM definitions of maternal deaths

increased the number by 10 percent above coding according to ICDA-9 (World Health Organization [WHO], 1979).

In general, however, records of mortality as reported by Divisions of Vital Statistics are more reliable than morbidity records, since death is easier to define than illness. Reports of death "from all causes" are more reliable than disease-specific mortality reports since the latter can be subject to change in diagnostic criteria.

Problems encountered in interpreting observed differences in mortality rates or ratios are similar to all vital statistics analysis and include: incomplete reporting, underregistration, ambiguous or overlapping classifications. Valid conclusions about differences must be based on comparable data that differs only with regard to the attribute(s) purported to be associated with the difference. The differences in vital rates and ratios are usually related to social, economic, biologic or medical factors, therefore, valid conclusions can only stem from data which are descriptive enough to allow proper assessment of comparability. Grove and Hetzel (1968) provide an excellent review of the analysis and interpretation of vital statistics and in the article state, "imperfections in data and inconsistencies between numerator and denominator do not necessarily make a rate useless. It is important that the imperfections be recognized and evaluated . . . all vital statistics measures should be used with full knowledge of their limitations in respect to the primary interest to be served" (p. 17). A recent editorial in the American Journal of Public Health (Zemach, 1984) reviewed "what the vital statistics system can and

cannot do." Vital records of births and deaths are a legal requirement and need only state the time and place of a vital event along with enough information to uniquely identify the individual who dies or is born.

The content of birth and death records has expanded far beyond these legal requirements to support the needs of researchers, demographers, and epidemiologists seeking statistical information and, as such, provides an invaluable resource for assessing population health status. But given the limitations of the registration process overall, most research that goes beyond broad trends or major categories must look to additional sources of data.

After commenting on a report (Smith et al., 1984) of the underestimation of national maternal mortality, Zemach (1984) contends that "a similar issue of how much to expect from the vital records system extends to the study of perinatal mortality." She suggests that with attention now focused on the core problems (preterm delivery and low birthweight) related to the small numbers of remaining deaths, it is perhaps time to reconsider the historical categories of the vital records system (i.e., include fetal death reporting with infant deaths; link maternal deaths with pregnancy outcome, etc.) and to enhance the role of the system as a multipurpose source of health-related data.

In any attempt to investigate change in mortality over time and to assess what diseases have contributed to change, problems related to the categorization of diseases by ICD coding format must be recognized. For example, the disease category reported may depend on any one of the

following: (a) the thoroughness of the investigation, (b) the diagnostic habits of the patient's physician, (c) the medical knowledge and opinion at any given time or place, (d) the ranking of importance between morbid anatomy and aetiology-focussed reporting, (e) the way in which borderline conditions are enumerated between two possible diagnoses, and (f) the way in which nomenclature and classification changes are handled following any ICD revision (Davis & Dobbing, 1974, Zemach, 1984).

Leck (1974) states "the rule that analysis of deaths by cause should generally be based on categories of the ICD must be questioned as far as perinatal deaths are concerned" (p. 709). The ICD represents a compromise between the anatomical (or histological) and aetiological concepts of diagnosis. Both concepts are accommodated although in a majority of cases preference is given to anatomical reporting. The problem of reporting only the morbid anatomy at death, or aetiology, is greatest for perinatal deaths and creates artificial distinctions between causes that can be one and the same. For example, a death certificate may describe an infant's condition at death as immaturity, growth retardation, or birth asphyxia, or may describe the maternal, placental, or cord conditions which may have led to the premature labor, growth retardation, or asphyxia, or both.

Leck (1974) goes on to suggest that "more may be achieved by collecting clinical and pathological summaries of representative series of perinatal deaths, or standard forms, and arranging for each case to be allocated to one carefully defined aetiological and (one carefully defined) pathological category by a single assessor

or team" (p. 709). Aetiological classification which distinguishes between obstetrical causes and environmental causes has proved valuable in identifying means for preventing perinatal death (Butler & Bonham, 1963).

In general, routine vital statistics, as currently reported, have the advantage of being based on larger numbers than special surveys, but the disadvantages of including fewer clinical and pathological details and being more susceptible to bias by the diagnostic discrepancies already noted. Where disorders are caused by a combination of many influences, clarification of the relative aetiological importance of the contributing influences is key to the preventive approach and cannot be achieved in the absence of descriptive reporting and investigation.

It has been well established that the two factors most closely associated with the death of an infant in the first weeks and months of life are the gestational age and weight of the infant at birth. In addition, infants with serious birth defects are at greater risk of dying. The questions of interest to this study relate to these factors, to the variables that are associated with an infant being born too small or too soon, and to the manner in which growth retardation is distinguished from birthweight and any differences in the variables associated with either. Further to this, the maternal characteristics associated with fetal death that are of interest relate to whether the reproductive history of a mother whose infant dies is different

from those whose infants do not die and are perceived to be healthy; whether the lifestyle characteristics of mothers whose infants die and are growth retarded, premature, or malformed are different; and whether the lifestyle of mothers whose infants die are different from mothers whose infants are alive and healthy or from mothers who experienced other reproductive problems. What questions can be answered from the current vital records system in BC?

Data from the vital statistics reports certainly confirm the association between infant and fetal deaths, birthweight and gestational age. Table 5 summarized the BC livebirth, fetal, and neonatal mortality statistics for 1978 and 1983, and Table 6 reports birthweight-specific mortality rates by age at death, for the years 1979-1983. Although a small gradual decline in infant mortality is seen over this time period, the risk of dying remains directly proportionate to an infant's weight category at birth. The 5 percent of infants weighing 2,500 g or less at birth [LBW] account for 60-70 percent of all perinatal deaths and 45-50 percent of infant deaths (RR:17.6) within the first year. Less than 2 percent of all births are reported in the 1,500 g and under birthweight category [VLBW], yet these infants account for 50-60 percent of perinatal deaths and 25-35 percent of all infant deaths (RR:40.0) in BC over these six years. One in 5 VLBW and 1 in 10 LBW infants die compared to less than 1 in 100 infants who weigh more than 2,500 g at birth—even in the later group, infants in the 2,501-3,000 g birthweight category have a mortality incidence which is twice that of heavier infants (RR:2.0).

TABLE 5

Total Livebirths, Total Population and Birthrate per 1,000 Population; and Total Infant Deaths by Six Age-Specific Categories (Fetal, Early Neonatal, Late Neonatal, Perinatal, Neonatal, and Infant) and Rate per 1,000 Livebirths (or per 1,000 Live and Stillbirths) in British Columbia, 1978-1983

Age-Specific Mortality Categories	Numbers and Rates of Birth, Fetal and Infant Deaths											
	1978		1979		1980		1981		1982		1983	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Stillbirths												
(Fetal Deaths)	330	8.8	298	7.8	297	7.4	368	8.8	309	7.1	312	7.3
Early Neonatal Deaths												
(0-6 days)	248	6.7	214	5.6	199	5.0	242	5.8	229	5.3	199	4.6
Perinatal Deaths												
(Stillbirths + 0-6 days)	578	15.4	512	13.2	496	12.3	610	14.5	538	12.4	511	11.8
Late Neonatal Deaths												
(7-27 days)	44	1.2	44	1.1	48	1.2	29	0.7	37	0.9	20	0.5
Neonatal Deaths												
(0-27 days)	292	7.8	258	6.7	247	6.2	271	6.5	266	6.2	219	5.1
Infant Deaths												
(0-365 days)	472	12.6	434	11.3	442	11.0	424	10.2	423	9.9	374	8.7
Total												
Livebirths	37,231	14.7	38,432	14.9	40,104	15.2	41,679	15.2	42,942	15.4	43,047	15.3
Total												
Population	2,530,100		2,571,200		2,640,100		2,744,467		2,783,200		2,812,900	

Source: Province of British Columbia, Division of Vital Statistics.

TABLE 6

Total Number of Livebirths and Infant Deaths: Early Neonatal, Late Neonatal, Post Neonatal, and Infant Death, and Rate per 1,000 Livebirths by Birthweight Category in British Columbia, 1979-1983

Age at Death	Year	Birthweight Categories in Grams										Total Deaths N
		≥500 M Rate	501-1000 M Rate	1001-1500 M Rate	1501-2000 M Rate	2001-2500 M Rate	2501-3000 M Rate	3001-3500 M Rate	3501-4000 M Rate	≥4001 M Rate	Unknown M Rate	
Early Neonatal (0-6 days)	1979	944.4	541.0	162.0	40.3	14.0	4.6	0.9	1.1	0.4	8	209
	1980	956.5	440.4	136.8	28.4	16.4	2.6	1.0	1.4	1.3	14	200
	1981	900.0	553.2	118.2	54.4	8.7	3.2	1.3	1.4	0.9	14	241
	1982	1,000.00	550.3	107.3	41.9	9.7	2.0	1.5	1.1	0.9	10	229
	1983	777.8	474.4	117.3	26.1	9.4	3.2	1.4	1.3	0.8	11	197
Late Neonatal (7-27 days)	1979	-	49.2	33.5	5.0	3.7	2.3	0.5	0.3	0.4	1	46
	1980	43.5	82.6	31.6	14.2	2.8	1.0	0.8	0.2	0.4	0	48
	1981	-	42.6	4.9	7.1	1.5	0.5	0.2	0.5	-	3	28
	1982	-	11.8	4.9	4.7	2.1	1.5	0.4	0.7	0.5	1	37
	1983	-	7.3	10.2	7.1	0.7	0.5	0.1	0.5	0.3	1	21
Post Neonatal (28-365 days)	1979	55.6	123.0	27.9	12.6	14.0	4.9	3.5	3.3	3.5	1	180
	1980	-	45.9	52.6	21.3	15.7	6.5	4.2	2.5	2.1	8	195
	1981	66.7	35.5	39.4	16.5	8.0	3.0	3.0	2.2	3.9	9	156
	1982	-	65.1	-	14.0	12.4	5.1	3.3	2.3	0.9	3	157
	1983	111.1	29.2	40.8	11.8	6.5	4.3	3.1	2.4	2.5	7	156
Total Infant Death (0-365 days)	1979	1,000.0	713.2	223.4	57.9	31.7	11.8	4.9	4.7	4.3	10	435
	1980	1,000.0	568.9	221.0	63.9	34.9	10.1	6.0	4.1	3.8	22	443
	1981	966.7	631.3	162.5	78.0	18.2	6.7	4.5	4.1	4.8	26	425
	1982	1,000.0	627.2	112.2	60.6	24.2	8.6	5.2	4.1	2.3	14	423
	1983	888.9	510.9	168.3	45.0	16.6	8.0	4.6	4.2	3.1	19	374
Livebirths		N	N	N	N	N	N	N	N	N		Total N Births
	1979	19	122	179	397	1,354	5,663	13,988	12,062	4,838		38,644
	1980	22	109	190	422	1,401	5,701	14,380	12,772	5,151		40,170
	1981	30	141	203	423	1,374	5,960	14,791	13,369	5,378		41,679
	1982	17	169	205	429	1,446	5,901	15,504	13,634	5,628		42,942
	1983	18	137	196	422	1,385	5,990	15,350	13,868	5,673		43,047

Source: Province of British Columbia, Division of Vital Statistics.

Thirty-three percent of all preterm liveborn infants (= <37 weeks gestation) are low birthweight, and half of these are very low birthweight. Less than 2 percent of liveborn term infants weigh under 2,500 g. These proportions increase for fetal deaths: 20 percent of stillborn infants of 38 weeks gestation or more are low birthweight; 85-95 percent of preterm stillbirths are low birthweight and 70-85 percent are very low birthweight in BC.

In addition, the available BC data can (and does) confirm other well known associations with low birthweight and with infant mortality —i.e., a positive association with younger and older parents, with single mothers and/or "illegitimate" births, with multiple births, with first births and with a history of previous pregnancy loss or stillbirth. All information reported in the registration of livebirth, stillbirth, and infant deaths (see Appendix) is available for analysis, given the constraints already mentioned. Using these data to determine variable-specific mortality rates or associations with low birthweight help to identify factors which describe high risk groups in the population, but the type of information currently reported does not help to explain why the particular group (e.g., mothers born in India) is at risk or why their infants are born too small or too soon.

An excess of low birthweight or mortality may be associated with lifestyle factors such as smoking and poor diet; with poor pregnancy gain and low pregravid weight; with particular medical and obstetric problems; etc., but documenting this type of information of potential etiological importance is not required at present. Without such

information, however, community resources cannot be knowledgeably allocated to areas of intervention which could be effective in improving reproductive and neonatal health.

An etiological perspective could also provide valuable support in assessing "cause of death" data. To recognize cause of death as short gestation and low birthweight as reported in some 15 percent of cases; or intrauterine hypoxia and birth asphyxia, in about 5 percent of cases; or congenital anomalies of major systems, in 35-50 percent of deaths; provides no insight into factors which contribute to this outcome. Recognizing maternal conditions or placental, cord or membrane conditions as the cause of death, recognizes contributing factors that are, in themselves, the outcome of earlier problems. Pneumonia was amongst the four leading causes of infant death in 1980 in BC. Do infants die of infection because of increased exposure or decreased resistance? Sudden Infant Death [SID] Syndrome now represents 40-50 percent of the postnatal deaths in BC—is the postnatal growth retardation associated with SIDs unique to the postnatal period or an extended profile of prenatal growth? We cannot say if records do not include other growth parameters besides birthweight.

With smaller numbers of deaths and improved technological support for data analysis, it seems the appropriate time to suggest a role for the vital records system in enhancing etiological research efforts. In this way a data base representative of the total community could be supplemented with a selected population data base assembled from in-depth case studies carried out by local health agencies and independent researchers.

Zemach (1984) concludes her editorial: "The challenge to public health and other researchers is to document the types of application that are and are not suitable for the vital records system, and to move toward the establishment of other supplementary uniform national data sets, instead of posing unrealistic expectations for birth and death registration." The index of reproductive health proposed in this thesis suggests the type of supplementary data which could provide direction to those planning intervention programs and valuable statistics for in-depth studies.

The following is concluded from this review: Data for the infant mortality component of a reproductive health index should include (a) the incidence of early, late, and postneonatal mortality; (b) birthweight-specific mortality; (c) mortality by birthweight for gestational age; and (d) variables consistent with the use of the index as a tool for measuring effect of factors, such as maternal weight, weight gain, and lifestyle habits, on both birthweight and mortality outcome.

Fetal Growth and Fetal Growth Retardation

The recognition of fetal growth, as measured by birthweight, as the most significant predictor of fetal and infant mortality, and of gestational age as the most critical determinant of birthweight has ensured a legitimate focus on reducing the incidence of low birthweight and premature birth in the population. Studies in the early 1970s demonstrated that infants who weighed less than 2,500 g at birth, regardless of their gestational age, accounted for over two thirds of the infants who died, and for this reason, low birthweight infants

(defined as <2,500 g) were singled out as a high risk group. Therefore, data regarding birthweight, gestational age, and the incidence of low birthweight and prematurity (<38 weeks) for the majority of live births, stillbirths, and neonatal deaths in the community are readily available.

Subsequently, it has been recognized that the birthweight of some infants is very low relative to the birthweight of other infants of the same gestational age and that this represents a failure to thrive. These small-for-gestational-age [SGA] or growth retarded [IGR] infants are shown to have an increased perinatal mortality and suboptimal postnatal development (Abdul-Karim & Sunderji, 1978; Usher & McLean, 1974; Walther & Ramaekers, 1982).

The recognition of growth retardation is dependent upon a standard of normal growth for infants at each gestational age. Most standards for fetal growth have been based on detailed clinical studies of perceived-to-be healthy mothers and infants but are derived, of necessity, from small populations. The accuracy of the percentile curves, in particular the calculation of gestational age, is an important attribute of these clinically derived standards, but this is offset by the concern that the population, being small, might not be representative of the general population. For example, the high geographic elevation and low socioeconomic status of the Denver sample (Lubchenco et al., 1963), which was for many years the most commonly used growth standard, is suggested as part of the reason for its now apparent difference from the majority of comparable standards (i.e., 100-300 g lower from 34 weeks gestation). In a review of various growth standards, Ulrich

(1982) found the least variation in mean birth length (about 2 percent, generally not exceeding 1 cm in individual gestational weeks) and head circumference measurements (approximately 3 percent variation), whereas differences in birthweight exceed 10 percent from one curve to another, particularly in the later weeks. Thus, mean values of length/head circumference ratios show general agreement but ponderal index curves, the ratio of length to weight, are likely to vary by 4-6 percent.

Postnatal measurements of biparietal diameter are effected by accommodation of the head during delivery (particularly first borns, and male infants) and, thus, intrauterine ultrasound measures are considered to more accurately represent growth after 36 weeks gestation—for example, Campbell and Newman (1971) report a growth rate of 1.2 mm/week after 36 weeks, whereas postnatal measurements show 1.0 mm/week growth.

The characteristics of the population that should be used in developing growth standards has also been a topic of controversy. Should growth standards depict average fetal growth in the population or optimal growth in the sense that the growth profile is associated with the lowest risk of an infant dying and/or the pregnancies perceived to be unaffected by any growth retarding characteristics? Both types of growth standards have been developed. The type of standard used, the degree to which the standard population is representative of the community and the criteria used to assess fetal growth retardation will determine the way in which infant health is described.

The assessment of infant health based solely on weight for gestational age is now suggested to be an inadequate measure (Miller

et al., 1977; Neligan et al., 1976; Ulrich, 1982). This is of particular concern when trying to establish the origins and consequences of fetal growth retardation. The SGA infants are not a homogeneous group in terms of growth dimensions, and their individual prognosis varies widely—some infants are proportionately stunted; others are of expected length, but wasted; and some exhibit a combination of the two types of retardation. It is generally thought that infants with a small ponderal index—ponderal index being $\text{weight in grams} \times 100 / \text{body length in centimetres}^3$ —have probably been growth-retarded over a relatively short period of time before delivery. Many SGA infants have appropriate ponderal indices, indicating expected weight for length proportions, but are symmetrically undergrown—the result, it is thought, of prolonged growth retardation of early pregnancy origin. Greater severity of growth deprivation is associated with a reduction in both head circumference and crown-heel length. It seems that infants who are both stunted and have a small ponderal index may be the most severely growth-retarded since they appear to have suffered a recent insult superimposed on prolonged growth retardation. Thus, measures of crown-heel length and head circumference (in addition to birthweight and gestational age), and an appropriate multi-measure standard of normal growth are required to identify and describe different types of fetal growth retardation. These data are not available for the majority of communities, including BC, and to date have been generated by a small number of large scale studies.

Problems are also seen in the available growth standards for premature births. Naeye and Dixon (1978) found evidence that most fetal growth standards based on body measurements of neonates born at various gestational ages (i.e., cross-sectional data) included inaccuracies in gestational age assessment. Standard deviation [SD] from mean birth weight values are relatively larger in preterm than in term infants in all of the major growth standards (Babson, Behrman, & Lessel, 1970; Brenner, Edelmann, & Hendricks, 1976; Gruenwald, 1966; Lubchenco et al., 1963; Tanner & Thomson, 1970; Usher & McLean, 1974). Because variations in fetal growth are greatest near term, relative values for standard deviations from mean birth weight values should progressively increase rather than decrease near term. Five of the six frequently used standards combined measurements from infants who died in the neonatal period with measurements from those who survived. Since fetal growth values are significantly larger in preterm infants who survive than in those who die, Naeye and Dixon (1978) suggest the standards are likely to be influenced by the inclusion of data from growth-retarded neonates and neonates that were older than their calculated ages. Although the corrected preterm growth standards conform to the logical (smaller) standard deviations, the authors suggest there is no completely valid method presently available to determine normal fetal growth using measurements from neonates because there is no assurance that prematurely born neonates are normally grown.

Williams and colleagues (1982) present a case for developing growth standards from vital statistics records in order to provide

accurate information on contemporary patterns of fetal growth and viability in a community. The populations used for clinically based growth standards are too small to allow the development of accurate weight- and age-specific viability standards. Large population-based studies can provide more stable mortality rates but this advantage may be offset by quality control problems with respect to the calculation of gestational age and the resulting distortion of percentile curves (particularly those below 37 weeks gestation).

Population-based studies have the advantage of being broad based and, thereby, more representative; their large numbers make it possible to control for confounding factors such as sex, race, and birth multiplicity and because they are based on vital records, they can be replicated periodically and economically to reflect ongoing improvement or change in mortality and birthweights. The California study (Williams et al., 1982), which developed methodology to minimize quality control problems, illustrates the clinical support that can be derived from the comparison of age-specific perinatal, neonatal, and fetal mortality rates across selected parameters of interest (e.g., sex, race, multiple births, fetal growth retardation).

The ability to use the same information as both a fetal growth standard (which reflects average fetal growth in the community) and a viability standard (which reflects optimal fetal growth for lowest mortality in the community) resolves the problems related to the exclusive use of either average or optimal growth standards and provides the opportunity to monitor growth-related improvements in infant health

outcomes. For example, the optimal birthweight-for-gestational age combinations for the California population is presently 500 g heavier and 2 weeks longer than the mean birthweight-for-gestational age. Thus, a target for improved infant mortality outcome would be to increase the mean birthweight for all gestational age groups in this community in addition to the reduction of LBW and preterm births.

Most recently, population studies of fetal growth have developed optimal standards as a means to examine the impact of maternal, infant and health care characteristics of pregnancy on fetal growth and viability outcomes. An example of this type of study was carried out in Odense, Denmark, and reported by Ulrich (1982). The object of the investigation was to study normal, as far as possible optimal, fetal growth in a representative population; to relate a number of maternal and pregnancy factors to fetal growth in preterm and term deliveries; and by measurement of several body dimensions, to contribute to the description of variations in the relative growth of body dimensions in normal and growth retarded infants.

Three groups of mothers and infants (all singleton births) were studied: (a) 358 normally grown newborns of healthy mothers with uncomplicated pregnancies, (b) 109 preterm infants delivered prior to 38 weeks gestation of "moderately" healthy mothers, and (c) 222 preterm and 130 low weight mature infants and their mothers. Criteria for inclusion in the study was primarily determined by maternal characteristics for groups one and two, and by infant characteristics for group three. The study was carried out at the Odense University Hospital which

covered 97 percent of all prenatal clinic care and subsequent deliveries in the municipality for the study period 1972-1974.

Mothers to be included in group one were selected prospectively from the prenatal clinic records according to the following criteria:

- 17.5 to 35 years at time of delivery,
- menstrual cycles with <6 days variation, not exceeding 21-35 days,
- >3 regular menstrual periods after discontinuing oral contraception,
- date of last menstrual period known,
- normal gynaecological examination,
- uncomplicated pregnancy,
- absence of maternal chronic disease,
- complications of earlier pregnancies limited to one abortion or one premature delivery or mild preeclamptic toxemia,
- smoking habits of <10 cigarettes/day,
- both parents born in Denmark.

Records were checked at each subsequent prenatal visit to ensure continued compliance with this criteria and at time of delivery randomization was carried out in term pregnancies. About 30 percent of all mothers met the above inclusion criteria and 3 out of 7 (13 percent of all deliveries) were included in the study. Preterm infants of mothers meeting this criteria were so few in number (47/358) that these births were not randomized and were supplemented by the 109 infants in group two (whose mothers met a less restrictive inclusion criteria) in order to obtain an adequate study sample. Exclusion criteria for potential group one and two infants—which included the presence of malformation, serious placental pathology or controversial gestational age (>3 weeks disparity between reported menstrual data and clinical assessment)—effected 34 infants. Group three was composed of all singleton infants, born to mothers living in the municipality,

with birthweights less than 2,750 g and/or a gestational age under 38 weeks (266 days). For all groups, data were collected prospectively from the prenatal through the immediate postpartum period.

Results from this and similar studies emphasize the importance of distinguishing between "normal" infant growth, resulting from healthy pregnancies, and infant growth patterns associated with less optimal prenatal conditions. For example, the fact that so few healthy mothers give birth prematurely and the fact that most fetal growth curves are cross-sectional curves, means that with decreasing gestational age such curves represent increasing proportions of abnormal, mostly undergrown, infants.

Ulrich (1982) found the following characteristics of "normal" growth: all body dimensions showed rising values with advancing gestational age (body length and head circumference measures similar to other fetal growth studies, birthweights above all but Swedish and Norwegian studies); ponderal index values declined after week 40 in firstborn infants but continued to rise in laterborn infants; laterborn infants were larger than firstborns with respect to all body dimensions, and ratios were similar except in the latest gestational weeks. A particularly interesting finding, that is of relevance in monitoring the adequacy of intervention programs, concerns the different growth patterns seen in boys and girls of similar weight—boys exhibited faster growth in body length and head circumference and ratios of body dimensions were consequently different. The results suggest that, with normal pregnancies and healthy mothers, girls may attain an

average weight similar to that of boys in fetal life, but tend to be plump while boys show faster skeletal and head growth.

When fetal growth patterns of the normal mature newborn infants were examined in relation to social status (upper/lower), maternal weight (heavy/light), employment outside the home (home working/outside employment), and smoking habits (25 percent smoked under 10 cigarettes/day versus non-smokers), the following results were reported: infants of light mothers were smaller than infants of heavy mothers except for head circumference and biparietal diameter; infants of upper and lower social status were of similar size; smoking reduced average birthweight by 145 g; boys and girls showed different growth patterns in the two maternal weight groups (infants of light mothers did not exhibit the growth variations between sexes as described above); and birthweight of firstborn infants varied with maternal pregravid weight. With lower social status, employment, and moderate smoking, a significant weight reduction (120 g) was observed in infants of light mothers, but not in infants of heavy mothers. The authors state that this marked difference between the two maternal weight groups, in the effect of maternal employment, social status, and smoking in pregnancy, indicates an interaction between maternal constitution and external influence rather than a mere summation of adverse factors—this interaction may, within the limits of normal uncomplicated pregnancy, result in newborns who are well-fed and others who show signs of undernourishment. In other words, one potentially adverse factor may produce results varying from

a considerable reduction in birthweight to no measureable effect depending on other circumstances of the pregnancy or characteristics of the mother.

In group three infants who were preterm or low-weight mature, growth patterns previously described in normally grown mature infants had largely disappeared and new growth patterns were evident: faster head growth in boys compared to girls remained for all groups and subgroups but faster linear growth was no longer observed; premature infants were shorter, and had higher ponderal index and smaller heads than low-weight mature infants of similar weight; both groups of infants of smoking mothers had disproportionate retardation of skeletal growth compared to infants of non-smoking mothers and sex ratio was lowered; and specific types of placental complications were associated with specific types of fetal growth retardation in both groups of infants. Based on the results, the authors suggest that male fetuses may be more sensitive to abnormal immunological and nutritional factors whereas female fetuses may be more sensitive to hypoxia—thus, the impact of a given adverse pregnancy factor may vary according to fetal sex.

A similar but retrospective study of a selected population was carried out by Miller and Merritt (1979) who developed normal fetal growth standards from a five year study of over 6,000 consecutive births at the Kansas Medical Center (tertiary care, high risk referral center), 1973-1978. Head circumference and birth length growth patterns compared favorably to the Danish study (Ulrich, 1982), but birthweight

and, thus, ponderal index dimensions were lower. The purpose of the Kansas study was to provide anthropometric data on newborn infants free from all known growth retarding influences in utero; to construct from these data standards of normal fetal growth for comparative use in determining newborn infants with atypical fetal growth; and to describe the causes and consequences of atypical growth.

A unique component of the study was the criteria established for identifying growth retarding factors. Four groups of growth retarding factors were outlined: fetal factors (including intrauterine infection, chromosomal abnormalities, malformations, multiple births); medical complications of pregnancy (including hypertension, pre-eclampsia, chronic disease, infection, anemia, medications, abnormalities of the placenta); environmental factors (including exposure to toxic substances); and maternal behavior (including abnormal low prepregnancy weight for height, low pregnancy gain, lack of prenatal care, delivery before 17 or after 35 years of age, smoking, and the use of addicting drugs or large quantities of alcohol during pregnancy). The presence of any of these factors excluded the mother-infant pair from the "normal" group—two out of three fullterm infants and 85 percent of all premature infants born during the study were so excluded.

Within the group free of known growth retarding factors, pregnancy outcome was excellent: less than 2 percent of infants weighed under 2,500 g and of the 2.4 percent born prematurely, 85 percent weighed more than 2,000 g. Within this group, babies born to women in the lowest socioeconomic group were at no greater risk of being low birthweight

or fetal growth retarded than those born to mothers in the highest socioeconomic group. Similarly, a mother's age, her marital status, race or level of education were not, per se, related to a higher risk of her baby being born too small or too soon.

Infants born to mothers with one or more growth retarding behavioral conditions were more likely to be premature, of low birthweight and growth retarded by each of the measures used (low ponderal index, short-for-dates, and small head circumference)—over half the low birthweight infants were born to women with behavioral conditions and no other known complications of pregnancy. Both premature and fullterm infants with low ponderal index and short-for-dates types of growth retardation were more likely to be low birthweight in this group compared to the group with no known growth retarding factors associated with pregnancy. Specific behavioral conditions were associated with specific types of fetal growth retardation.

Pregnancy outcome was significantly worse if multiple behavior conditions were present. For example, mothers whose only known growth retarding factor was low weight gain had a significantly increased proportion of preterm births (RR:2.9), short-for-dates growth retardation (RR:1.8) and full-term infants who weighed less than 2,500 g (RR:2.8)—if low weight gain and low pregravid weight-for-height occurred together, the proportion of preterm and short-for-dates infants was significantly greater than for low weight gain alone (RR:12.1 and 4.5 respectively). Similarly, increase in preterm births (RR:4.1) and short-for-dates growth retardation (RR:3.5) occurred when smoking and

low weight gain occurred together. When low weight gain occurred with two or more other behavioral risks, the relative risk for preterm birth was 8.8 and for short-for-dates growth retardation was 8.2.

Mothers with a single medical complication had a significantly increased proportion of premature birth and growth retarded fullterm infants (all types) when compared to mothers with no complication or adverse behavioral conditions. Many were taking prescribed drugs for their medical conditions. Mothers with single obstetrical problems had a significantly increased proportion of premature births (50 percent were medically induced) and of low ponderal index infants—and these infants were more likely to be low birthweight. Infants born to mothers with both obstetric problems and behavioral conditions were twice as likely to be short-for-dates and three times as likely to have a small head circumference as those born to mothers with no such problems.

Miller and Merritt (1979) concluded from the study results that intrauterine growth retardation was not uncommon and is generally underreported; that it is important to differentiate between the two main types of fetal malgrowth (low ponderal index and short-for-dates) since their pathogenesis are probably different and their prenatal and postnatal courses are definitely different. The authors support previous proposals that low ponderal index infants have a milder form of growth retardation (most exhibited "catch-up" growth within 6 months) of later pregnancy origin than that of short-for-dates infants—many of whom remained growth retarded at the end of their first year. Short-for-dates growth retardation was most closely associated with

low weight gain, short maternal stature, and smoking, and the proportion was significantly higher when any of these conditions occurred together.

Fetal growth retardation is, of course, not a disease entity, but the final result of a number of adverse conditions which determine a less than optimal growth and/or development and/or nourishment of the fetus. With the use of multi-measures of fetal growth, these studies delineate heterogeneous growth profiles in both the "normal" healthy infants, those "at risk" of dying, and those who demonstrate adverse and longterm associations with their fetal growth experience. As well, they can describe more precisely the associations between the different types of fetal growth retardation and the numerous variables affecting growth.

In comparison to such studies, there are major gaps in the currently available data with respect to assessment of fetal growth. Data for BC are limited to birthweight for gestational age. Of the 2,090 livebirths born in BC in 1983, at 25 weeks gestation or later and weighing 2,500 g or less, 608 (29.1 percent) were growth retarded (defined as $-2SD$) using Usher's and McLean's (1969) fetal growth standards; and of the approximately 6,000 livebirths weighing 2,501-3,000 g, 1.8 percent were growth retarded. Overall, 8.8 percent (715/8,080) of infants weighing 3,000 g or less, and born at 25 weeks gestation or later, were growth retarded. Both the Odense and Kansas studies found that only 30 percent of their population could meet criteria for the development of a "normal" fetal growth standard.

At present, there is no way of identifying the "normally" grown infants in the BC community.

The following is concluded from this review of fetal growth retardation: Data for the fetal growth component of a reproductive health index should include (a) the incidence of different types of fetal growth retardation—low ponderal index, short-for-dates and small head circumference; (b) fetal growth retardation-specific mortality and morbidity incidence rates; (c) variables which will enable the development of a population growth standard for normal infants born to healthy mothers with uncomplicated pregnancies; and (d) variables consistent with the use of the index as a tool for measuring effect of factors, such as maternal weight, weight gain, and lifestyle habits, on the various dimensions of fetal growth.

Birth Defects and Malformations

The study of birth defects has been characterized by a dichotomy between knowledge of many of the fundamental aspects of genetic regulation and developmental processes, and limited understanding of the mechanisms which underlie many of the developmental abnormalities that are clinically recognized. Emphasis has been given to the need to delineate specific disorders and develop appropriate diagnostic terminology as a basis for clinical management and counselling, and for the determination of incidence and prevalence between and within populations, and as a prerequisite to the study of the mechanisms of abnormal development and to the collection of epidemiological information.

This emphasis is reflected by the fact that in most developed countries annual natality statistics include incidence data for specific, as well as general, categories of birth defects based on the system of classification recommended by WHO (1979). There is often, in addition, an ongoing surveillance system established to monitor the occurrence and prognosis of birth defects (regardless of when diagnosed) which provide accessible supplementary data.

Although information about birth defect incidence in a community is usually readily available, there are recognized problems in ensuring the data are accurate and complete. The primary data source is determined by the routine clinical examination of the newborn and is susceptible to errors of misdiagnosis, inadequate reporting, and the failure to screen the whole population. The most common problems are related to diagnostic difficulties which most often result in underreporting. Very conservative estimates are derived from hospital records and birth notices, while more accurate estimates are associated with a system of prospective standardized data collection which can allow for delays in diagnoses. Results of the Collaborative Perinatal Project (Myrianthopoulos & Chung, 1974) supported earlier observations that less than half of all major or minor malformations present at birth and diagnosed by age 1-2, were detected at birth.

To be complete, the incidence of defects and malformations in a community should cover early and late fetal deaths as well as live births—for reasons discussed earlier, this composite picture is not generally available and reporting becomes progressively less complete

from live births to stillbirths and from late to early fetal deaths. Estimates are often assumed from the results of large scale studies of spontaneous abortion.

In terms of the ability to investigate causes and the potential for prevention of birth defects, the manner in which these defects are reported is of particularly importance. Within the framework of established terminology birth defects can be reported according to classification systems which emphasize the anatomical characteristics of the defects, the period of development of the defects, or the clinical significance of the defect. This results in a lack of standardization and definition of the terms and nomenclature used in the field and diminishes the comparative value of research and study findings.

An example, given by Polani (1978), refers to anomalies—congenital defects can present as "anomalies" or in other ways such as the presence of foetal disease, perinatal illness, birth trauma, or biochemical derangement. Anomalies in turn can be "malformations" or embryopathies if they are defects originating during the period of organogenesis, or "deformations" or foetopathies if they are defects arising after completion of major organogenesis—both represent alternations in form or structure but with very different outcomes. The incidence of deformities is higher in earlier intrauterine life (approximately one-third of congenital anomalies are musculo-skeletal deformities), perinatal mortality of infants with malformations is about 40 percent compared to 5 percent with deformations, and in the latter, spontaneous

recovery or recovery with treatment is common. Recovery is rare with malformations. Other terminology may be needed to distinguish structural abnormalities which are due to delay (or error) of transition from foetal to postnatal life (e.g., undescended testis) or unusual variation in structural size or function.

"All in all," Polani (1978) concludes, "there are 3 different methods of classifying birth defects. The first is based on the clinical significance of the defect in terms of survival, handicap and correctability. A second method depends on the prenatal time at which the defect is likely to have arisen. The third depends on the cause of the defect. The simultaneous use of some or all of these guidelines of classifications may help to clarify studies on birth defects" (p. 423).

Smith (1982) recommends a method of classification for patterns of malformations which describes infants according to three clinical sub-categories: deformations; malformations (the consequence of a single localized defect in morphogenesis) which present as an anomaly (a single defect at birth) or an anomalad (multiple defects but still related to a single loci); and malformations syndromes (anomalads which are the consequence of multiple defects in morphogenesis). This type of classification is of benefit to the clinician in counselling since the recurrence risks are fairly consistent for deformities (low) and anomalies of all kinds (1-5 percent), while for syndromes the risk varies according to the specific aetiology of the particular syndrome. It also has potential as a classification system to examine causation, if differences and similarities in factors associated with anomalies/anomalads as a syndrome.

When data from the Collaborative Perinatal Project (prospective study of 54,452 pregnancies) was re-examined according to this classification system (Smith, 1982), 587 of the 1,488 infants with malformations were considered to have significant multiple malformations (incidence rate, 10.7/1,000 births). Of these, the conditions in 251 infants (43 percent) could be interpreted as the result of a single loci producing multiple defects (anomalad); in 143 (24 percent) a specific syndrome was identified, caused either by chromosomal abnormalities (74 infants, 59 with Down's Syndrome), single gene defects (24 infants), environmental (34 infants) or unknown factors (11 cases); and in 193 infants (33 percent) the pattern of malformation could not be readily interpreted. The fact that anomalads as a category were responsible for almost half of all multiple defect conditions underscores the importance of a developmental approach to classification which can support epidemiological and aetiological study.

Classification systems supporting studies of causation and prevention must also be designed to help distinguish between the role of genetic factors and environmental/lifestyle factors since few diseases or defects can be attributed entirely to one or the other, but the contributing influence can vary greatly between and within specific conditions. Most cases of severe genetic disorders are not familial. Phenomena like genetic heterogeneity, where different genes can produce apparently identical outcomes; and phenocopies, where environmental factors can produce abnormalities in the fetus which resemble known hereditary

conditions, cannot be distinguished without skilled clinical investigation (Emery, 1979).

There are many recognized causes of congenital abnormalities that include both environmental/lifestyle factors (e.g., infections such as rubella, toxoplasmosis, and cytomegalovirus; drugs such as thalidomide and alcohol; exposure to radiation; maternal disease) and genetic factors (e.g., single gene defects such as the autosomal recessive form of microcephaly; chromosome abnormalities such as the autosomal trisomy syndromes). However, the causes of 65-70 percent of developmental defects are still unknown—Childs (1978) reports the proportion of defects associated with known causes by categories: 20 percent caused by genetic transmission, 3-5 percent of chromosomal origin, and 6-9 percent caused primarily by environmental factors (radiation, <1 percent; infections, 2-3 percent; maternal metabolic conditions, 1-2 percent; 2-3 percent).

Ultimately, it is believed that the cause of developmental aberrations will be understood in terms of their association with abnormal molecular processes (the processes which operate through the medium of macromolecules and related substances to control development) since both epigenetic and environmental factors are presumedly mediated by molecular events (Epstein, 1978). Knowledge of normal biochemical processes and of their genetic control has permitted an understanding of how a genetic abnormality results in metabolic abnormalities, and of how metabolic processes (the biological element of the health field

concept) may be adversely influenced by environmental and lifestyle elements.

Recent publications underscore the importance of being able to document the relationship between environmental and lifestyle risk exposure during the preconception period and the overall occurrence of anomalies (i.e., associated with spontaneous abortion, stillbirth, and live birth) in the population (International Commission for Protection against Environmental Mutagens and Carcinogens [ICPEMC], 1983; Obe, 1984; Wynn & Wynn, 1984).

Questions of interest to this study relate to the total incidence of birth defects in the community, the proportion associated with livebirths and the timing of the insult; whether there is a difference between the population who abort or do not abort abnormal karyotypes; whether the reproductive history of women are different if their pregnancies are/are not associated with birth defects, whether available data are descriptive enough to discriminate between the influence of environmental/lifestyle element versus the biologic/genetic element on abnormal development and if so, whether there is an association between abnormal fetal development and the lifestyle of women or men.

British Columbia has established a surveillance system in the province which, through a multiple source reporting procedure and an extended ascertainment period, enables a reasonably comprehensive coverage of the occurrence of birth defects in the community. For the period 1966-1980, the average annual rate among total births for both

sexes combined was 47.3 cases per 1,000 (4.73 percent of total births); for male births was 53.1 cases per 1,000 (5.3 percent); and for females was 41.2 per 1,000 (4.1 percent). Birth defects are defined by the ICD-9 codes 740-759. The average rates among live births are slightly lower than among total births (52.5 per 1,000 male live births and 40.1 per 1,000 female live births) due to the high rate (125.4 per 1,000) of congenital anomalies reported in stillbirths (Province of B.C., 1981). The surveillance system has developed the potential for assessing factors which could contribute to the occurrence of birth defects, but lacks comparative data from a reference population and standardized assessment measures for many of the variables (e.g., lifestyle factors).

Tables 7 and 8 describe the incidence of congenital anomalies in BC for the period 1971-1980 as reported by the Division of Vital Statistics and the Health Surveillance Registry.

TABLE 7

Total Number of Livebirths and Total Number of Congenital Anomalies (ICD 740-759) and Rate per 1,000 Livebirths by Major Diagnostic Categories and for Male and Female Births in BC, 1971-1980, as Reported by Year End 1981

Major Diagnostic Categories of Congenital Anomalies	Reported Congenital Anomalies			
	Male N	Female N	Total N	R
1. Nervous System	517	461	978	26.9±2.2
2. Eye	253	246	499	13.7±1.5
3. Ear, Face & Neck	382	340	722	19.9±2.2
4. Heart & Circulatory System	2,280	2,021	4,301	118.3±7.3
5. Respiratory System	194	157	351	9.7±3.3
6. Cleft Palate & Cleft Lip	406	299	705	19.4±2.2
7. Upper Alimentary Tract & Digestive System	1,436	664	2,100	57.8±3.8
8. Genital Organs	2,476	167	2,643	72.7±6.0
9. Urinary System	506	418	924	25.4±6.4
10. Musculo-Skeletal System	5,235	3,794	7,029	193.3±14.3
11. Integument	404	418	822	22.6±6.7
12. Chromosomal Anomalies	254	251	505	13.9±1.4
13. Other & Unspecified Congenital Anomalies	152	139	291	8.0±1.3
Total Congenital Anomalies in Livebirths	12,495	9,376	21,871	601.5±20.1
Number of Livebirths in British Columbia	186,703	176,930	363,633	

Source: Province of British Columbia, Division of Vital Statistics, Health Surveillance Registry Annual Report, 1981.

TABLE 8

Major Diagnostic Categories of Congenital Anomalies
(ICD 740-759) by Incidence Rate per 10,000 Livebirths
and Proportion of all Congenital Anomalies Reported
in BC Livebirths for the period 1971-1980

Major Categories of Congenital Anomalies	Reported Congenital Anomalies in British Columbia		
	ICD-9 Code	Rate/10,000 Livebirths	% Total Anomalies
1. Nervous System	740-742	26.9	4.5
2. Eye	743	13.7	2.3
3. Ear, Face & Neck	744	19.9	3.3
4. Heart & Circulatory System	745-747	118.3	19.7
5. Respiratory System	748	9.7	1.6
6. Cleft Palate & Cleft Lip	749	19.4	3.2
7. Upper Alimentary Tract & Digestive System	750-751	57.8	9.6
8. Genital Organs	752	72.7	12.1
9. Urinary System	753	25.4	4.2
10. Musculo-Skeletal System	754-756	193.3	32.1
11. Integument	757	22.6	3.8
12. Chromosomal Anomalies	758	13.9	2.3
13. Other & Unspecified Congenital Anomalies	759	8.0	1.3

Source: Province of British Columbia, Division of Vital Statistics,
Health Surveillance Registry Annual Report, 1981.

Infant Morbidity (Longterm Growth and Development)

While infant mortality will always remain of major concern because of the human suffering involved and the loss of productivity to the community, of equal if not greater importance is the impact on the individual, family, and community of survival accompanied by disability—the more severe the disability, the higher the cost in human and economic terms.

For the most part, morbidity is now concerned with disorders of growth and development, such as those associated with malformations, intrauterine growth retardation, short gestation and neoplasms, rather than the acute infections of year's past. Many more infants now survive major insults of perinatal origin and require extra support from medical and community services for continued survival and/or to minimize their handicaps. Continuing attention must be directed toward whether reductions in perinatal mortality are accompanied by similar reductions in morbidity, or since the increased survival rate includes children with birth defects (e.g., Down's Syndrome) and, thus, increases the prevalence of these disorders in the community, whether such increases are offset by the reduction of other preventable disorders. To assess the magnitude of these problems and to monitor any change in their incidence or prevalence in the community requires good morbidity data. Vohr and Hack (1982), in a review of developmental follow-up of low birthweight infants, state that very low birthweight (<1,500 g) continues to be an important factor in development of subsequent handicap in the

1980s, with risk of sequelae inversely related to birthweight. Short term results are often more optimistic than followup of longer duration which report an increased incidence of intellectual handicap and learning difficulties even in infants without major sequelae. The paper outlines the potential risk factors to be considered and the type of followup schedules and evaluation procedures that are needed to monitor quality of outcome beyond survival. A systematic infant surveillance system has not been established in British Columbia. The Infant Monitoring Program of the Calgary Health Services (1984) provides an excellent working example of such a system.

It is even more difficult to determine and interpret morbidity data than many other reproductive health outcomes. For example, the distinction between health and illness is much less objective than between life and death or birthweight categories; diagnostic standards vary much more for non-fatal compared to fatal illnesses since pathological changes are less extreme in the former and less easily confirmed; and morbidity is more difficult to summarize since it has different lengths of duration, can occur more than once to the same individual and can take many forms (Leck, 1974).

One method of obtaining morbidity data is through the use of health service contacts such as hospital discharge by cause reports. These data measure the frequency of an event in the population but because the same individual may be admitted more than once during the study period, they may require a supplementary survey to determine the frequency and duration of hospitalization, and type of health problem

experienced by a particular group of individuals. Prevalence or bed occupancy rates are more useful than incidence or discharge rates in determining the burden of the illnesses on the health care services. The illness incidence, however, is the more important in studying causal associations, or in assessing the effects of intervention. Hospital data are always biased in favor of what is currently available in terms of type and numbers of beds. Given the appropriate reporting system, a similar method for determining frequency of physician contact (other than for routine checkup), of need for prescription drugs, and/or the use of special community services (i.e., infant development program) might be used to measure morbidity by determining the size of the "affected" group.

A second method of obtaining morbidity data is by screening whole populations through routine or special surveys. Routine screening is carried out in most communities at birth, at the beginning and end of school life and often screening of intellectual ability is carried out some time during school years—some countries have instituted routine preschool screening. Data from routine screening are usually limited to quantitative variables such as weight, height, intelligence quotient, and the determination of lasting disabilities such as malformations and impaired hearing or vision. The main advantage of screening data is that knowledge is gained about the entire population and the proportion and distribution of disorders within it. The reason for routine screening is generally to detect unrecognized health problems at an opportune time for preventive treatment. Screening, as well as

health service contacts, can be biased by misdiagnoses, by inadequate reporting and by some individuals being excluded.

Special surveys of particular types of morbidity are likely to be either cross-sectional (retrospective or case-history) or longitudinal (prospective or cohort) studies. Problems associated with these surveys include inadequate reporting by parents of the study children and inadequate followup of the survey population if families move or are unwilling to participate.

With particular reference to morbidity of children of low birthweight or preterm birth, and the measurement of the frequency of related problems in later years, Leck (1974) identifies three areas of bias: (a) sources of inaccuracy of the measurement recorded (i.e., single measures, rounding-off); (b) the heterogeneity of the conditions which an abnormal measurement may reflect; and (c) the artificiality of classifying individuals into normal and abnormal on the basis of a fixed threshold.

Murphy, Nichter, and Liden (1982) review a number of different methodological issues in infant development outcome studies. Factors which make this type of research difficult include: limited knowledge of "normal" human development; the lack of distinction between delayed development, specific developmental disorders and functional deficits; the problem in separating transient from longterm outcomes; and the changing nature of the high-risk population over the past 20 years. The final set of problems involve quality of assessment in terms of

the stability of developmental examinations, the comprehensiveness of assessment batteries, and serial observations of the children.

With the many inherent problems of longitudinal and developmental studies, it is not surprising that very few special surveys are carried out and even fewer provide solid evidence of longterm perinatal effects except at the extremes.

An exceptional study chosen for review in this section was reported by Neligan and colleagues (1976) and is important because the results can be generalized to other populations and because the infants studied were of moderate rather than high risk. The results are, therefore, applicable to the large number of infants who are low weight or preterm.

Neligan and colleagues outline the special features which characterize the study:

1. The population studied was selected specifically for the purpose of comparing a group of children who had been born too soon and a group who had been born too small, both with each other and with a suitable comparison group, in terms of many aspects of their later performance during school years. The groups represented the two abnormalities of intrauterine growth which account for low birthweight and which present clinicians with different practical problems.

2. The two abnormal groups and the comparison group were selected from a larger, geographically defined population for whom standardized obstetric, paediatric, and social data were available through the Newcastle Survey of Child Development (Neligan, Prudham, & Steiner, 1974). The selection was, therefore, free of the biases due to medical,

social or personal factors which so often prevent generalization of study results.

3. The methods of assessment were sufficiently sophisticated, comprehensive, and specific to detect very minor differences between individual children over a very wide range of measures of performance, and care was taken so that results could be quantified in terms of continuous variables.

4. The methods of statistical analysis enabled identification of the specific and independent effects of the two abnormalities of intrauterine growth, after allowing for a large number of associated and potentially confounding factors, and to compare the magnitude of the effects of these factors.

The study population consisted of a randomly selected comparison group of 187 five year old children from amongst one year of births of the Newcastle Survey group; 141 children whose birthweight was below the 10th percentile for gestational age which were separated into two groups—birthweight between the 5th and 10th percentiles and birthweight on or below the 5th percentile ($n = 74$); and 59 children who were born at less than 37 weeks gestation. The groups were studied at 5, 6, and 7 years of age using a wide range of specific psychometric, behavioral and temperamental, neurological and physical growth assessments against a known background of biological and social variables. After careful analysis of the results, the authors came to the following conclusions:

1. Both the short-gestation and the very light-for-dates groups

of children performed significantly less well than those in the random sample over the whole range of measures of performance at ages 5, 6, and 7 years. This conclusion was not altered by the effects of 15 associated factors.

2. The suggestion that prenatal impairment of growth may be directly responsible for the later impairment of performance is strongly supported by the findings—the scores from the rather light-for-dates group (mean birthweight of 2,701 g) were almost always intermediate between those of the very light-for-dates (mean birthweight 2,397 g) and the random controls for both over-all scores and individual subtests. Birthweight made an important contribution to the over-all performance scores of the children within all groups including the random sample and short-gestation groups.

3. The over-all performance of the children in the very light-for-dates group is significantly worse than the short-gestation group. In the study population, impairment of the net rate of intrauterine growth had a direct adverse effect upon the later performance of the children which was greater than the effect of a comparable degree of shortening of its duration.

4. The effects of some of the associated factors (e.g., social class, mother's care, mother's expectations) which were investigated appear to be of much greater magnitude than those of the variables in intrauterine growth and their relative importance tends to differ in the different groups.

5. The impaired performance of the children in the two extreme abnormal groups persists with very little modification after the effects of six biological, clinical, and environmental associated factors have been allowed for.

6. The associated factors grouped under the heading of "family factors" (in particular, social class and mother's care of child) were of overriding importance in the random sample and very light-for-dates group: biological and clinical factors combine to produce effects of almost equal importance in the short gestation group.

Due to the careful design and implementation of this study, Neligan and colleagues have provided sound evidence that both children who are born too soon and those who are born too small show some impairment of performance when they reach school age—those born too small are at a greater disadvantage and seem less likely to benefit from recent advances in paediatric care, whereas those born too soon seem able to benefit from adequate nutrition and care in the postnatal period. The adverse effects attributable to the two disorders of intrauterine growth (representing 10 percent of the total study population) cover a wide range of measures of performance and are of a similar pattern in both groups. These groups seem particularly vulnerable to other biological, clinical, and social factors which may also have adverse effects.

This study reinforces the need for an index of reproductive health that will identify the proportion of infants at risk for longterm developmental impairment; that will provide a tool to measure the

effect of factors on fetal growth and ultimately help to determine intervention strategies which can reduce the preventable portion of fetal growth complications.

Summary

In summary, this chapter has reviewed the key outcome measures of reproductive and infant health; the problems of accurate measurement; the outcome data available for British Columbia; and the type of data required for the development of an overall index of reproductive health which would reflect the association between the different outcomes in the community and provide support for surveillance and intervention strategies. This information will be further summarized in chapters four and five.

CHAPTER III: THE EFFECT OF LIFESTYLE ON REPRODUCTIVE HEALTH

Chapter two began with the proposition that the extent to which a population encounters problems producing healthy, living infants is influenced to varying degrees by each of the four elements of the health field concept—human biology, environment, health care organization, and lifestyle. The chapter then reviewed the outcome measures which are used to document the reproductive casualties occurring in a population, the problems associated with this documentation, and whether the available information was comprehensive enough to allow for the assessment of the impact of the lifestyle element on these outcomes.

This chapter examines the extent to which these outcome measures might be affected by lifestyle. The purpose of the chapter is to review the evidence that lifestyle factors do affect reproductive outcome and to examine what proportion and to what degree might the population be affected. Where data are available, the prevalence of these lifestyle factors in the BC population of childbearing years will be reported.

The focus of the review will be to determine what type of an effect, if any, a lifestyle factor has on reproductive outcome—i.e., whether there is a growth retarding influence and if this is associated with increased mortality and/or morbidity; whether there is an associated teratogenic, mutagenic, abortifacient, or fetotoxic influence;

whether the effect varies with early or late pregnancy exposure; and whether the impact can be measured across all the reproductive outcome measures or only a select number. In the next chapter, the issue of "cause and effect" will be examined in detail.

Only the literature concerning the effect of smoking (tobacco and cannabis), nutrition and diet, and alcohol on reproductive health will be reported in this study. An equally substantial set of literature on the relationship between reproductive health outcomes and exposure to drugs, chemicals and other toxins, and to physical and psychological stress could have been reviewed. Given limitations of space, it was decided that a comprehensive assessment of a representative group of lifestyle factors was preferable to a less comprehensive review of all. For the same reason, a representative set of studies for each of the three lifestyle factors and seven reproductive outcome measures were selected for discussion—these highlight human population studies with reference to associated animal, metabolic, and cell culture studies.

Smoking and Reproductive Health

It is about 50 years since clinicians first warned of the detrimental effects of smoking on reproductive health. Human and animal research linked maternal exposure to tobacco with increased stillbirth and decreased birthweight (Bernard, 1948; Essenberg, Schwind, & Patras, 1940; Schoeneck, 1941; Sontag & Wallace, 1935).

Over the past 40 years, an extraordinary amount of research has been conducted in the area. Comprehensive literature reviews have

been published (Abel, 1980; Landesman-Dwyer & Emanuel, 1979; Sidle, 1982; US Public Health Service, 1972, 1980; Wynn & Wynn, 1981) which provide structure to the assessment of the strength of association between smoking and reproductive health, mechanisms of action, and interactions with other lifestyle and demographic risk factor variables.

One of the most recent and comprehensive reports on the health consequences of smoking during the reproductive period, based on a critical review of the literature by basic scientists and clinicians, was published as a report of the US Surgeon General in 1979 (US Public Health Service, 1980). This report summarized the evidence of the adverse effect of smoking on reproductive outcome measures in the following way:

A. The effect on fetal growth. Babies born to women who smoke during pregnancy are, on the average, 200 g lighter than babies born to comparable nonsmoking women. There is a dose-response relationship between maternal smoking and reduced birthweight: the more the woman smokes during pregnancy, the greater the reduction in birthweight. If a woman gives up smoking early during pregnancy, her risk of delivering a low birthweight baby approaches that of a nonsmoker. The pattern of fetal growth retardation that occurs with maternal smoking is a decrease in all parameters including body length, chest circumference, and head circumference.

The relationship between maternal smoking and reduced birthweight is independent of all other factors that influence birthweight including

race, parity, maternal size, socioeconomic status, and sex of child; it is also independent of gestational age. Maternal smoking during pregnancy exerts a direct growth-retarding effect on the fetus which does not appear to be mediated by reduced maternal appetite, eating, or weight gain.

The ratio of placental weight to birthweight increases with increasing levels of maternal smoking, reflecting a considerable decrease in mean birthweight and a slight increase in mean placental mass; this may represent an adaptation to relative fetal hypoxia.

B. The effect on fetal/infant mortality and morbidity. The risk of spontaneous abortion, fetal death, and neonatal death increases directly with increasing levels of maternal smoking during pregnancy; interaction of maternal smoking with other factors which increase perinatal mortality may result in an even greater risk. Excess deaths of smokers' infants are found mainly in the coded cause categories of "unknown" and "anoxia" for fetal deaths, and the categories of "prematurity alone" (defined by birthweight) and "respiratory difficulty" for neonatal deaths; suggesting that the excess deaths are due to problems of the pregnancy, rather than to abnormalities of the fetus or neonate.

Although there is little effect of maternal smoking on mean length of gestation, the proportion of fetal deaths and live births that occur before term increases directly with maternal smoking level. Up to 14 percent of all preterm deliveries in the US may be attributable to maternal smoking.

Increasing levels of maternal smoking result in a highly significant increase in the risk of abruptio placentae, placenta previa, bleeding early or late in pregnancy, premature and prolonged rupture of membranes, and preterm delivery—all of which carry high risks of perinatal loss.

Maternal smoking during pregnancy may adversely affect the child's long-term growth, intellectual development, and behavioral characteristics. An infant's risk of developing the "sudden infant death syndrome" is increased by maternal smoking during pregnancy. Infants and children born to smoking mothers may experience more long-term morbidity than those born to nonsmoking mothers; however, studies usually cannot distinguish between the effects of smoking during pregnancy and the effects of the infant's or child's passive exposure to cigarette smoke after birth.

C. Effect on birth defects. There are insufficient data to determine whether maternal and/or paternal cigarette smoking increases the risk of congenital malformations.

D. Effect on other reproductive outcome measures. Studies in women and men suggest that cigarette smoking may impair fertility.

While it may be fair to assume that this is an appropriate representation of the evidence to 1979, this report, along with most other reviews of the literature in this field, does not provide a review of the design, implementation, and statistical analysis of the referenced studies and, thereby, does not allow the reader to weigh the evidence provided. Since evidence from large, prospective cohort

studies with carefully documented levels of exposure would provide the most convincing results, a selected review of these studies is reported.

Smoking in pregnancy has a dual effect on the mother and fetus—it is difficult to evaluate the effect of smoking on the fetus, and equally as difficult to evaluate the effect of smoking on the mother and her reproductive capability. Butler (1975), in an address to the Third World Conference on Smoking and Health, summarized these difficulties well. He stated:

First, in the majority of studies, smoking habits in pregnancy were inquired about after delivery and were, therefore, subject to fallacies of memory. Second, smoking is not a constant phenomenon, as women may begin to smoke or give up smoking during pregnancy, and there may be frequent changes in the number of cigarettes smoked. Third, there are differences in degree of inhalation and in type of tobacco smoked. Fourth and perhaps most important, different types of women have different smoking habits. Smoking habits will differ with social background, parity and even with the height of the mother. Some obstetric conditions may occur more often in women who smoke than in women who don't smoke. The changing components of smoking and also the effect of other sociobiological influences may completely obscure the pattern and effects. Special techniques of analysis and statistical treatment can be used to exclude the effects of other variables which could affect birthweight, perinatal mortality or even child development, where these data are available. It has also been difficult to correlate the clinical situation with experimental findings. A great deal of work has been done with animals . . . but it must be remembered that the experimental animal is not the same as a pregnant human female. (pp. 43-44)

Fertility

Many studies suggest that smoking exerts an adverse effect on fertility for both women and men (US Public Health Service, 1980). There are many ways that fertility can be affected and, in the case of smoking, the following associations have been reported: a reduction

in years of fertility for women through early onset of menopause; a reduction in level of fertility through impaired spermatogenesis in men and increased prevalence of menstrual disorder in women, and a delayed return of fertility after discontinuation of contraception.

Two studies are selected to examine the association between smoking and early onset of menopause. Willett and colleagues (1983) prospectively evaluated the experience of 66,663 female registered US nurses who were pre-menopausal in 1976 and the 5,004 women who became post-menopausal over the following two years. Data were collected by mail questionnaire. Of the 121,964 original study participants, 78,678 were pre-menopausal and received a questionnaire two years later. Of this group, 89 percent (69,906) responded, 2,887 were post-menopausal for surgical or therapeutic reasons, 356 did not report menopausal status, leaving a sample size of 66,663 women. Analysis was carried out according to four age groups, three smoking classifications and four levels of smoking, two "weight for height" classifications and five quintiles of relative weight. Within sample followup suggested accurate reporting of menopausal and relative weight status. Thirty-one percent of the sample were current smokers which is similar to the estimate of 32 percent as the prevalence of regular cigarette smoking among US women in 1976 (US, Department of Health Education & Welfare, 1977).

Independent effects of current smoking, number of cigarettes smoked daily, relative weight and nulliparity were confirmed by multiple

logistic regression analysis. The rate ratios of menopause for current smokers versus never smokers (95 percent confidence limits) 1.90 (1.10-3.28) for women between 30-39 years, 2.16 (1.73-2.69) for 40-44 year olds, 1.53 (1.41-1.67) for those aged 45-49 and 1.20 (1.12-1.28) for women aged 50-55 years. Median ages at menopause by level of smoking were 52.4 for never smokers, 51.9 for those smoking 1-14 cigarettes per day, 51.0 for 15-24 cigarettes/day smokers, 50.7 for those smoking 25-34 per day, and 50.4 for women smoking 35 or more cigarettes per day. Any significant relationship between earlier menopause and ex-smokers was confined to those who had quit within the past two years. After adjustment for current cigarette exposure, a weak linear relationship between relative weight and menopause remained among women who smoked but not among nonsmokers. Extremes of underweight were not seen in the study population. The potential effect of a non-response bias was not discussed in this paper but careful consideration was given to potential confounding by other variables.

The relation of cigarette smoking to natural menopause was also evaluated by Jick, Porter, and Morrison (1977) in a retrospective cross-sectional survey of two independent groups. Women between the ages of 44-53 years who were hospitalized for medical or surgical reasons were interviewed—one group of 3,076 women being derived from a survey of 25,000 hospital patients from 24 Boston-area hospitals and the other group of 2,479 women from 32,000 inpatients in seven countries participating in the Boston Collaborative Drug Surveillance Program. It is not clear that all eligible women aged 44-55 years

were interviewed. After exclusion of those with a history of surgical menopause, analysis included data from 2,143 women for group I and from 1,391 women for group II—no discussion of the differences between the study women and those excluded for lack of information was presented. Three smoking classifications, two smoking levels, and five age group classifications were used for analysis. Data were examined for confounding by variables other than age and smoking (e.g., medical versus surgical admission, diagnosis, parity, alcohol intake). Results showed a progressive rise in the proportion of women who were post-menopausal in all age categories except the youngest (44-45 years) according to amount smoked. The association between smoking and natural menopause was consistent in each of the seven countries contributing to study II. For the group of women from Boston, the age-standardized proportions who were post-menopausal by smoking classification were 35 percent, 36 percent, 43 percent, and 49 percent, respectively, for never smokers, ex-smokers (>1 year), and current smokers of one-half pack cigarettes per day or one pack or more per day. Corresponding proportions for the group II women were considerably higher at 53 percent, 59 percent, 60 percent, and 65 percent.

The consistency of a difference between the menopause experience of nonsmokers and current smokers seen in these two studies and others studying different population samples (Bailey, Robinson, & Vessey, 1977; Lindquist & Bengtsson, 1979), and the demonstration of a dose-response relationship provides good reason to assume the association

between smoking and early menopause is valid. These results are pertinent to a number of public health issues, but, for this study, they serve as an example of the effect of smoking on the female reproductive system per se (as compared to an effect on fetal growth) and provide reason to speculate that smoking may be a contributing factor to a range of reproductive problems.

The retrospective case-control study of Olsen and colleagues (1983) provides another example. In this study, the association between tobacco use, alcohol consumption, and subfecundity was investigated in couples who were examined or treated for an infertility problem at Odense University Hospital and couples who had a healthy child born at the hospital within the same time period (1977-1980). Since hospital policy required hospital admittance for infertility work-up, all eligible couples (infertile, fertile with healthy child, no indication of chronic disease) could be identified from the hospital registry. Data were collected by self-administered mailed questionnaires and, for all infertile cases, enhanced by information from hospital records. A response rate of 87 percent for each group was reported providing 927 case and 3,728 control couples. Analysis involved two classifications of smoking (yes/no), and four categories of alcohol consumption (by grams of pure alcohol) during the time of hospital admission. Three different analytical approaches were used as a way to address methodological problems—between group comparison of infertile and fertile couples, within-group comparison of infertile couples, and within-group comparison of fertile couples. Odds ratios

for estimating the relative risk of smoking and alcohol consumption are adjusted for the effects of parity, age, residence, education, and oral contraceptive use.

A positive association between smoking and primary and secondary subfecundity (OR:1.6, CI:1.1-2.2; OR:2.1, CI:1.3-3.6, respectively) in the between group comparison of cases and controls was supported by a positive association between smoking and delayed conception of at least one year within the control group—delayed conception in a past pregnancy (OR:1.6, 1.3-2.0), in present pregnancy (OR:1.5, 1.2-3.0), and in both past and present pregnancies (OR:2.0, 1.4-2.8). The odds ratio for all cases compared to controls for smoking (OR:2.1, CI:1.7-2.5) and alcohol consumption (OR:1.6, CI:1.2-2.1) was similar to the odds ratio for the subgroup of cases excluding couples with a diagnosed male fertility problem compared to controls—for smoking this was 2.3 (1.8-2.9) and for alcohol consumption, 1.7 (1.3-2.4).

Methodological problems were reviewed in the study: selection bias which might affect case-control comparison was unlikely to affect within-control analysis; non response bias and reporting/selective memory bias would be less likely to affect within group analysis. The reduction in use of tobacco and alcohol during pregnancy is a very real possibility in the pregnant control group, but does not affect the significant positive association between smoking and delayed conception within the control group. In general, results which are supported by both between and within group analysis provide reasonable evidence of real association. The evidence for an association between

smoking and infertility/conception delay was consistent and suggests a real association whereas the association between alcohol consumption and infertility is not fully supported.

Community health surveys (cross-sectional retrospective studies) in the US (Sloss & Frerichs, 1983), Australia (Wood, 1978), and Finland (Kaureniemi, 1969) show an association between smoking and the prevalence of menstrual disorders for which a woman sought medical attention (e.g., dysmenorrhoea and menstrual irregularity). These studies have not ruled out a spurious association with low body weight or low percent body fat and face the common problems of response and memory bias in retrospective studies. Nevertheless, menstrual disorders are of sufficient significance in the population (Kistner, 1979) that a preventable association is worth examining further. Smoking appears to have an affect on the reproductive system of men as well as women, an association supported by animal and biological studies (US Public Health Service, 1980).

Given the range of studies reporting an adverse association between smoking and reproductive health, albeit of varying weights in terms of strength of evidence, it is difficult not to speculate that the association is real and pervasive. The extent of many of these potential problems cannot yet be estimated.

Spontaneous Abortion

Problems of ascertainment in measuring the incidence of spontaneous abortions have been discussed in chapter two. Retrospective studies are more likely to allow for complete ascertainment but are subject to

errors of recall, while prospective studies may introduce bias if groups do not enter the study at comparative times since the early abortions may be missed. While there are a number of studies of both types which report an excess of spontaneous abortions associated with smoking (Downing & Chapman, 1966; Himmelberger, Brown, & Cohen, 1978; O'Lane, 1963; Underwood et al., 1965; Zabriskie, 1963), few provide a basis for sound estimates of risk.

A prospective study on the effect of smoking on pregnancy (Kullander & Kallen, 1971) obtained data on smoking habits throughout 6,363 pregnancies via self-administered questionnaires completed at each subsequent prenatal visit to the physician from diagnosis of pregnancy. Forty-four percent of the women (2,806) smoked during their pregnancy—almost all of these smoked during the entire pregnancy (97 percent), only 20 percent smoked more than 10 cigarettes per day and 1 percent more than 20 per day. The women whose pregnancies ended in spontaneous abortions (<28 weeks gestation) were more likely to be smokers (51.0 percent) than those who delivered a live healthy child (43.3 percent) ($\chi^2 = 12.5$, $p < 0.001$). The observation of the effect of smoking on spontaneous abortion showed no difference in smoking habits of women aborting during the second or third gestational month but after this time, an increasing proportion of women who aborted at each subsequent gestational month were smokers. Graphs (mean percentage smoking, standard error) illustrating these results were not accompanied by data on numbers of spontaneous abortions. A later study of 5,272

women from the same community (Persson et al., 1978) did not confirm an association between smoking and spontaneous abortion.

Kline and colleagues (1977) sought to provide estimates of risk in a case-control study of cigarette smoking during pregnancy among 574 women who aborted spontaneously (cases) and 320 women who delivered live infants after 29 weeks gestation (controls). Cases were derived from a consecutive series of women between the ages of 18-40 years hospitalized for spontaneous abortions at any of three Manhattan hospitals (82 percent of 703 eligible cases agreed to participate). Controls were selected from women attending public prenatal clinics of the same hospitals prior to 22 weeks gestation and matched within two years of age (86 percent of controls selected for 371 cases consented to interview). Non-respondents were reported to be similar to participants, cases and controls were found to be comparable. Previous reproductive history was not discussed in the report. Analysis controlled for age (3 age groups), number of previous spontaneous abortions (3 classifications), induced abortions (2 classifications), and number of previous live births (3 classifications) and examined the association of smoking according to three categories (none, 1-19 cigarettes/day, 20+/day). Analysis did not include the potential effect of different levels of smoking in the non-respondents.

Study women who aborted spontaneously reported smoking during pregnancy more often than those who delivered a livebirth after 28 weeks gestation: 41 percent of cases and 28 percent of controls

smoked. The odds ratio for the highly significant association with smoking ($X^2 = 19.4$, $p < 0.001$) was 1.8 (1.3-2.5). The association of spontaneous abortion with smoking is similar in all age groups and for obstetric history. This study provides the best available estimate of risk.

Fetal Growth, Mortality and Morbidity

Of the many epidemiologic studies of smoking and pregnancy over the last three decades, all have shown that pregnant women who smoke have babies of lower birthweights than comparable women who do not smoke and many have demonstrated a dose-response relationship—on average, smokers' infants are 150-250 g lighter and are twice as likely to weigh less than 2,500 g. In populations where 34-54 percent of mothers smoked during pregnancy, from 21-39 percent of the incidence of low birthweight could be attributed to maternal smoking (AR:1.64-2.21) (Andrews & McGarry, 1972; Butler & Alberman, 1969; Fabia, 1973; Meyer, Jonas, & Tonascia, 1976; Niswander & Gordon, 1972).

Given that there is universal agreement about a smoking effect on birthweight, it seems appropriate to proceed from this point to examine the implications of the birthweight effect on aspects of fetal survival, growth and development, and to examine the possible interaction between smoking and other fetal growth retarding factors.

The study by Andrews and McGarry (1972) of the pregnancies of all women in the city of Cardiff between 1965 and 1968 was designed to avoid errors due to sampling and small numbers. Obstetric and social

data were recorded for the 18,631 pregnancies. Information on smoking habits was unfortunately not documented until the postpartum period and the authors suggest this may have resulted in a conservative estimate of cigarettes smoked for some pregnancies. The study results confirm the consistent weight reduction among infants born to smoking mothers (average 170 g, singletons); an increased proportion of low birthweight infants (10.4 percent among smokers, 6.1 percent among nonsmokers); and a dose-response effect on birthweight with average weight for infants of ex-smokers (quit before or during first trimester) between that of nonsmokers and light smokers—there was a progressive fall in average birthweight of infants and increase in low birthweight percentage with number of cigarettes (4 categories) smoked by the mother. Smokers had an increased proportion of preterm births (9.2 percent versus 6.7 percent; $X^2 = 28.2$, $p < 0.001$). Birthweight was adversely affected by other factors such as social class, presence of anaemia, low maternal weight, age and parity, but in all cases, smoking exhibited an additional independent effect.

The study results show a decrease in perinatal mortality among low birthweight infants born to smokers but an overall small and significant increase in mortality of infants of smoking mothers (3.1/1,000 versus 2.5/1,000) associated with antepartum hemorrhage, with stillbirths and pneumonia, respiratory distress syndrome and immaturity with neonatal deaths. The incidence of congenital anomalies, with the exception of cleft lip and palate, was not significantly

associated with maternal smoking. The incidence of hypertension and pre-eclamptic toxæmia was reduced in pregnancies of smoking women.

The prospective cohort study of Kullander and Kallen (1971), described in the discussion on smoking and spontaneous abortion, also reported increased mortality among infants of smoking mothers as well as reduced birthweight and increased proportion of low birthweight infants. All fetal growth dimensions—body length, head circumference, and shoulder circumference—and placental weights decreased with increases in amount smoked, while the placental weight/body weight ratio increased.

Excess mortality related to smoking was more likely to occur in infants of birthweights greater than (not less than) 2,500 g and to occur after the first week of life (RR:2.7). By the end of the first year, 1.9 percent of infants born to nonsmoking mothers had died, whereas 3 percent of those born to smoking mothers had died (RR:1.6).

In 1975, Goujard, Rumeau, and Schwartz reported on a study of maternal smoking and stillbirth using data from the 100 stillbirths which occurred to 9,169 women who were participating in the prospective study of pregnancies and births in 13 Paris maternity hospitals in the mid-sixties. The study showed a substantial increase in stillbirths among smokers—the rates per thousand of still-born for the study population were 23.3 among smokers and 9.2 among nonsmokers ($p < 0.001$; RR:2.5), with the highest incidence occurring to high parity (4+) smokers. Stillbirths according to cause were significantly related

to smoking during pregnancy in two categories: abruptio placentae (smoking proportion:46 percent, $p<0.0005$), which represented 13 percent of stillbirths, and "unknown" cause (smoking proportion:35 percent, $p<0.0005$) which represented 37 percent of the stillbirths. Study analysis does not rule out interactions with other factors (in addition to parity) important to outcome.

A smoking-related increase in mortality has not been reported by all studies and it has been suggested that this may be due to problems of sample selection, size, and methods of analysis (Butler et al., 1977; Meyer & Comstock, 1972). Meyer, Tonascia, and Buck (1975) suggest that the failure of some studies to find a significant increase in perinatal mortality may be due to selection of low risk study populations where light smoking is associated with only a slight increase in perinatal risk, whereas other studies may select higher risk populations where the influence of smoking on mortality is stronger. The significance of the results will depend on the magnitude of the difference, the amount smoked, and the size of the study.

Data from the Ontario Perinatal Mortality Study (Ontario, Department of Health, 1967) which collected information on antecedent, prenatal, and perinatal factors and events from all single births in ten teaching hospitals in Ontario during 1960-1961 was selected as an appropriate sample to evaluate further the association between smoking and fetal/infant mortality (Meyer, Tonascia, & Buck, 1975; Meyer, Jonas, & Tonascia, 1976). A total of 51,490 births, including 701 fetal deaths and 655 neonatal deaths are recorded. The original purpose of

the study was to obtain information concerning the causes of perinatal loss. Interviews with the mother, which included information regarding the maximum number of cigarettes smoked during pregnancy, were conducted in the early postpartum period. During this same period obstetrical/medical information was confirmed with attending physicians.

For analysis, three levels of smoking frequency were established (none, less than one pack/day, one or more pack/day) for nine population subgroups (37 subgroup categories) and five outcome measures were used. Binary variable multiple regression analysis provided for simultaneous adjustment of outcome rates for multiple factors important to outcome and unevenly distributed among smoking-level groups. Smoking information was available for 98 percent of study participants—57 percent were nonsmokers, 30 percent less than one package of cigarettes per day, and 13 percent smoked at least a pack per day.

Significant smoking-related increases in percent low birthweight, and preterm births; placenta previa, abruptio placentae, and perinatal mortality were found, independent of mother's height, weight, hospital status, age-parity group, birthplace, previous pregnancy history, weight gain, time of registration, and sex of child. Maternal smoking had the strongest effect on birthweight in the 8 factor regression (weight gain excluded), and percent low birthweight increased directly with smoking level from 20 percent to 340 percent in the 37 data subgroups. Preterm births of less than 38 weeks increased 20 percent and 50 percent and perinatal mortality, 20 percent and 35 percent for infants of less than one pack/day and one or more pack/day smokers,

after adjustment. Placental complications increased consistently with smoking level in all but one of 37 data subgroups—adjusted rates for placenta previa increased to 25 percent and 92 percent; abruptio placentae, 23 percent and 86 percent for the two levels of smoking compared to rates for nonsmokers. These placental complications accounted for one-third to one-half the perinatal deaths attributable to smoking.

Relative [RR] and attributable risks [AR] for smoking compared to nonsmoking outcomes were reported as follows: birthweight under 2,500 g, RR:2.02, AR:31 percent; preterm birth, RR:1.36, AR:14 percent; perinatal mortality, RR:1.27, AR:10.5 percent; placental complications, RR:1.43, AR:16 percent. Confidence intervals for relative risk were not reported analysis. Apart from the aspect of risk estimates for smoking, these analyses of the Ontario data show that in each case where a maternal risk factor was related to poor reproductive outcome, smoking increased the probability of poor outcome occurring.

Data from the Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke, a large prospective study of pregnancy carried out in the United States, also confirms an association between smoking and fetal and neonatal deaths that varies with maternal risk status (Niswander & Gordon, 1972). This study followed the course of 53,518 pregnancies in 12 hospitals affiliated with US medical schools between 1959-1966 and recorded events of gestation, labor, delivery, and the neonatal period.

As in the Ontario study, maternal smoking was associated with particular causes of fetal and infant death.

Naeye, Harkness, and Utts (1977) analyzed factors that might be involved in abruptio placentae using the data from the Collaborative Project. The perinatal mortality rate due to abruptio placentae was 3.96/1,000 births and was the second most frequent cause of perinatal death in the study population. After the first trimester of pregnancy, enough information was available for 86 percent of deaths to provide a primary diagnosis regarding the disorder initiating death. Of the 3,987 deaths reported, 138 stillbirths and 74 postnatal deaths were attributed to abruptio placentae—the disorder had peak frequencies between 20–29 weeks and after 38 weeks of gestation. From over 1,000 demographic, hereditary, social, medical, and postmortem variables analyzed in the study, the variables which had a significant influence on the frequency of fatal cases of abruptio placentae without having significant interactions with other variables were found to be: seizures by gravida, low hemoglobin, low pregnancy weight gain, number of cigarettes smoked per day, intrapartum hypertension, sex of infant, number of previous abortions, number of prior perinatal deaths, and number of prior preterm deliveries. Decidual necrosis at the placental margin and large placental infarcts were the most characteristic placental abnormalities in fatal abruptio placentae cases. Decidual necrosis was seen twice as frequently in women of very low pregnancy weight gain (<10 lb) than with those who had gained more than 19 lb, and was most common in the heaviest smokers. The association with

smoking was greatest at the lower gestational ages, and in pregnancies where the mother had a low weight gain, was anemic or had a history of prior unsuccessful pregnancies. A relationship between smoking and large placental infarcts occurred only with women who had a history of prior spontaneous abortion. Normal pregnancies also had a positive correlation between smoking and/or low weight gain and decidual necrosis at the margin of the placenta and smoking and placental infarcts. The fetuses and neonates who died following abruptio placentae had a pattern of growth retardation characteristic of antenatal undernutrition, however, no information is available on growth patterns of infants who did not die where the placenta was characterized by decidual necrosis or infarcts. The results from this study emphasize the importance of recognizing that lifestyle factors may be influential in determining cause-specific fetal or infant mortality rates. Moreover, they emphasize that these effects may go unrecognized in situations where only general mortality rates are investigated, where key maternal risk variables are not reported or reviewed, and where diagnosis of death does not reflect the disorder that initiated the cause of death.

Further to this study, Naeye (1979) found that in the three placental conditions most influenced by smoking and related to poor outcome—placenta previa, abruptio placentae, and large placental infarcts—the frequency of the disorders were influenced by both the numbers of years mothers had smoked (increased frequency with duration of over 6 years) and their current smoking habits. The same

Collaborative data were used to look at past and present smoking habits on birthweight (Wainright, 1983) in the group of 319 white women who changed smoking patterns between two consecutive pregnancies (cases) and 319 women who did not report a change (controls). Pairs were matched by birthweight of their first infant (reproductive potential), age, sex of infant, parity and time interval between pregnancies. The infants of women who started smoking in their second pregnancy, weighed less (not statistically significant) on average than the infants of their nonsmoking control pair or their previous infants. The infants of women who stopped smoking prior to the second study birth were significantly heavier (average, 171 g; $p < 0.01$) than infants of controls who continued to smoke. These study results, and those of a similar study by Silverman (1977) suggest the birthweight deficit between consecutive pregnancies is greater when smoking was continued over the two pregnancies than when smoking began just prior to the second and that a smoking duration effect on birthweight should not be discounted.

Another example of specific "cause of death" investigation showing smoking during pregnancy to be a mortality-related factor comes from attempts to understand the etiology of the Sudden Infant Death Syndrome [SIDS]. While there is much still to be learned about this syndrome, studies that have reported on both maternal smoking habits and SIDS have shown an association between the two (Bergman & Weisner, 1976; Steele & Langworth, 1966). Results from the case-control study of 125 SIDS victims from the Collaborative Project (Naeye, Ladis, & Drage, 1976) are typical. A search for predisposing factors for SIDS (i.e.,

events that might have damaged fetal or infant brains) compared information collected during the Collaborative Study for 375 infants matched with SIDS victims for place of birth, date of delivery, gestational age, sex, race, and socioeconomic status, and 53,721 liveborn infants who survived the neonatal period (unmatched controls) against data collected for the 125 SIDS victims. Infants with congenital anomalies were excluded from all groups. The demographic profile of SIDS families were the same as those of families with excessive perinatal mortality. Evidence of neonatal brain dysfunction could not be related to events in labor and delivery, and there was little evidence of genetic or hereditary influence. A greater proportion of infants who later died of SIDS were mildly growth retarded at birth or showed postnatal growth retardation prior to death. Their mothers were more likely to be young, of low socioeconomic status, anemic; to have had vaginitis or puerperal infection during pregnancy, to have had prior fetal losses, and to have smoked at least 6 cigarettes/day during pregnancy (46 percent versus 25 percent, $p < 0.001$). A variety of neurologic abnormalities were more common in future SIDS victims than in the selected controls and multiple evidence of probable brain dysfunction was found. The mechanism by which smoking might contribute to the risk of SIDS is not known although the frequency with which fetal growth retardation occurs in relation to both smoking during pregnancy and fetal or infant mortality has provided a major focus for such investigations.

The type of fetal growth retardation which occurs may itself be a clue to the underlying mechanism of action (or perhaps to a common pathway of growth retardant action)—two main types of fetal growth retardation were discussed in chapter two. Smoking is associated with a higher incidence of growth retarded infants with short crown-heel length and proportionately smaller weight, head circumference, and other body dimensions. In the 1974-1975 Swedish prospective study of 5,272 pregnant women described earlier (Persson et al., 1978), ultrasound measurements of fetal biparietal diameter [BPD] were made from the 18th-20th week of gestation, growth curves were constructed separately for term births of the smoking (51 percent) and nonsmoking group (49 percent). The BPD increased faster during gestation in the nonsmoking group, the difference being apparent at 22 weeks, significant after the 28th week and positively correlated to number of cigarettes smoked. The study found a lower birthweight, smaller head circumference, and shorter over-all length at birth in the smokers than in the nonsmokers—the heavy smoking group (>20 cigarettes/day, 3 percent smokers) compared with the nonsmoking group showed a 6 percent reduction in birthweight and a 2 percent reduction in length, head circumference, and BPD growth. The study confirmed that fetal size at birth is directly influenced by maternal size and weight gain during pregnancy. The importance of this study is its demonstration of an early onset of overall size reduction in the infants of smoking mothers.

The disproportionate retardation of skeletal growth in premature and low-weight infants of smoking mothers compared to comparable

infants of nonsmoking mothers is reported by others who have carried out broad-based population studies of large numbers of pregnancies (Kullander & Kallen, 1971; Ulrich, 1982) and many who have carried out studies on selected pregnant populations (Luke, Hawkins, & Petrie, 1981; Miller, Haasanein, & Hensleigh, 1976; Miller & Merritt, 1979). Different fetal growth retardation profiles seem to be associated with smoking and low maternal weight gain during pregnancy—higher proportions of short-for-dates infants in the former and of low ponderal index in the latter (although both types occur in either situation)—and with different patterns of early postnatal growth (Miller, Haasanein, & Hensleigh, 1976).

Where studies have subclassified the growth retarded or small-for-gestational age infant for purposes of followup, retarded growth in the postnatal period has been associated with the short-for-dates as well as the low ponderal index infants (Ounsted et al., 1971), with those who did not achieve a "catch-up" growth by 6 months (Fitzhardinge & Steven, 1972), with low birthweight infants of longer gestation (Beck, 1974), with those of significant skeletal stunting in height and/or head circumference (Lubchenco et al., 1976), and with short rather than lean infants (Holmes, 1977; Miller & Merritt, 1979). It might be expected then that infants of smoking mothers who are more likely to be short-for-dates would exhibit signs of growth retardation in the postnatal period.

The results of the longitudinal study of the 17,000 British children who were first studied as part of the Perinatal Mortality

Survey (Davie et al., 1972) and then investigated at the ages of 7 and 11 years confirms a link between prenatal smoking and impairment of both mental and physical growth after adjustment for maternal height, age, social class, parity and sex of child. These effects were seen at both age 7 and age 11 and the deficits increased with the number of cigarettes smoked after the fourth month of pregnancy. Children of mothers who smoked 10 or more cigarettes a day are on average 1.0 cm shorter and between 3-5 months retarded on reading, mathematics, and general ability compared with offspring of nonsmoking mothers. While these results are statistically significant, the smoking-nonsmoking differences are considerably smaller than the differences associated with other sociobiological factors and would unlikely be detected at a level of significance in studies of smaller populations (Butler & Goldstein, 1973). Given the results of the Newcastle Survey of Child Development (Neligan et al., 1976) showing both short-gestation and light-for-dates groups of children perform significantly less well than the random sample comparison over the whole range of measures of performance (psychometric, behavioral and temperamental, neurological and physical growth assessment) studied at ages 5, 6, and 7 years and given that smoking during pregnancy increases the proportion of these two groups, longterm smoking-related impairment in growth and development is very plausible.

A further example of longterm effects related to maternal smoking during pregnancy is reported by Rantakallio (1978). From a study of 12,068 births (96 percent of all births in two provinces of Finland),

1,819 mothers were smokers (83 percent of these smoked <10 cigarettes/day) according to data collected from the sixth month of pregnancy to early postpartum. The infants of these 1,819 mothers and a subgroup of 1,819 infants from the total group matched for mother's age, parity, marital status, and place of residence were followed for a period of 5 years to examine differences in mortality and morbidity. Results show postneonatal mortality to be higher among infants of smokers (RO:3.78 for <2,500 g infants; RO:2.22 for >2,500 g infants). An advantageous position of the low birthweight infants of smokers during the perinatal period when mortality was compared with those of controls, was totally lost during the postneonatal period when both heavier and low birthweight infants of smokers were more affected than controls, and the low birthweight infants more so than the heavier infants. Morbidity was significantly higher ($p<0.001$) among children of smokers, as measured by number of admissions to hospital (higher for all birthweights) and incidence of disease. Diseases in which the difference between the smokers and controls was significant included: respiratory, blood and skin diseases, and those of the nervous system and sense organs. Taken together, the ratio between the smokers and controls was 3.02 among the low birthweight infants and 1.65 among the infants with birthweights of 2,500 g or more.

Clues to the underlying mechanisms of smoking-related reproductive problems are sought in pathological and physiological studies of the placental, membrane, circulatory, serum, cell and tissue changes seen

to be associated with smoking (e.g., Asmussen, 1978; Christianson, 1979; Meyer, Jonas, & Tonascia, 1976; Naeye, 1978b; Oschner, 1976; Resnik, Brink, & Wilkes, 1979).

The effects of three constituents of smoke—carbon monoxide, nicotine, and cyanide/thiocyanate—have been extensively investigated and are reviewed by Sidle (1982).

Carbon monoxide, in combining with haemoglobin, decreases the available oxygen supply from the blood. Carbon monoxide mediated hypoxia is one of the most accepted potential mechanisms by which smoking could influence pregnancy outcome. Consideration is given to the possibility that placental pathology linked with smoking is an adaptation to smoking induced hypoxia.

There is evidence that nicotine has both independent and synergistic effects when combined with carbon monoxide (Boyle et al., 1957; Krisna, 1978; Krous et al., 1981; Sidle, 1982). Nicotine is seen to produce vasoconstriction via sympathetic stimulation, leading to a reduction in uterine blood flow.

The presence of both nicotine and cyanide has implications for the availability and requirements of essential nutrients, for the level of metabolic activity, and for the subsequent growth and development potential of the fetus (Andrews & McGarry, 1972; Crosby et al., 1977; Olubadewa et al., 1978; Rowell & Sastry, 1978; Sontag & Wallace, 1935).

Smoking causes a significant increase in maternal cyanide and thiocyanate and in fetal thiocyanate levels (Pettigrew et al., 1977).

A negative correlation between maternal thiocyanate levels and birthweight is seen (Meberg et al., 1979). It is not known if the fetus is exposed directly to cyanide and if the exposure is at toxic levels, or if only to the detoxified product thiocyanate, which is itself an anti-thyroid agent that could effect thyroid dependent organ development.

In a review of the effect of smoking on placental and maternal immune competence, Wynn and Wynn (1981) state "failure to retain the fetus appears in many cases to be a failure in immunological mechanisms involving both the placenta and the mother" (p. 30). The studies of Naeye and colleagues (Naeye & Blanc, 1970; Naeye et al., 1971) associate placenta and membrane infection to fetal growth retardation, bleeding, preterm birth, stillbirth, and perinatal death. This infection can indicate either increased exposure or reduced resistance to infection.

Many constituents of smoke have independent immunosuppressive effects (Esber et al., 1973; Gulsvik & Fagerhol, 1979; Kraal, 1978; Silvette, Larson, & Haag, 1957; Thomas, Holt, & Keast, 1975). Smokers are seen to have a higher prevalence of infections than nonsmokers (Holt, Thomas, & Keast, 1973; Martin-Boyce, David, & Schwartz, 1977) and in the Collaborative Study (Naeye, 1978b) mothers who smoked had an increased incidence of vaginal, cervical, and amniotic fluid infections.

Immune status, as has been discussed, is modified by nutritional status. Since an intimate relationship exists between the endocrine and immune systems (Castro, 1978) it could be speculated that depression

of maternal endocrine function relating to smoking, nutrition, or other factors may lead to reduced cell replication of embryo, fetus, and placenta, and, in turn, to reduced immune competence in the infant (Wynn & Wynn, 1981).

Consideration of the interaction between immune system function, and the changes in nutrient availability and requirements with smoking and/or infection, as well as the interactive effects of other known risk factors provides a theoretical explanation of the many types and variations in smoking-related pregnancy outcome (Meyer & Tonascia, 1977; Naeye et al., 1973; Naeye, Harkness, & Utts, 1977). Examples of variation in outcome include the increased risk (doubled) to children of the lower socioeconomic groups attributed to maternal smoking (Meyer, Tonascia, & Buck, 1975) and the 6-fold increase in abruptio placentae with heavy maternal smoking or alcohol intake reported by Goujard (1978) that becomes a 30-fold increase when both occur together.

Smoking Prevalence

The most recent broad-based data concerning the prevalence of smoking amongst women of childbearing age in British Columbia is reported as part of the results of the 1978-1979 Canada Health Survey (Ottawa, Canada, 1981). This cross-sectional survey was intended to provide health statistics compatible with the outline of the health field concept—in particular, to provide missing data about the distribution of risk factors of lifestyle origin in the Canadian population.

The sample design consisted of approximately 12,000 households from 100 geographical clusters (stratified representation of the population by provincial region and population, urban centers and rural areas), representing 40,000 persons to be interviewed by specially trained personnel, and a subset of 4,200 households to provide physical measures information. Budget constraints required that the initial survey design be altered somewhat prior to its initiation by a reduction in subset participants. The response rate was 86 percent (10,571/12,218 households) for the physical measures component. Non-response adjustments at the household level in effect replaced the non-respondent with an "average" household from the same cluster and month of survey. Non-responses at the person level were excluded (determined as a negligible effect on results) and non-response for individual items was weighted in a manner that assumed respondents and non-respondents from the same province-stratum-age-sex group were the same, although a study of non-response indicated that non-respondents tended to be slightly less healthy. The data are considered to be from a representative, non-volunteer sample of the non-institutionalized population of Canada that do not live in the Territories, in remote areas, or on Indian Reserves (3 percent of total population).

In general, the survey found differences between the sexes in terms of both the rate and level of exposure to lifestyle risks, as well as a change with age, and variation with social status (defined by occupation and income).

Data on tobacco use were collected from persons 15 years of age and over by self-administered questionnaire. The survey reports about 40 percent of adult Canadians smoke cigarettes daily, and one-third of these smoke 23 or more cigarettes per day, and nearly one-quarter of adult Canadians are former smokers. Smoking was most prevalent among those with low education, among the unemployed, and among those in blue collar jobs. Income was not strongly related to daily cigarette smoking. Heavy smokers were the least likely to have recently tried to cut down on their smoking. Current drinkers were the most likely to be current smokers; heavy drinkers were most likely to be heavy smokers.

The percentage of women reporting daily cigarette smoking according to the data from the Canada Health Survey is compared to data from the Smoking Habits of Canadians Surveys conducted in 1977 and again in 1979 (Ottawa, Canada, 1979, 1980), as follows.

TABLE 9

Proportion of Female Population 15 and over Reporting
Daily Cigarette Smoking, by Age, in the Smoking Habits
of Canadians Survey, December 1977 and December 1979,
and Canada Health Survey, 1978-1979

	Percentage of population who are daily smokers		
	Smoking Habits of Canadians 1977	Smoking Habits of Canadians 1979	Canada Health Survey 1978-1979
Women:			
All ages	31.1	30.1	35.8
15-19 years	26.7	26.0	35.6
20-24 years	40.7	39.8	46.5
25-44 years	36.6	36.0	38.9
45-64 years	30.5	28.9	34.8

Source: Adapted from Canada Health Survey, Table IV, p. 48.

A previous study which examined the results of the Smoking Habits of Canadians Surveys from 1965-1975 (Thompson, 1978) found total cigarette consumption to be underreported by 14-20 percent when compared to tobacco sales data. This suggests that the higher estimates of the Canada Health Survey may provide a closer approximation of the prevalence of smoking in Canada.

The proportion of men and women smokers under 25 are virtually the same, after this, relatively more men than women smoke. Over half the women under 25 are likely to have started smoking before age 16, which contrasts with their mothers who were less likely to begin before age 21 and, in fact, were less likely to smoke.

Table 10 compares the prevalence of smoking among women of different age groups in Canada and in British Columbia.

TABLE 10

Total Female Population 15 Years and Over and Percent Distribution by Type of Cigarette Smoker and by Number of Cigarettes Smoked Daily, by Age Group, for Canada and for British Columbia, Canada Health Survey, 1978-1979

Type of Smoker	Numbers of Women in Population (in thousands)					
	BC Total	Age Groups: Canada				
		15-19	20-24	25-44	45-64	65+
	%	%	%	%	%	%
Never smoked	38.8	38.4	27.9	33.2	40.2	58.7
Former smoker	21.6	16.6	19.8	21.3	17.3	11.2
Current smoker						
Occasional	1.8	6.2	4.3	4.0	2.1	1.3
Daily	30.8	33.9	45.2	37.3	31.9	13.8
# Cigarettes/day						
1-12	10.8	16.8	16.9	11.0	9.8	7.4
13-22	14.0	11.6	18.9	14.5	12.9	3.3
23-32	4.0	4.4	7.2	9.9	7.0	1.2
>33	1.6	0.0	0.2	2.7	1.7	0.0
Type of smoker unknown	6.9	4.9	2.8	4.1	8.3	14.9
Total Population %	99.9	100.0	100.0	99.9	99.8	99.9
N	974	1146	1108	3242	2279	1132

Source: Ottawa, Health & Welfare Canada, Statistics Canada (1981).

It can be seen from these data that from 20-45 percent of the female population of childbearing years are regular smokers. At least as high

a proportion of the male population are regular smokers as well. The percentage of women smoking throughout pregnancy is unknown, although it can be speculated that some will quit when pregnancy is confirmed. The prevalence of smoking around the period of conception and during pregnancy is at a level where even a low relative risk of adverse reproductive outcome from exposure can be of public health significance. The implications of this will be examined in the following chapter.

Cannabis and Reproductive Health

Cannabis is identified as an independent health hazard in this study for two reasons: (a) millions of young people of reproductive age currently use the drug and, thus, adverse consequences, even if infrequent, could be of public health significance; and (b) recent documentation of the health hazards associated with cannabis use (Fehr & Kalant, 1983) provides an exemplary model for investigating and reporting the effects of lifestyle factors on health and reproductive outcome. However, since large prospective cohort studies to examine the effect of cannabis on reproductive outcome in humans have not been conducted, it is not yet possible to determine a causal relationship.

During the early 1980s three expert committees published reports on the health implications of cannabis use—the Addiction Research Foundation of Ontario in collaboration with the World Health Organization (Addiction Research Foundation, 1981); the Institute of Medicine, National Academy of Sciences, USA (National Academy of Sciences, 1982); and the Advisory Council on the Misuse of Drugs, UK (Home Office, 1982).

These reports came to similar conclusions, namely:

That cannabis is clearly capable of causing adverse effects on health, that some of these have already been recognized clinically in heavy users, that others have been produced in experimental animals but do not necessarily occur in humans at the dose levels that have been employed by voluntary users until now, and that there is a serious lack of systematic epidemiological information about the incidence and prevalence of such effects in different parts of the world, as a function of the extent of cannabis use in those regions. (Fehr & Kalant, 1983, p. 10)

The 1983 proceedings of the Addiction Research Foundation/World Health Organization Scientific Meetings provides a comprehensive review of the adverse effects of cannabis use (the text of 800 pages includes over 2,000 references) including general and cellular toxicity; the immune system; effects on endocrine function, reproduction and development; epidemiology and consideration of the clinical relevance of effects seen in animal experiments. This publication is the primary reference for the following overview. Other key references, in addition to the previously mentioned expert committee reports, include Nahas (1976) and Nahas and Paton (1979). A number of extensive reviews have focused on the interaction of marihuana and cannabinoids with endocrine and reproductive function in animals and humans (Bloch, 1983; Nahas & Paton, 1979; Rosenkrantz & Esber, 1980; Rosenkrantz & Hayden, 1979; Smith et al., 1979b).

There are approximately 60 compounds of cannabinoid structure within the group of 421 compounds identified in the cannabis plant (Turner, Elsohly, & Boeren, 1980). It is the euphoric effects of Δ^9 -tetrahydrocannabinol [THC] that attracts its users (Mechoulam et al.,

1980) and although other compounds are also implicated, toxicity appears related to the THC content of cannabis products (Fehr & Kalant, 1983). In general, marihuana (dried leaves) preparations contain 1-8 percent THC, hashish (resin and flowers) contains up to 15 percent, and hashish oil (solvent extracts of leaf, flower, or resin) can contain up to 60 percent THC.

When cannabis products are smoked, the health consequences are considered similar to those associated with tobacco smoke—the important difference is that the concentration of toxic compounds is greater in cannabis smoke and the smoke contains the additional toxicity of the cannabinoid compounds (Leuchtenberger, 1983). The common constituents in tobacco and marihuana cigarette smoke considered to be health hazards by virtue of their known carcinogenic, cocarcinogenic and toxic properties (US, Department of Health, Education, & Welfare, 1972, 1979) are: tar, phenols, cresols, and polynuclear aromatic hydrocarbons in the particulate phase (Hoffman et al., 1975; Lee, Novotny, & Bartle, 1976; Magus & Harris, 1971); and nitrous oxide, carbon monoxide, hydrogen cyanide and nitrosamines in the gas vapour phase (Leuchtenberger, 1983). Those smoking tobacco and cannabis concurrently are seen to be at greatest risk for pulmonary disease and lung cancer (Tennant, 1983). Lung biopsies from young males using both tobacco and hashish had precancerous lesions generally found only after years of heavy tobacco smoking (Tennant, 1980).

In animals, THC decreases cardiac output and cerebral blood flow; in humans, tachycardia and postural hypotension are consistently

reported (Hardman & Hosko, 1976; Tennant, 1983). Since similar amounts of carbon monoxide are found in cannabis and tobacco smoke, impaired oxygenation of the myocardium due to the formation of carboxyhemoglobin is likely.

Other general toxic effects are associated with reduced growth and body weight (animals) (Rosenkrantz, 1983), gastrointestinal distress (Halikas, Goodwin, & Guze, 1971; Rosenkrantz et al., 1975; Tennant, 1974; Thompson et al., 1973), enhancement of alcohol-induced liver toxicity (human) (Tennant, 1983), decreased resistance to infection (Munson & Fehr, 1983; Nalin et al., 1978), and altered endocrine function (Bloch, 1983).

In vivo and in vitro studies of cellular toxicity associated with cannabinoids have focused on the potential for mutagenicity, carcinogenicity and impairment of biosynthesis of nucleic acids and proteins (Leuchtenberger, 1983). In both animal and human tissue culture studies purified cannabinoids were linked with a higher proportion of hypoploid cells during the period of exposure with no measurable increase in chromosome breaks or gaps (Bloch, 1983; Leuchtenberger, 1983; Matsuyama et al., 1977; Morishama et al., 1979; Nichols et al., 1974). Marijuana smoke, on the other hand, is associated with both chromosome aberrations and hypoploidy (Leuchtenberger, 1983), mutagenicity, and impaired development in the second generation of treated animals (Dalterio, 1980; Fried & Charlebois, 1979).

Cannabis smoke is considered to have significant carcinogenic potential, not because of evidence that it has produced cancer in

humans, but because cannabis produces the same sequence of cellular abnormalities produced by tobacco smoke. Abnormalities in mitosis, DNA complement, chromosome number and cell division were more severe after exposure to cannabis smoke than to tobacco smoke (Leuchtenberger, 1983; Munson & Fehr, 1983).

In animals, a decrease in DNA content of immature sperm as well as inhibition of RNA synthesis and of protein synthesis (Munson & Fehr, 1983) is attributed to the cannabinoids in marihuana smoke. Cannabinoid-induced inhibition of both cell growth and division is consistently reported for all cell types as is inhibition of the intracellular synthesis of macromolecules, and inhibition of the incorporation of precursors of nucleic acids and protein across systems. The relevance of these in vitro findings to the general population is not yet known, although abnormalities in morphology and/or nucleoproteins of sperm from marihuana smokers has been reported (Hembree et al., 1979). Issidorides (1983) proposes a hypothesis regarding the possible biochemical mechanism of cannabis which provides:

a single explanation both for the deficiency in nuclear histone synthesis and for the ultrastructural alterations encountered in the leukocytes and spermatozoa of chronic human users of hashish. These cells are characterized by a depletion of the amino acid arginine and by abnormal chromatin condensation. According to this hypothesis, the biological depletion which, in itself, can cause chromosomal aberrations, decreased sperm maturity and motility, defective ovulation, growth retardation, immunosuppression and the reactivation of latent viral infections, and CNS effects such as anorexia, motor incoordination, and lethargy. Furthermore, the enzymes reported to be affected by cannabis possess essential arginine residues at their active sites, which would permit a THC/arginine interaction. (p. 13)

There is consistent evidence that THC and marihuana induce immunological defects in mice and rats (Morahan et al., 1979; Munson & Fehr, 1983). Both humoral and cell-mediated immune suppression are reported. The effects are greater when exposure occurs during the early phase of antibody formation, in young animals (Luthra et al., 1980; Pruess & Lefkowitz, 1978).

There is suggestive evidence of similar immune dysfunction in humans based on in vitro studies (Issidorides, 1979; Juel-Jensen, 1972; Petersen et al., 1975; Stefanis & Issidorides, 1976). Munson and Fehr (1983) state:

It is likely that the degree of immunosuppression produced by different doses of cannabis, like that of other immunosuppressants, will vary along a continuum, ranging from slight effects on resistance to infections, to a marked decrease in resistance resulting in death of the host. It is likely that we would now be aware of profound changes in the resistance of human cannabis smokers if these occurred frequently. However, we lack the epidemiological observations on large numbers of users that would be necessary to establish the occurrence of small degrees of impairment that are suggested by the animal experiments. (p. 339)

The Addiction Research Foundation/World Health Organization report concludes:

A minor degree of immunosuppression in a substantial number of cannabis users might result not in any sudden and dramatic increase in incidence of unusual infections, but rather in a slight increase in incidence, severity, and duration of common ones. Cumulatively, this could have considerable significance for public health and health care delivery systems. (Fehr & Kalant, 1983, p. 16)

Effects of cannabis on endocrine function are seen consistently in animals—particularly with respect to gonadal and adrenal hormone production and hypothalamic-pituitary regulation—but inconsistently

in humans (Bloch, 1983; Bloch et al., 1978). The Addiction Research Foundation/World Health Organization expert committee (1981) suggest that since the endocrine responses of animals to most drugs are at least qualitatively similar to human response, animal studies showing a consistent reaction across species and classes are likely to be relevant to humans.

There still remain critical gaps in animal work examining endocrine response and reproductive outcome associated with cannabis exposure and there are few human studies. Bloch (1983), in his review of the 200 key references in this field, summarizes the available evidence that cannabis adversely effects (or has potential to) reproduction.

The most substantial work has been with rodents. The conclusions that can be drawn from these studies are as follows (Bloch, 1983):

1. In male animals, cannabinoids disrupt normal reproductive physiology and are associated with a reversible decrease in testicular metabolic activity and in vitro testosterone synthesis; and lowered plasma testosterone and LH levels (Bloch et al., 1978; Fujimoto et al., 1978; Huang, Nahas, & Hembree, 1979; Rosenkrantz & Hayden, 1979). With chronic exposure the androgenic target tissues show functional and morphological involution and spermatogenesis is diminished. The mechanism of action may be via reduced cholesterol esterase activity or prostaglandin synthesis, and through diminished metabolic activity and macromolecule synthesis.

2. In non-pregnant female animals, Δ^9 -THC inhibits functioning

of the hypothalamic-pituitary-gonadal axis resulting in decreased plasma LH and prolactin; suppressed pre-ovulatory LH surge and delayed estrus (Nir et al., 1973). With chronic exposure, the uteri and vagina show functional and morphological involution and ovulation may be interrupted or blocked (Cordova et al., 1980). As with males, these effects are seen to be reversible.

During pregnancy, exposure to high doses is associated with reduced maternal weight gain, a reduction in prolactin levels and with continued exposure, inadequate lactation in the postpartum period (Bloch, 1983).

3. Cannabinoids stimulate adrenal cortical function, resulting in an increase in adrenal weight and a decrease in thymus weight, and diminish thyroid function (Bloch et al., 1978).

In animals, exposure during the first two trimesters is associated with increased incidence of fetal resorption and growth retardation in the survivors (Bloch et al., 1978; Sofia, Strasbaugh, & Banerjee, 1979). The growth retardation was linked to exposure during the embryogenic and organogenic phases of development, not the fetal phase. When THC is administered during pregnancy, the uptake by the placenta is greater than that of the fetus and release is slower. This suggests the placenta acts both as a barrier to and a reservoir for cannabinoid transfer (Bloch, 1983). THC may disrupt placental development and function (Sassenrath, Chapman, & Goo, 1979) and in this way influence the potential for fetal abnormalities.

Large doses of Δ^9 -THC can increase the incidence of malformations in mice and hamsters (Bloch, Morrill, & Fujimoto, 1979; Geber & Schramm,

1969; Harbison, Mantilla-Plata, & Lubin, 1977; Joneja, 1976; Mantilla-Plata, Clewe, & Harbison, 1975; Persaud & Ellington, 1968). But since the incidence of malformations associated with THC varies across species and between studies, the question of teratogenicity of cannabinoids per se and cannabinoids versus other toxins in cannabis smoke remains unresolved.

Studies on monkeys and nonhuman primates have not been extensive, but tentatively confirm the suppressive effect of cannabinoids on pituitary gonadotrophin release and on ovulation (Asch et al., 1979; Besch et al., 1977; Smith & Munson, 1976; Smith et al., 1979a).

A number of mechanisms for cannabinoid action have been proposed, but conclusions cannot be drawn at present. The fact that the effects of cannabis are not exclusive to the cannabinoid compounds suggest a variety of mechanisms must be clarified. It is known that Δ^9 -THC concentrates in tissues rich in lipid components (Bloch, 1983) and that in some respects cannabinoids mimic estrogen action and in others, act as estrogen antagonists (Chakravarty & Sengupta, 1980; Chakravarty et al., 1976; Harmon & Aliapoulios, 1972).

Bloch (1983), in answer to the question, "How well have animal studies served as models for the human situation?", states:

Where a particular endpoint or system reacts uniformly to cannabinoid exposure in several species of several classes, including monkeys, a qualitatively similar response in humans may be inferred. This uniformity seems to be the case for acute and short-term responses of the reproductive system, including lactation. (p. 416)

Rosenkrantz and colleagues (1974, 1975, 1976, 1979) have developed a methodology for relating animal study dosages to human marihuana intake. According to these calculations, most studies approximate the daily smoking of .5-1 marihuana cigarettes given the current (and rising) Δ^9 -THC content of marihuana (US Secretary of Health, Education, & Welfare, 1980). It is suggested that approximately 10 percent of the marihuana-smoking population equal or exceed this level of daily exposure (Smart, 1983).

In humans, marihuana acutely depresses the activity of the male pituitary-testicular axis (Hembree et al., 1979; Kalodny et al., 1974) and, according to Bloch (1983), a similar inhibitory affect may be expected to exist in females based on animal studies. One of the few human studies in this area (Bauman et al., 1979) provides preliminary evidence that marihuana-smoking women exhibit an abnormal proportion of menstrual cycles that are anovulatory or have an inadequate luteal phase. Further to this, there is no evidence as yet that cannabis exposure is associated with infertility in humans or animals (Grilly, Ferraro, & Braude, 1974; True et al., 1980; Wright et al., 1976).

Human studies have not examined in any comprehensive manner the relationship of cannabis exposure to reproductive outcomes such as spontaneous abortion, stillbirth, birthweight, or perinatal death (Adamec, 1976; Bloch, 1983). Teratogenicity in humans exposed to cannabis is presently under study (Zukerman et al., 1981) as is the question of postnatal morbidity (Fried, 1980). Studies suggesting

marihuana exposure concurrent with alcohol, tobacco, other drugs or poor nutrition enhances the adverse effects of these health hazards have been reported (e.g., Benowitz & Jones, 1977; Siemens, 1980).

Until further research is available, an assumption that the profile of adverse effects of marihuana smoking on reproductive health is best represented by the profile associated with tobacco smoking seems reasonable.

Estimates of the prevalence of cannabis use in Canada are derived from several large surveys of grade 7-13 students and household surveys of adults 18 years of age and older, between 1975 and 1979. The student surveys found that 20-27 percent of female and 25-36 percent of male students had used cannabis within the year of the survey, compared to 2-7 percent of female adults and 8-12 percent of male adults (Rootman, 1979; Smart & Fejer, 1975; Smart & Goodstadt, 1976; Smart et al., 1979). The percentage of adults (usually between 18-25 years of age) using cannabis daily is estimated at 2 percent for females and 5 percent for males. In the United States, higher prevalence of cannabis use is seen among students (45-50 percent) and adults (10 percent) with smaller differences between male and female users (Abelson & Atkinson, 1975; Blackford, 1977; Johnston, Bachman, & O'Malley, 1979). Cannabis use is associated with alcohol, tobacco, and other drug use. The high prevalence of cannabis use in teenagers and young adults provide ample justification for further study of the effect of cannabis exposure on reproductive health in humans.

Diet and Nutrition

The measurement of the impact of nutrition and diet on reproductive performance presents problems not encountered in studying other lifestyle factors. Food intake is essential to survival; diet is an integral component of human metabolism and the functioning of all cells, tissues, organs and systems; and dietary requirements vary widely according to each individual's physical, physiological, biochemical, genetic makeup, age and his/her health status. At present, there is no simple standardized method of determining whether a specific diet is optimal, adequate or inadequate for an individual (let alone a study population) and, thus, no straightforward method of determining the impact of an optimal versus adequate versus inadequate diet on reproductive performance. This has led to a heavy reliance on animal and cell model studies which allow precise measures and manipulation of nutrients but can only provide grounds for speculation of a nutritional impact in humans. More recent clinical studies of nutritional status and functional effects represent potential for the future. For all of the reproductive outcome measures identified by this paper, animal and cell research describe a significant role for nutrition—but in most cases, the appropriate human studies have yet to be conducted. For this reason, apart from an independent section on nutrition and infertility, a review of the association between nutrition and reproductive outcome with a focus on birthweight and perinatal mortality is presented. Despite the considerable literature on nutritional status and placental function; on maternal-fetal exchange; on postnatal consequences of

maternal malnutrition; on specific nutrient deficiencies; and on the potential mutagenic, teratogenic, and growth retarding effects of malnutrition during the preconception period, these areas will not be reviewed. The material which follows is considered an ample demonstration of the difficulty of estimating nutrition-related reproductive casualties without sufficient knowledge of the nutritional and anthropometric status of the population who do and do not experience reproductive problems and of the importance of baseline assessment.

Background Information

To briefly illustrate the complexity involved in assessing the functional consequences of malnutrition, the following section reviews the interrelationship between nutrition and the endocrine system (since the importance of the relationship between endocrine function and reproductive performance is well established) and examines some specific problems and new concepts in measuring nutritional status.

Nutrition and the endocrine system. The endocrine system, comprised of a number of different glands each having a specific function (e.g., thyroid, adrenal medulla, adrenal cortex, gonads, parathyroids, and pancreas), adjusts and correlates the activities of the various body systems to meet the changing demands of the external and internal environment (including reproduction, growth and development) and does this by the secretion of hormones which regulate the metabolic processes of various cells. In pregnancy, maternal, placental and fetal endocrine function is distinct yet interrelated.

The involvement of any hormone in the control of cellular function depends on a series of reactions, beginning with the synthesis of hormones from their precursors and ending with extrinsic or intrinsic feedback control mechanisms—each stage can be extremely complex because of the many interactions involved, and, thus, there are many possibilities for disruption at various levels in the system (Laycock & Wise, 1983).

Hormones influence the synthesis and catabolism of carbohydrates, protein and fat in a variety of ways (Goodhart & Shils, 1980). In turn, hormonal balance can be profoundly changed by malnutrition—protein-energy malnutrition [PEM] is a well documented example.

Since vitamins are required as precursors of hormones, as activators of steps in hormonal synthesis, and as potentiators of the interaction of hormones with cell membranes,

it follows that an excess or deficiency of specific vitamins must induce some modification in the quality of hormones which they help synthesize, or some change in the effect of those hormones on their target cells. In addition, defective vitamin status may modify the capacity of the target cell to react to normal hormonal stimulus. (Jennings, 1970, p. 113)

Most, if not all, metabolic reactions also require the assistance of enzymes to facilitate and accelerate the reaction. The enzymes with the assistance of coenzymes (usually vitamin derivatives) or cofactors (electrolytes or trace mineral cations) significantly affect cellular function like the synthesis of new protein, through their control of the metabolic processes which regulate these functions. Many of the enzymes are highly specific and catalyze only one step in a complicated metabolic pathway. In pathological states, such as vitamin deficiencies

in which essential coenzymes are missing, there may be a buildup of reaction products, or even a reversal of the reaction.

The synthesis of new protein which is vital to successful reproduction and which requires the activation of particular gene sequences (structural gene DNA to ribosomal RNA, messenger RNA and transfer RNA) in the cell nucleus, is dependent on both hormone and enzyme regulation, which are, in turn, dependent on an adequate supply of nutrients.

In an excellent review of the actions and interactions of hormones, vitamins, and minerals in the human system, Kutsky (1981) states:

The chief difference between a vitamin and a hormone seem to be the site of biosynthesis, the types of organic compounds present in vitamins as opposed to the hormones, and some of the modes of action. These differences between vitamins and hormones in essential properties are small compared to their similarities. (p. vi)

The similarity is made obvious by the following definitions:

a hormone is defined as:

a biologically active, organic compound, a controlling agent essential for normal health and growth (its absence causing a deficiency disease or disorder), synthesized within the human organism in ductless glands which release the agent in very small concentrations into the circulatory system to act on target organs or tissues. (Kutsky, 1981)

and a vitamin is defined as:

a biologically active, organic compound, a controlling agent essential for normal health and growth in humans (its absence causing a deficiency disease or disorder), not synthesized within the organism, available in the diet in small amounts, and carried in the circulatory system in small concentrations to act on target organs or tissues. (Kutsky, 1981)

The differences between certain hormones and vitamins are becoming more difficult to differentiate given the recent evidence that small amounts of Vitamin D and niacin can be synthesized, that some steroids are active in a dietary form, and that the same molecule (e.g., Vitamin C) functions as either a hormone or vitamin depending on the species.

Both vitamins and hormones can be divided into a fat-soluble and water-soluble series. The fat-soluble vitamins [ADEK] and hormones (steroids) are similar in function—both groups affect the permeability of cell membranes, the redox potential, the activation of enzymes—but in addition, the hormones affect RNA transcription in the cell nucleus. The water-soluble vitamins (B-complex, C) and hormones (pituitary, thyroid-pancreas-ovary, adrenal, hypothalamic releasing factors) share the common traits of enzymes activation or action (vitamins directly, hormones indirectly via cyclic AMP), and affect on the cell nucleus—but in addition, some of these vitamins have redox potential.

Trace elements and mineral cofactors are required for the function of some hormones and of most coenzyme systems. The interaction, antagonism and synergism among these vitamins, hormones, and minerals is well recognized. Further evidence regarding the role of specific amino acids, essential fatty acids, and the local tissue regulators (vascular, neurotransmitter, mitogenic agents) is likely to clarify and enlarge this picture of interdependence.

Given these complex interactions and the pattern of intimate and controlled balance, it is small wonder that efforts to measure the isolated influence of one component are less successful in human studies

where components cannot be knowingly manipulated. The insight gained from animal studies and tissue cultures confirms that significant change occurs at the cellular level in the absence of, or prior to, overt clinical measures and that the system is most vulnerable to insult at times of physiological stress—particularly during the maturation period of the sperm and ovum, and during embryogenesis.

To date, abnormalities in metabolic performance in humans can only be measured at the extremes of the continuum. Thus, although the pattern of adaptive interaction within and between systems has been recognized for a long time, the distinction between adaptative versus optimal performance and the relevance of adaptive change at the cellular level has yet to be clarified.

Further to this point, the following section details some of the basic methodology involved and problems encountered in determining the nutritional status of individuals and groups.

Nutritional assessment. Although the first principles for the studies on the nutrition of populations were documented in the mid-1930s and for standardization of survey methodology in the early 1960s, the focus of concern was the nutritional problems of the populations of underdeveloped nations. It was not until the late 1960s and early 1970s that recognition was given to the fact that malnutrition was also a health problem in developed countries. Population surveys (e.g., Ten-State Nutrition Surveys, HANES survey, Nutrition Canada) in the US and Canada revealed vulnerable groups and individuals with evidence of clinical and subclinical malnutrition and linked undernutrition with

growth cessation and developmental handicaps, poor outcomes of pregnancy, susceptibility to infectious diseases, delayed recovery from illness and shortened life expectancy (Simko, Cowell, & Gilbride, 1984). Since this discovery, there have been increased efforts to apply and improve methods of nutrition assessment for surveillance and monitoring (mandated by US Congress, 1977) and for nutritional intervention and preventive health care (Simopoulos, 1982).

Common procedures for individual nutritional assessment in a clinical setting include anthropometric measurements for serial readings, qualitative and quantitative dietary evaluation, observations of physical signs and symptoms, review of medical and socioeconomic factors, and selective biochemical tests. Although nutrition screening and diagnosis is the exception rather than the rule in antenatal care, this is not for lack of established methodology (NAS [The National Research Council], 1978; Simopoulos, 1982).

Techniques for community surveys or population studies, on the other hand, are usually streamlined (i.e., 24-hour diet recall as compared to multiple 7-day prospective diet history) in accord with cost, convenience, and concern for minimizing invasiveness. However, the selection of screening measures that are convenient, yet adequately sensitive and specific, is far from straightforward. Regardless of choice, these findings must be correlated with clinical, anthropometric, dietary, biochemical, and ecological factors to ensure accuracy. The report of a recent conference (Simopoulos, 1982) on assessment of nutritional status reiterates the difficulties of assessment in

epidemiologic studies and surveys of populations. Primarily the difficulties arise from the complexity of interactions among dietary, and other environmental factors with genetic, personal, and other social variables that influence the occurrence of the various conditions of concern. Realistically, these difficulties are unlikely to be satisfactorily overcome. Practically, the associations of importance for epidemiological study should be clearly identified by prior clinical and applied public health research.

More optimistic evaluation of recent advances in food consumption methodology and systems (Hegsted, 1982; Nesheim, 1982; Schucker, 1982; Schultz, 1982; Schwerin et al., 1982) suggest these techniques could be used to investigate relationships between food consumption and nutritional status of a representative or target population integrated with measures of health status indicators, morbidity, mortality, regional economic estimate of food availability, and other characteristics of the population (e.g., health habits and nutrient composition of the food supply). Such systems have been developed in the context of applied public health research.

Malnutrition. Jelliffe (1966) identified four types of malnutrition: (a) undernutrition resulting from lack of sufficient food over a period of time; (b) overnutrition caused by an excess of food over time; (c) specific deficiency states resulting from a lack of individual nutrients; and (d) imbalance caused by a disproportionate amount of required nutrients, either through diet or supplementation. Primary malnutrition

refers to inadequacies and imbalances in the diet, while secondary malnutrition is the result of disease and disability. Failure in nutritional health has been categorized by inadequate intake, inadequate absorption, defective utilization, increased losses (excretion), and increased requirements (Wellman, 1978). The effects of these conditions present clinically as weight loss, delayed wound healing, electrolyte and fluid imbalance, depressed cellular immunity, progressive weakness, skin breakdown, and endocrine abnormalities.

Increased understanding of the correlation between nutritional assessment, intervention, and outcome parameters has resulted from increased interest within the clinical and hospital setting—an interest stemming in part from the "discovery" by the medical profession of hospital malnutrition (Butterworth, 1974; Butterworth & Blackburn, 1975), the advent of hyperalimentation, the introduction of computer-assisted nutritional assessment support, and advanced research on the effects of nutritional status on functional states.

One of the results relevant to community-based studies is the recognition of a particular malnutrition syndrome, described by Blackburn and Bistrian (1977) as "a visceral attrition state or kwashiorkor-like syndrome," where a patient who appears well-nourished and has maintained normal anthropometric measurements, has depressed serum levels of albumin, transferrin and other circulating proteins, as well as compromised cellular immunity. Recommended therapy includes protein and protein-sparing regimes such as "more than adequate" calories, fluid, electrolytes,

and vitamins and minerals. It is likely that the methods of assessment used at the community level are not sensitive enough to identify this type of syndrome although studies have not been carried out to clarify this.

A second result of clinical studies which has relevance to the community is the recognition that a consistent relationship between the parameters of nutritional assessment and prognosis is not always seen. In a hospital setting this can be partly explained by the non-nutritional aspects of the illness and treatment. But Russell and Jeejeebhoy (1983) suggest that another reason for the discrepancy may be that the functional aspects of malnutrition are often not manifested by significant changes in traditional measurements of body composition. Morbidity and mortality, they suggest, may correlate better with the adverse effects of malnutrition on organ function than with the changes in body composition which occur much later. The authors review the effects of malnutrition on three vital organ functions—hepatic secretory protein function, immunocompetence, and skeletal muscle function—by way of explanation (Russell & Jeejeebhoy, 1983).

This review would suggest that screening for a "visceral attrition" state of malnutrition might appropriately incorporate the measurement of serum levels of pre-albumin and retinol-binding protein (which respond to short term changes in protein and energy intake) in combination with some form of dietary intake (to help distinguish between dietary inadequacy and disease processes).

Since malnutrition is the commonest cause of secondary immunodeficiency and infection is one of the most frequent complications of undernutrition, an additional support to screening could come from the measurement of immune function. Cell-mediated immune response is affected earlier and more severely by undernutrition (Chandra, 1979), but severe undernutrition also alters serum immunoglobulins (Chandra, 1979b, 1981; McFarlane & Hamid, 1973). In fact, almost all facets of host resistance are known to be affected (e.g., the complement system, opsonic function of plasma, polymorphonuclear cell function) by malnutrition. Selected nutrient deficiencies can also alter immune function—these include zinc (Driezen, 1978), iron and magnesium (Chandra & Dayton, 1982), pyridoxine, folic acid, Vitamin A and Vitamin E (Biesel, 1981). In a treatise on the immunology of nutritional disorders, Chandra (1980) states that nutritional modulation of immunity has wide-ranging clinical, biological and therapeutic implications. The fact that immunological changes occur in advance of the "visible" chain-reaction outcomes of poor reproductive health signals a potential use for them as a screening measure (Chandra, 1980; Metcalf, 1977), although accurate interpretation of these measures still present difficulty (Harper & Simopoulos, 1982).

Similarly, recent studies of the effects of nutritional status on autonomic and sympathetic nervous system function, which may precede some of the changes in other organ function that accompany alterations in nutritional status and which can, in part, be assessed by norepinephrine turnover rates, speak to the future availability of more sensitive

screening measures of malnutrition than those of current and past use.

A third aspect of clinical studies relevant to the community and reproductive outcomes is the relationship between nutritional status and behavior. It is suggested that behavioral consequences may be among the most important consequences of inappropriate dietary practices (Harper & Simopoulos, 1982), but that these require measurement of specific functions (e.g., memory, problem-solving) rather than the global measures (e.g., cognitive function) used previously in followup studies of infants and children.

One study in particular has provided us with a benchmark for the effect of severe, acute malnutrition on reproductive performance in a human population. Through a detailed investigation of the consequences of undernutrition for 40,000 children conceived and born during the Dutch "hunger winter" of 1944/45, Stein and colleagues (1975) provide clear evidence of relationships between severe food shortage, birthweight, and other reproductive casualties when famine is abruptly imposed on an adequately nourished population. Under these conditions, malnutrition was associated with a fetal growth deficit of 300-400 g, excess prematurity (defined as low birthweight), excess perinatal and neonatal mortality, and an excess of congenital abnormalities.

Similar but less detailed accounts of epidemics of malformations, low birthweight, and infant death have been associated with acute war-related famine conditions since the siege of Paris in 1870 (Wynn & Wynn, 1979). These same adverse outcomes have been consistently

demonstrated across animal species with a broad spectrum of energy deficient, single and multiple nutrient deficiency conditions (Hurley & Eckhert, 1981; Hurley, Keen, & Lonnerdal, 1983).

The unique strength of the Dutch study conducted by Stein and colleagues lies in the quality of data (events surrounding the Dutch famine were carefully and systematically documented as part of populations statistics, food rationing records, birth and death registration, maternity hospital records, etc.); the fact that this cohort data represents the total rather than a sample population; and the fact that famine conditions existed in a defined area of the Netherlands for a specific and measurable time period. These data allowed the researchers to compare reproductive outcomes in famine areas against those in non-famine area of the Netherlands during the same time period, to compare famine effects during early versus late pregnancy, and to compare outcomes in the famine area before, during and after the famine occurred. Followup of the male cohort at the time of their military medical examination was possible for all but 3 percent of the survivors.

The study clearly shows that maternal nutrition can adversely affect all measures of reproductive performance, from the ability to conceive and maintain a pregnancy to the number of malformations, stillbirths, and infant deaths. It also determined that maternal nutrition affects maternal weight, placental weight, and fetal growth dimensions seemingly in a time-ordered chain of events. Thus, with reinstatement of food supplies, maternal weight gain and placental weight gain preceded increases in infant birthweight.

The data suggest a threshold phenomenon which reflects a shift from adaptive to maladaptive state below a certain level of caloric intake. For example, below a threshold value of food rations, fertility (and infecundity by inference) in the population declined parallel with the availability of food and by virtue of a social class gradient effect, affected the lowest classes to the greatest degree. The data did not, however, support the presence of famine effects in those who survived to adulthood.

Some observations of the Dutch famine help to differentiate between the effect of malnutrition around conception and in early pregnancy from the effect of malnutrition later in pregnancy. For example, food shortage in the third trimester had the greatest impact on intrauterine growth and early postnatal mortality (7-90 days). Partial regression coefficients indicate a change in daily average rations of 100 calories predicts a change of 1.2 deaths/1,000 live births at age 7-89 days. Birthweight was more sensitive to nutritional effects than length and head circumference. Slowed fetal growth was the mediating factor between malnutrition and excess deaths in the first three months of life and affected a substantial number of infants. Food shortage in the first trimester had the greatest effect on abnormal development of the central nervous system, preterm birth associated with very low birthweight, stillbirth, and first week death. Smaller numbers of infants were affected by first trimester famine. The data suggest a different low birthweight syndrome is associated with third versus first trimester nutrition deprivation.

Susser (1981) has suggested the latter association may have to do with a famine-refeeding combination. Wynn and Wynn (1981) reviewed the same data in an investigation of the effect of food shortage around the time of conception and present a different perspective. They report that the peak incidence of perinatal mortality (stillbirths and deaths from "prematurity") and infant mortality from malformations of the central nervous system and from "other" malformations, occurred when famine conditions coincided with the period around conception. Further to this, they found that excess deaths (particularly those associated with malformations) persisted at famine levels among babies conceived during the first four months following the restoration of food supplies and remained above pre-famine levels for up to 12 months. Although fertility rates returned to pre-famine levels and above immediately following food restoration, there seemed to be a time lag of at least four months before recovery from the effects of malnutrition on other reproductive outcomes was complete. It is speculated that this finding may reflect the sensitivity of the maturing ovum and sperm to insult, as identified by current mutagenic research (Wynn & Wynn, 1984).

Infertility and Impaired Fecundity

In the Dutch famine cities, the relationship between food rations and fertility (number of births) was convincing below a threshold of 1,500 calories ($r = 0.92$) (Stein & Susser, 1978). Amenorrhea was commonly experienced but not quantified. Non-manual classes were less effected than manual—the social class variation is suggested by the

author to represent a greater access to the limited food supplies in the higher socioeconomic population.

The work of Frisch (1977) and others (Crisp, 1979; Fries, 1974; Holmberger & Nylander, 1971; Nillius, 1978) with small population groups, which indicated that onset and maintenance of regular menstrual function in the human female is dependent on a minimum weight for height (reflecting a particular body composition of relative fatness) has led to the suggestion that 47 kg is a "critical weight" below which menarche does not occur in the North American population. Similar critical weight ranges have been suggested for other countries (Wynn & Wynn, 1981). However, Garn and LaVelle (1983) investigated the "critical weight" theory in a pooled sample of 79,000 North American females (from four different surveys) which included 3,549 women at or below 47 kg. The authors concluded that low body weight may represent a delaying factor to menarche and effect reproductive outcome in terms of birthweight, but because menarche, conception and multiparity occurred within the low weight group, it could not be considered "critical". They observed that non-nutritional genetic components play a role, along with nutritional status, in the timing of menarche. Others (Wynn & Wynn, 1983) have suggested that ponderal index (as a percentile grid) may provide a more appropriate screening tool in identifying those approaching the "infertility threshold" but this has yet to be studied in a representative population.

The findings of Garn and LaVelle do not contradict studies of

malabsorption, caloric deprivation or chronic malnutrition related to delayed menarche or prolonged postpartum amenorrhea, and acute malnutrition related to the interruption of menstrual cycles (Ellison, 1981; Garn, 1979).

The effects of severe malnutrition on fecundity are unequivocal and include disturbed endocrine function in both adult males and females; delayed puberty in the young; cessation of menstruation and ovulation; underdeveloped genitalia and atrophy of the seminiferous tubules in young boys; significant reduction in semen volume, sperm count and mobility, and libido; and morphologic changes in gonadal tissue (Calloway, 1983; Rechcigal, 1981). The recovery period after refeeding, which is consistently reported as four to six months for adult males (Jacobs, 1948; Klatskin, Saltler, & Humm, 1947), is likely to be between two to four months for adult females.

The evidence that moderate, chronic malnutrition affects fecundity is more equivocal, but similar changes have been reported in controlled experiments on adult males (Crisp et al., 1982; Keys et al., 1950; Smith et al., 1975) and studies of anorexia nervosa patients (Crisp, 1979; Fries, 1974) with weight loss of 10-15 percent below initial normal weight. Hypothalamic, pituitary and Leydig cell function all are involved in the response to chronic undernutrition. Hormonal characteristics return toward normal with restoration of body weight but full recovery may take an extended time (Crisp et al., 1982; Woolam, 1981).

Hormonal levels are known to be very responsive to acute food deprivation. In men of normal weight, and even in obese men, fasting for only a few days leads to reduced serum levels of FSH and testosterone, decreased excretion of 17-ketosteroids, and decreased responsiveness to LHRH (Klibanski et al., 1981; Miller, Mickelsen, & Keys, 1948).

Much has been reported about the prevalence of amenorrhea and infertility in women following or concurrent with self-imposed weight loss (Bergh, Nillius, & Wide, 1978; Crisp, 1979; Fries, 1974; Frisch, 1977; Hirvonen, 1979; Nillius, 1978). Bates, Bates, and Whitworth (1982) found, in a small clinical study of 47 women with unexplained infertility or menstrual dysfunction who practised weight control, that even 5-10 percent reductions in weight were associated with subtle alterations in the menstrual cycle and reproductive failure. Of the 36 study women who agreed to follow a diet designed to increase their weight to within the "ideal" range (Metropolitan Life Standards, 1968), 73 percent of those who were infertile conceived spontaneously and 90 percent with secondary amenorrhea resumed menstruation when weight was restored to within 5 percent of ideal. Differences in the serum gonadotrophin luteinizing hormone:follicle stimulating hormone ratio [LH:FSH] were found to be significantly related to differences in the percentage of ideal body weight.

There is also an association between impaired fecundity and quality of diet or specific nutrient deficiencies (as compared to general undernutrition or energy deprivation reflected in weight loss). Animal models indicate important and specific roles for Vitamin A and E, each

of the B-complex vitamins and for essential fatty acids. In a review of nutrition and reproductive function in males, Calloway (1983) concludes:

Of the essential nutrients, only zinc has been linked unequivocally to gonadal development and function in men . . . [but] almost all nutrients involved in metabolism can affect gonadal function directly, or indirectly via the pituitary-hypothalamic axis. Several trace elements are toxic to the gonads, as are excess Vitamin A and ethanol. (p. 377)

Single nutrient deficiency studies in human populations are virtually impossible (as in the case of zinc, the opportunity for natural experiments occasionally occur) since inadequate diets will be deficient in more than one essential nutrient and standards of ethics no longer allow the imposition of a nutrient deficiency.

It is of interest that when Nelson and colleagues (1951, 1954), in one of a series of studies on nutrition and reproduction in rats, used hormone injections to treat diet-related endocrine dysfunction, the hormones successfully supported conception and offset most of the fetal effects related to the dysfunction (e.g., embryo resorption) but did so at the expense of the mother's health and nutritional status. The relevance of this study to humans is unknown. Given that nutritional assessment is not a common component of current infertility investigation and that there is a substantial body of knowledge linking nutrition to the integrity of the endocrine system which is believed pertinent to mammals and humans (Campbell, 1981), investigation of the nutritional status of some couples receiving medical attention for infertility problems seems warranted. Until this occurs it is not possible to determine the incidence of nutrition-related infertility.

At best one could only speculate from population estimates of the number of men and women who are anorexic, bulimic, chronic dieters, substantially underweight, or have nutrient-related diseases or deficiencies.

Birthweight, Perinatal Mortality and Fetal Growth

Studies of groups of pregnant women have consistently shown that an increase in weight gain during pregnancy is associated with a parallel increase in birthweight and a progressive decrease in the number of infants under 2,500 g. Increased prepregnancy weight is also associated with increased birthweight and reduced incidence of low birthweight infants (Gormican, Valentine, & Satter, 1980; Naeye, 1981; Niswander & Jackson, 1975; Ounsted & Scott, 1981; Peckham & Christianson, 1971; Simpson, Lanlow, & Mitchel, 1975). One of the largest series to confirm these correlations was carried out by Eastman and Jackson (1968) for full-term pregnancies of over 11,000 pregnant women (6,675 white, 5,236 black women) delivering at the Johns Hopkins Hospital, Baltimore. Cases associated with fetal deaths, multiple pregnancies, toxemias, and maternal disease states were not included in the study. Weight gain and prepregnancy weight are found to act independently of each other. When they vary in the same direction, their effects are additive; when they vary in opposite directions, their separate effects tend to offset each other. Thus, the largest infants are born to women whose pregravid weight and pregnancy weight gain is high, the smallest to women whose pregravid weight and weight gain were both low, and infants of intermediate weight are born to women with either a low pregravid weight or pregnancy weight gain. In the Baltimore study, for example,

no low birthweight term infants were born to women (black or white) of high maternal weight with adequate pregnancy gain whereas the percentage of low birthweight term infants associated with low maternal weight and pregnancy gain was 16 percent in the group of black women and 5.8 percent in the group of white women. Other studies also report an increased number of preterm births (X4) associated with low weight gain (Miller & Merritt, 1979). From a nutritional perspective, it has been inferred that women with both an adequate pregravid weight for height and an adequate pregnancy weight gain (11-12 kg), enter their pregnancy with adequate maternal nutrient stores and maintain a level of nutrient intake to support pregnancy needs.

Tompkins, Wiehl, and Mitchell (1955) were some of the earliest investigators to report that underweight women who gained more than an average amount from mid-pregnancy had fewer low birthweight infants. This has been further substantiated (Brown et al., 1981; Higgins, 1976; Simpson, Lanlow, & Mitchel, 1975). Postpartum weight as a percentage of ideal body weight/height is considered to be a reflection of the nutritional status of a woman at the conclusion of the gestational period. Luke and Rosso (1978) studied the relationship between postpartum weight and optimal infant birthweight in 254 Black and Hispanic singleton, term deliveries and found a linear correlation up to 110 percent ideal weight/height, at which point the curve begins to level off, reaching a plateau at about 125 percent. To achieve a postpartum weight of at least 110 percent meant a minimum weight gain of 20 kg for underweight gravida in the study group, but was reached by the obese group in spite of some weight loss.

In a group of 467 term, singleton deliveries whose low-income mothers had been referred for dietary counselling, Rosso and Cramoy (1977) examined the influence of maternal weight gain on the incidence of fetal growth retardation. Based on pregravid weight/height, the mothers were classified as underweight, normal, or obese. Low weight gain was classified as underweight, normal, or obese. Low weight gain was defined as 13 kg or less for the underweight group and 7 kg for the other two groups. The incidence of intrauterine growth retardation among women (with no pregnancy complications) was 2 percent in those with adequate gain, compared to 33 percent among women with low gain. The overall incidence of IUGR was 9.8 percent (46 cases) of which 41.3 percent (19 cases) were delivered of women with low gain alone and an additional 30.4 percent (14 cases) were from women with low gain plus one other influencing factor (e.g., preeclampsia, smoking, hypertension); 13 percent (6 cases) of IUGR occurred in gestations of normal weight gain and no complications, and 15 percent (7 cases) attributed to a pathological condition other than weight gain. Thus, inadequate gain, either alone or in combination with other factors, was present in 72 percent of the cases of intrauterine growth retardation.

In addition, studies have demonstrated that the usual excess of low birthweight infants is not found in teenagers or underweight women if they attain an above-average pregnancy gain. This apparent "weight gain protection" may apply in cases where women smoke or are under stress as well. (Garn, Hoff, & McCabe, 1979; Luke, Hawkins, & Petrie, 1981; Picone et al., 1982; Rush, 1974). From a nutritional

perspective, these women and those who are underweight are seen to be at risk by virtue of increased nutritional requirements or of decreased utilization of nutrient intake.

Body weight is affected by both height and maternal caloric intake, height being more important except at the extremes of variation in weight-for-height. Numerous studies have demonstrated a relationship between maternal height and the incidence of stillbirths and labor difficulties, birthweight and perinatal mortality (Baird, 1952; Butler & Bonham, 1963; Thomson, 1959a; Thomson & Billewicz, 1963). From a nutritional perspective, it is inferred that women who were favored by good nutrition and health in childhood are likely to have reached their full potential for height, whereas those less favored may be stunted and more vulnerable to reproductive problems (NAS [The National Research Council], 1970).

The association between height-adjusted maternal weight and infant birthweight identifies the role of prior caloric intake. An example of this type of study is that of Peckham and Christianson (1971) of 3,939 pregnant white women who were members of the Kaiser Foundation Health Plan in California. From this group, all women within the height range of $64 \pm .3$ inches were selected and those with weights in the lowest ($n = 394$), highest ($n = 395$), and mid ($n = 393$) 10 percent of the group were studied. The results are confounded by "opposite effect" differences in maternal age and parity between the light and heavy group (more under 20 years and primigravida in the lightest group) and by differences in weight gain (higher in the lightest group). The mean birthweight of infants

increased with maternal weight for height (3,191.6 g, 3,388.7 g, and 3,531.8 g for the light, medium, and heavy groups, respectively) while the proportion of low birthweight decreased with increasing maternal weight for height (7.8, 4.2, and 2.3 percent). Thus, in stepwise multiple linear regression analysis of the determinants of birthweight (controlled for gestational age and fetal sex), prepregnant weight for height and maternal weight gain are most important (e.g., Blidner, Anderson, & Sinclair, 1982; Niswander & Gordon, 1972) with other anthropometric measurements explained by prepregnant weight.

Consistent correlations between particular dietary components and weight gain, pregravid weight, or birthweight have not been shown across studies (Leader, 1983; NAS, 1970; Rosso & Cramoy, 1977). In a prospective longitudinal study of 95 pregnancies of 54 women, Beal (1971) investigated the food intake of the study women monthly. Throughout pregnancy, there was a positive correlation of caloric intake to weight gain, but the coefficient was statistically significant only for caloric intake in the second trimester. No significant relationship between dietary components and birthweight or birth length were found. However, the author described the women as being generally well nourished before and during pregnancy. Both birth length and birthweight were significantly correlated with maternal weight and pregnancy weight gain (third trimester only for length).

A similar correlation coefficient (+.30) for caloric intakes during the last half of pregnancy was reported by Thomson (1959b) in a study of the influence of maternal body size and caloric intake on birthweight

(489 primigravidas). In this study, caloric intake was directly related to birthweight, but also to social class and to height. The authors interpreted their results as indicating that maternal body size was the antecedent factor. In a multivariate analysis of birthweight in a low-socioeconomic black population, Rush, Davis, and Susser (1972) found maternal weight gain during pregnancy correlated with caloric intake and birthweight independent of "maternal size" and interpreted these results as indicating that caloric intake determines fetal size and birthweight.

Studies with women from low-socioeconomic groups (whose nutritional status is more likely to be inadequate) over time have shown significant correlation between food intake and birthweight. Many do not meet the standards of research design that would allow the results to be regarded as "evidence" but the studies are historically important and put perspective on the later, more rigorous investigations of the effect of nutrition on reproductive performance.

An often reported nutrition intervention study of the early 1940s was carried out in Toronto by Ebbs, Tisdall, and Scott (1941). A 7-day prospective dietary history was completed by 380 women attending the prenatal clinic of the Toronto General Hospital and analyzed by the staff dietitian. Those with a poor diet record and poor income were alternately left on a poor diet (120 cases) or given daily food supplements beginning the 5th-6th month of pregnancy to provide a good diet (90 cases); those with sufficient income were provided with

nutrition counselling to improve their diet (170 cases). A second 7-day food record was analyzed at eight months which showed improvement in all three groups but substantially better diets in the supplemented and counselled group. Initial records for the poor diet group showed a mean daily intake of 56 g protein and 1,627 calories with an increase to 62 g and 1,837 calories by the second review; the supplemented group began at a level of 56 g protein and 1,690 calories and increased to 94 g protein and 2,424 calories; and the good diet group began with 81 g protein and 2,206 calories which increased to 92 g protein and 2,521 calories. The poor diet and supplemented groups were similar in terms of socioeconomic, demographic and obstetric history; the good diet group contained more primips, had higher incomes, and better obstetrical histories. Pregravid weight, height and pregnancy gain were not reported. Obstetric and nursing staff were not informed of the women's diet group. Results showed the incidence of abortions, low birthweight, stillbirths, and neonatal deaths was higher in the group on a poor diet. The women in the groups with supplemented and good diets had fewer obstetrical complications including toxemia, and had fewer difficulties during labor, delivery, and the postpartum period (reduced infection, increased ability to nurse). The infants born to mothers on a poor prenatal diet were more susceptible to infections and nutritional diseases for the first six months and experienced a below normal growth rate even though their mean birthweight was not significantly different. The study has been critiqued for

methodological problems—e.g., noncompliance not adequately controlled, sample size too small to show statistical significance. By today's standards some of the outcome measures lack specificity and the timing of the intervention is late (preconception or first trimester intervention would be seen to be more appropriate) but the approach is sound.

A study of the stillbirth rates in England and Wales from 1928-1944 showed a sharp decline in all counties (greatest in the poor counties) after the institution of war-time prenatal food rations by government. Neonatal death rates and low birthweight also declined but to a lesser degree. Since these changes occurred at a time when all conditions other than nutrition had deteriorated, the result was considered to be due to the improved nutritional status of the poorer women (Baird, 1947; Sutherland, 1946). Descriptive dietary studies in England seemed to support this explanation (Cameron & Graham, 1944). Following this, a series of studies were conducted at the Boston Lying-In Hospital (Burke, 1948; Burke et al., 1943; Burke, Harding, & Stuart, 1943) to determine the influence of diet during pregnancy on growth and development of the fetus or the course of pregnancy, labor and delivery, or the postpartum period. The diets of a group of 216 pregnant women attending the hospital prenatal clinic were carefully assessed over the last two trimesters and a formula used to rate them as excellent or good (14 percent), fair (46 percent), poor (23 percent), or very poor (17 percent). An independent pediatric appraisal of the infants was carried out and then examined against the dietary rating

of the mother. The length and weight of the infants, their overall physical condition and osseous development were closely associated with the protein content of the mother's diet, and the occurrence of toxemia was related to the quality of the diet. A sibling study (Burke et al., 1949) reported that the diets of the mothers entering subsequent pregnancies remained at the same level of adequacy or inadequacy. This allowed for speculation of a nutritional component in the "repeater" syndrome of reproductive outcome in which a mother with a history of a previous low birthweight infant, for example, is at greater risk of giving birth to a second low birthweight infant.

The need for more rigorous research design and larger, more representative study populations led to a series of supplementation studies which have failed to clarify the effect of nutrition on reproductive outcome. Some have demonstrated a clear beneficial effect of food or nutrient supplementation, others have been less conclusive, and some have shown no effect.

In the early 1970s a number of major studies of nutrition and pregnancy were conducted on the premise that if inadequate diet contributed to low birthweight and poor reproductive performance, nutrition supplement/non-supplement comparison would help quantify this relationship. Three representative prospective studies—the New York study of 769 singleton births (Rush, Stein, & Susser, 1980), the Bogota study of 413 births (Mora, Clement, & Christiansen, 1977; Mora et al., 1978, 1979), the Guatemala study of over 1,500 pregnancies

(Habicht et al., 1974; Lechtig & Klein, 1980), and the Taiwan study of 225 women over two consecutive pregnancies (Blackwell et al., 1973; Wohlleb et al., 1983) have been critically reviewed by Lechtig and Klein (1981), Rush, Stein, and Susser (1980), Stein, Susser, and Rush (1978), and Susser (1981).

The New York study closely conforms to the experimental model with random double-blind assignment of an adequate sample of high risk women, to a control or one of two beverage supplemented groups. The Bogota study used randomized assignment of malnourished families to six prenatal and postnatal control and treatment groups using regular food as a prenatal supplement from the sixth month of pregnancy; the Guatemala study used two different liquid diet supplements with treatment assigned by residence in one of four small villages; and the Taiwan study randomly allocated pregnant women to a beverage supplement or placebo group from the second or third trimester of the initial study pregnancy through to the weaning of a subsequent birth.

The results from these major studies were mixed and emphasize the complexity of the nutrition-birthweight relationship. The New York study showed no significant supplement effect on birthweight except in infants of women who smoked. Susser (1981) concludes from these studies, that among women at risk of producing low birthweight infants, prenatal dietary supplementation can lead to a modest rise of 40-60 g in birthweight. The degree of effect on birthweight seems to be conditional and depends on the nutritional status of the women. In adequately nourished or heavy women, supplements are likely to show no

effect, whereas in thin or undernourished women, the birthweight effect is likely to be in the upper range. Supplement effects on maternal weight gain did not consistently reflect improved fetal growth nor were perceived nutrition-related benefits in cognitive function or psychological test results necessarily associated with improved fetal growth. A best time for supplement initiation and a best nutritional content for supplements was not fully clarified. The latter reflects the inherent problem of supplement studies where total dietary intake and nutritional needs are not taken into account.

In the Guatemalan study, the average non-supplemented diet of women during pregnancy was about 1,500 kcal and 40 g protein (mostly from vegetable sources) and the average pregnancy gain was only 7 kg. The two types of supplements compared protein-caloric versus caloric effects. In both supplemented groups, birthweight showed a consistent association with the number of calories received during pregnancy but no relationship to protein. The mean birthweight of infants of women receiving more than 20,000 kcal of supplement over their pregnancy was 3,105 g compared to 2,994 g when supplementation was less than 20,000 kcal. The proportion of low birthweight infants in the former groups was 9 percent compared to 19 percent in the later. The relationship between caloric supplement and birthweight remained after controlling for maternal height, parity, or gestational age. Supplements were taken under supervision at the village clinics, but since attendance at the center was voluntary, this resulted in a wide range of supplemented intake among and within the groups of women. The difficulty in

successfully implementing the study as designed created obvious problems concerning the strength of evidence of results.

On the other hand, the New York City study was able to implement a research design of high standard but has been widely criticized in terms of its nutritional design. Jacobson (1980) has suggested that the intervention was too late to allow meaningful rehabilitation to occur; others have criticized the protein content (which, at the higher levels, may have had detrimental effects) in the absence of supportive calories (Barnes, 1980) and the vitamin-mineral balance (Hegsted, 1980)... Wynn and Wynn (1980) noted that the ponderal index of the women (20.32 ± 2.18) was at a level cited by Frisch (1978) as the infertility threshold, and that poor nutrition at conception could be a component of the poor health of the study infants (e.g., overall perinatal mortality rate of 65.5/1,000). Leader (1983) comments that since protein deficiency may not have been the nutritional problem (Bowering, Lowenberg, & Morrison, 1980), "the New York Study was analogous to a field trial of a new antibiotic in a population not suffering from infections sensitive to the new drug." He continues: "With the benefit of hindsight, the study raises more questions than it answers. Whatever its suggested shortcomings, the study was valuable in pointing out that there is a need for a balanced and individualized approach to nutrition in pregnancy" (p. 38).

There are some interesting similarities between the findings in some of the supplement studies and observations by Stein and colleagues

(1975). For example, when food was restored post-famine, maternal weights increased before birthweights increased—some supplement programs were associated with significant increase in maternal gain but not in birthweights. Male birthweights at the height of the famine were affected more than female birthweights—some supplement programs were seen to affect male fetal growth to a greater degree than female fetal growth. These observations contribute to the questions raised as to the timing and type of supplementation selected for the studies.

Why the disparities in the results of the major supplement studies of the 1970s? It is now recognized that additional nourishment for the already adequately nourished pregnant woman bestows no measurable benefit on infant health and growth, nor does inappropriate dietary intervention of the malnourished. When the "nutritionally at risk" woman is correctly identified, her nutritional status, if unaltered, becomes predictive of adverse fetal growth outcome but if improved, shows significant fetal growth and health benefits. The work of Wharton and his colleagues (Bissenden et al., 1981a, 1981b; Viegas et al., 1982a, 1982b; Wharton, 1983) in England and Higgins (1984) in Canada are reviewed as examples.

In a series of studies starting in 1974, Wharton, Bissenden, and colleagues (Bissenden et al., 1981) found evidence that undernutrition was a factor in the aetiology of poor intrauterine growth seen in infants of many Asian mothers delivering in their Birmingham hospital. Their initial question was a familiar one—did low weight Asian babies

reflect ethnicity (i.e., were they simply "light" normals) or growth failure? A comparison of weight, length, head circumference, skin folds, and arm circumference dimensions in 28 normal European babies, 8 growth retarded European babies from medically compromised pregnancies, and 12 low weight Asian babies from normal pregnancies showed the Asian babies deviated from normal in exactly the same way the growth retarded European babies did (Bissenden et al., 1981a). In addition, both light Asian babies ($n = 21$) and growth retarded European babies ($n = 30$) showed significantly raised cord blood plasma triglycerides—analygous to the raised plasma triglycerides of children with marasmus—when compared to normally grown babies of either race ($n = 35$) (Bissenden et al., 1981b). The similarity in anthropometric and biochemical variables suggested growth failure. Following a systematic investigation of factors associated with growth failure in the Asian population, a nutritional hypothesis was established based on observed food customs and weighed dietary intake studies. A prospective study was designed to compare the nutritional status of mothers having normally grown and light for gestational age babies. Mothers who produced light babies put on less weight and less fat during the second trimester (triceps skinfold was the best predictor of a growth retarded infant) and had biochemical measures suggestive of poor nutritional status (Viegas et al., 1982a).

The final study in the series by Wharton attempted to confirm the nutritional cause of growth retardation through dietary intervention. One hundred and ninety-seven women were alternatively assigned to one

of three supplement programs (control = vitamins; energy plus vitamin supplement; protein and energy plus vitamin supplement) prior to their 20th week of pregnancy. When all mothers were considered together, the prenatal diet supplements provided no fetal growth benefits. Within this group, infants of mothers who had laid down fat adequately during pregnancy (determined not to be nutritionally at risk) showed no fetal growth benefits from the protein-energy supplement but infants of mothers who had not put on fat adequately (triceps skinfold increment <0.02 mm per week) showed significantly enhanced intrauterine growth with protein-energy supplementation. The authors comment that the results illustrate a general principle of therapeutics—treatment should be given only to those who have the disorder; unselective or "blind" treatment of all patients is not cost-effective and may be detrimental (Viegas et al., 1982b; Wharton, 1983). Wharton suggests the differential effect of supplementation in the major studies of the 1970s is likely to reflect the initial nutritional status of the study women.

This point is also emphasized by the results of the Montreal Diet Dispensary-Royal Victoria Hospital [MDD-RVH] collaborative sibling study (1963-79) (Higgins et al., 1984). This prospective, longitudinal study was designed to examine the effect, if any, of a nutrition assessment and intervention program on pregnancy outcome among a low socioeconomic unselected population derived from the RVH public maternity clinics. Prior to the study in 1963, the MDD had developed a standardized outcome-related nutrition rehabilitation method (known as The Higgin's

Nutrition Intervention Method) based on 15 years of experience providing nutrition counselling for disadvantaged women with poor obstetric histories and poor nutritional status. Baseline data showed a small mean difference in birthweight (120 g) between the public and private patients at the RVH hospital but a large difference in the incidence of low birthweight and perinatal mortality (60% and 50% higher in the public patient group, respectively). The purpose of the Montreal study was to demonstrate a means of reducing the birthweight disparity between the infants of advantaged and disadvantaged women (i.e., break the poverty cycle) and to test the effectiveness of different components of the nutrition intervention method.

Criteria for enrollment in the study included attendance at public clinics for antenatal care and delivery at the RVH, initiation of the MDD program for referred women (all women from two public clinics) during the first two trimesters of pregnancy, and singleton live birth at or after 28 weeks of gestation. Since multiple regression analysis had shown that only 45 percent of the variance in infant birthweight could be explained by parameters known to influence birthweight, the study examined the effects of the MDD program using "within mother" rather than "between mother" comparison using sibling controls. Analysis of program effect used least squares methods, with appropriate correction for infant sex and birth order. The MDD treatment groups (cases) were defined as singleton, live, RVH-born infants, gestation 28 weeks or more, with the mother being enrolled in the MDD

program before the 27th week of pregnancy and having been counselled by the dietitian at least 5 times. The control groups of siblings born to the 1,139 mothers with treated pregnancies were divided into those born prior to the mother receiving MDD treatment (Pre-MDD; $n = 872$) and those born after a MDD-treated pregnancy (Post-MDD; $n = 326$). Cases had a mean birthweight of 3,352 g, which was 129 ± 30 g greater than controls ($p < 0.001$), had a lower perinatal mortality rate (7.8 compared with 14.3/1,000; $p < 0.01$) and lower birthweight proportion (4.1 compared with 7.9 percent; $p < 0.01$).

The MDD nutrition intervention program is built around an initial comprehensive nutrition assessment (diagnosis) with subsequent dietary treatment tailored to the needs of each individual mother. The fact that mean birthweight (3,469 g) and weight gain (13.4 kg) was highest, and low birthweight less frequent (2.9 percent) for those assessed as having a good initial nutritional intake demonstrates the assessment method is accurate for selecting mothers who do not need a corrective dietary allowance. Significant improvements in birthweight and infant outcomes were specific to those women (79 percent of total) determined to be nutritionally at risk. The results support the assumption that infants of women who are underweight pregravid, with a low rate of pregnancy weight gain, with a prior poor obstetric history, etc., benefit if maternal nutrition is improved. However, 46 percent of the study group who were determined to be undernourished by virtue of the protein content of their diet at initial intake (a "leader" nutrient

criterion) and who were the most malnourished of the study risk groups (by 540-650 kcal and 17-30 g protein at initial assessment) were not underweight (the majority were overweight) and would most likely be missed as a high risk pregnancy in studies where dietary intake is not assessed. This group showed the most significant birthweight increase compared to their sibling controls (161+/-39 g).

That the study group was economically disadvantaged is revealed by the fact that 80 percent of the cases required an income supplement (given in the form of basic foods) to meet their nutritional requirements. It is reasonable to suggest that the women were chronically malnourished prior to intervention. Initial mean intakes ranged from 51-79 g protein and 1,800-2,400 calories depending on the risk category and were increased to 99-105 g protein and 2,600-2,950 calories through the counselling program. Relative to the Dutch famine study this is not an extreme level of malnutrition and yet major benefits in terms of birthweight and infant mortality were realized through appropriate assessment and improved diet prior to the third trimester.

The need for a comprehensive nutritional assessment (which requires time and special skills) in measuring the impact of nutritional status on reproductive outcome; the recognition that adverse effects of malnutrition can be associated with single or multiple nutrient inadequacies, excesses or imbalance; the knowledge that nutritional needs are modified by a wide range of factors (e.g., infection, drug use, activity patterns, etc.); that nutrition-outcome relationships may vary at the extremes (e.g., high pregnancy gain in the overweight

may reflect poor rather than good diet); and that nutrition can have a mediating influence on the affect of other reproductive risk factors (e.g., rate of detoxification, endocrine function, immune status) identify limits to the ability to quantify the total impact of nutrition on reproductive performance. The new generation of post-70s nutrition studies provide a more detailed multimeasure examination of maternal-reproductive outcome-related variables in smaller populations compared to the indirect or less specific measures of the previous large scale studies. There are, of course, inherent research design problems in studying smaller populations across a larger set of variables. However, they can provide increased detail which seems necessary to bridge the gap between animal studies and tissue or cell culture studies and human nutrition studies.

Metcoff and colleagues (1980, 1981) in Oklahoma, working through a series of stages in a complex, carefully executed study of over 400 "apparently" health pregnant women attending the University Obstetric Clinic show that birthweight can be predicted from a set of maternal characteristics and nutrition-related measurements obtained at mid pregnancy. Intervention to prevent predicted low birthweight and fetal malnutrition is currently being tested.

A number of aspects of the Oklahoma studies are notable. First, their applied use of the leukocyte (neutrophil) indicator as a cell model, based on earlier work by Metcoff and colleagues (1979). Measures of maternal leukocyte metabolism were used as an indication of nutrient

effects on rapidly replicating fetal cells, on the hypothesis that the nutrient microenvironment regulates the growth and metabolism of all rapidly dividing cells (such as fetal and placental cells) in the mother. Study results show that maternal leukocyte bioactivities make a significant contribution to the prediction of birthweight and that 65 percent of the variance in the components of leukocyte metabolism can be explained by the maternal nutrition-related measurements.

From a prevention perspective, the potential for identifying cost effective and time specific (i.e., preconception, midpregnancy, postpartum, interconception) predictor variables that allow for successful intervention is of great public health significance.

The Oklahoma studies also suggest that malnutrition caused by imbalances among nutrients, without a deficiency state, may be a more common association with fetal growth retardation in the developed countries. Others have suggested this possibility as well (Naeye, 1983). Distinct differences were found by Metcalf and colleagues (1981) between mothers of small, average, and large babies for many of the 33 independent maternal nutrient measures studied, and while these included lower weight gain, protein and energy intakes for mothers of small babies, gross nutritional deficiencies or excesses were not seen in any of the groups. The authors state: "it appears that birthweight (adjusted for non-nutritional factors) may be related more closely to the nutrient pattern or profile present in the mother, rather than to excesses or deficiencies of specific nutrients" (p. 717). Further

study is required to put this mid-pregnancy "snapshot" into perspective, but these initial data further alert us to re-examine the relevance of traditional screening measures.

Part of this perspective is an understanding of the relative contribution of various nutritional and non-nutritional factors to the variance in fetal growth. Numerous studies have attempted to quantify these contributions via various statistical techniques (see, e.g., Kaminsky, Goujard, & Rumeau-Rouquette, 1973; Keeping et al., 1979) using birthweight as the measure of fetal growth. Metcoff and colleagues (1981) summarize the factor-variance profile as follows: maternal genetic factors (individual variation) approximately 25 percent of the variance; paternal genetic factors, 1-2 percent; maternal age, education, prior low birthweight infant, about 8 percent; maternal height and prepregnancy weight, about 8 percent; coffee and alcohol intake, approximately 2 percent; smoking (tobacco), 3-6 percent dependent on dose; and pregnancy weight gain, approximately 3 percent from mid-pregnancy to term/3-6 percent total pregnancy gain. The Oklahoma maternal nutrition birthweight-predictor equation accounted for about 75 percent of the variance in adjusted birthweight ($R^2 = 0.74$) and the maternal leukocyte measures contributed 8-9 percent of the prediction of birthweight [$F(4,124) = 10.3, p < 0.0001$].

Emphasis has been given to the importance of a multimeasure fetal growth assessment in helping to differentiate the growth retarding effects of nutritional and the many non-nutritional factors and in

helping to differentiate between different types of fetal growth retardation. Although low birthweight remains the most significant predictor of mortality and morbidity, as a single measure it provides no diagnostic support. Miller and Hassanein (1971) demonstrated a variance of up to 1,100 g in birthweight among infants of the same body length, sex, race, and gestational age. These variations related primarily to differences in soft tissue mass, including fat and skeletal muscle. The authors comment that no clinician would evaluate growth in older infants, children, or adults on the basis of body weight for age. Fetal growth retardation is present in infants heavier than 2,500 g but is not recognized as such without sufficient anthropometric data.

The degree to which an infant is determined to be growth retarded in utero is, of course, dependent on the standard of normal growth that is used as a comparative measure. Most investigators have excluded infants with major malformations or those born to diabetic, hypertensive, or pre-eclamptic mothers although the exclusions vary and lack uniformity (Babson, 1970; Babson & Benda, 1976; Gruenwald, 1966; Hendricks, 1964; Hoffman et al., 1974; Lubchenco, Hansman, & Boyd, 1966; Tanner & Thomson, 1970; Thompson, Billewicz, & Hytten, 1970; Usher & McLean, 1969). These standards provide fetal growth profiles of a particular population, but they do not describe "normal" growth profiles of infants free from intrauterine growth retarding factors. In attempting to determine what type and proportion of fetal growth retardation can be prevented by

removing particular intrauterine growth retarding factors, a "normal" or optimal growth standard should be used for comparison.

Miller and Merritt (1979) developed a "normal fetal growth standard" through a cross-sectional retrospective approach as part of a five year study of over 6,000 consecutive births at the Kansas Medical Center, 1973-1978. The purpose of the Kansas study was to provide anthropometric data on newborn infants free from all known growth retarding influences in utero, to construct from this data standards of normal fetal growth for comparative use in determining newborn infants with atypical fetal growth; and to describe the causes and consequences of atypical growth. The study population of black and white mothers and their infants reflected a wide range of socioeconomic circumstances, medical and obstetrical problems, and behavioral habits and attitudes. The group was unrepresentative in respect to the fact they were drawn from a large urban setting and attended the obstetric clinic of a designated tertiary care institution and some cases delivered during the study period were not included or discussed in the report. Thus, while the approach merits attention, the study design limits the applicability of the results.

The infants were categorized by the two main types of fetal growth retardation— (a) Low Ponderal Index [LPI] where an infant's crown-heel length at birth is normal for gestational age but subcutaneous fat is deficient. This is suggested to be growth retardation of late pregnancy origin and is characterized by postnatal growth "catchup" within a 3-6 month period; (b) Short for Dates [SHFD] where an infant is symmetrically

small in external body dimensions and may or may not be deficient in subcutaneous fat. This is suggested to be growth retardation of earlier pregnancy origin and is not associated with any consistent "catchup" growth phase in the postpartum period; by two types of accelerated fetal growth; by occipitofrontal head circumference [OC]; by classification as a fullterm or premature (<37 completed weeks of gestation) birth and by birthweight of less than 2,500 g or 2,500 g and over.

The study differentiated between factors that effect fetal growth in all pregnancies (i.e., parity, height, race, gestational age, sex of infant) and those that occur only in some, which they describe as growth retarding factors. Four groups of growth retarding factors were identified: (a) Fetal Factors which included intrauterine infection, chromosomal abnormalities, malformations, multiple births; (b) Medical Complications of Pregnancy which included hypertension, pre-eclampsia, chronic disease, infection, anemia, medications, abnormalities of the placenta; (c) Maternal Behavior (i.e., conditions which are dependent on maternal choice/action which included seven distinct variables—abnormally low prepregnancy weight for height, low pregnancy gain, lack of any prenatal care, delivery before 17 years of age, delivery after 35 years of age, cigarette smoking, and the use of addicting drugs or large quantities of alcohol during pregnancy; (d) Environmental Factors which included exposure to toxic substances and high altitude.

Two out of every three fullterm infants and 85 percent of all premature infants had to be excluded from the control group because

of some fetal or maternal growth retarding factor. In the white only population, 1,399 mothers and their fullterm infants had no known growth retarding factors (there were too few premature infants born to control mothers to construct a functional preterm fetal growth standard), 1,269 mothers were associated with one or more behavioral conditions, but no other growth retarding factors, and 429 mothers whose pregnancy was complicated by medical problems (210 of whom had no other fetal growth retarding factor).

Within the "control" group, pregnancy outcome was excellent: less than 2 percent LBW infants, 2.4 percent prematurity with 85 percent of the preterm births weighing more than 2,000 g, and by study definition, a 5 percent incidence of fetal growth retardation measured as LPI or SHFD. An important observation in the study is that control group babies born to women in the lowest socioeconomic group had as little risk of being low birthweight [LBW] or fetal growth retarded [FGR] as those born to control group mothers in the highest socioeconomic group. Similarly, a control mother's age, her marital status, race, or level of education were not related to a higher risk of her baby weighing less than 2,500 g at birth.

Infants born to mothers with one or more growth retarding behavioral conditions were more likely than "control" infants to be premature, low birthweight [LBW] and fetal growth retarded [FGR] by each of the measures—low ponderal index [LPI], short-for-dates [SHFD], and small occipital circumference [OC]; the incidence for each fetal growth

indicator was significantly different from the controls and pregnancy outcome for the "behavioral condition" group was comparatively poor—over half of the total group of 230 LBW infants were born to women with behavioral conditions and no other known complications of pregnancy. Both premature and fullterm infants with LPI and SHFD types of growth retardation were more likely to be low birthweight when born to the "behavioral condition" group of mothers than to the "control" group of mothers. Specific behavior conditions were associated with specific types of FGR. Pregnancy outcome was significantly worse if multiple behavior conditions were present. Associations between fetal growth dimensions and the occurrence of medical and of obstetric complications (with and without the presence of behavioral conditions) were also reported.

Two of the growth retarding behavior conditions were identified in the study as indirect measurements of inadequate maternal diet—abnormally low pregravid weight (>15 percent below normal, based on Sargent's table of weight-height relationships for young women) (Sargent, 1963); and low pregnancy gain (mean weight gain of 227 g or less per week in the last two trimesters). Infants of 69 women who were underweight but had no other growth retarding factors associated with their pregnancy were compared to the infants of the control group mothers. Control group mothers were categorized as obese, overweight, average weight and slender for comparison with the underweight mothers and their infants. Like other studies, the Kansas study found a

positive relationship between the prepregnancy weights of mothers and their infants' birthweights.

Even the lowest prepregnancy weight-for-height had no significant effect on the incidence of premature birth, or of LBW in either premature or fullterm infants when not accompanied by any other known fetal growth retarding factors. There was, however, a significant difference between the incidence of small OC infants in the highest and lowest weight-for-height categories (ten-fold increase in infants of underweight and slender mothers). Slender (7.5-15 percent below normal) and underweight women were more likely to have SHFD infants and LPI infants than obese women, but numbers born to the obese women in these categories were too small for statistical analysis.

Low pregnancy weight gain was identified as a behavior condition in 15-20 percent of the women in the study, most of whom (70 percent) were multips with average weight-for-height. Mothers whose only known growth retarding factor was low weight gain had a significantly increased incidence of premature births, of SHFD and LPI infants and of the proportion of premature and fullterm infants who weighed less than 2,500 g when compared to the controls. If low weight gain and low pregravid weight-for-height occurred together, the incidence of prematurity and SHFD growth retardation was significantly greater than when low weight gain occurred alone as a growth retarding factor. A similar increase in premature births and SHFD growth retardation occurred when smoking and low weight gain occurred together during the prenatal period.

Miller and Merritt concluded from their study data that intrauterine growth retardation is not uncommon and is generally underreported; that it is important to differentiate between the two main types of fetal undergrowth since their pathogenesis are probably different and their prenatal and postnatal courses are definitely different.

This study illustrates a technique for assessing the impact of specific lifestyle factors like dietary intake (alone, in combination with other lifestyle factors, or in combination with other known factors) on reproductive outcome in a total or representative population. The use of this technique is, of course, dependent upon having adequate prevalence and outcome data for the population of childbearing years.

The Prevalence of Nutritional Problems in the Population

Between 1970 and 1972, the first (and only) national nutrition survey—Nutrition Canada—was conducted (Nutrition Canada, 1973). The objective of Nutrition Canada was to provide a sound body of precise scientific information on the nutritional status of the Canadian population. The survey was designed to provide estimates of nutritional characteristics in (a) the residents of 10 provinces, (b) Indians in bands on reserves and crown lands, and (c) Eskimos living in four settlements in the Territories. Sampling for the provincial populations included five regions, one of which was British Columbia. The survey design allowed for assessment of nutritional status of a representative sample of the total population stratified according to region, population

type, income, and season. In addition, the survey planned to examine and interview up to 1,000 women who were in their last trimester of pregnancy. The pregnant sample were referred by public health units and because of the mode of selection were not considered a probability sample. In total, 27,332 individuals were selected for the Nutrition Canada survey. Of those persons initially selected, 12,795 (46 percent) attended the survey clinics.

A survey team of physicians, dentists, nurses, nutritionists, dental hygienists, laboratory technologists, and support staff were trained to carry out a comprehensive set of procedures which included: clinical, dental, and anthropometric examinations; dietary interviews; and blood and urine analyses. Prior to this, expert groups were convened to develop valid and practical procedures for nutritional status assessment and for developing an interpretive standard for the data.

Table 11 summarizes the dietary and biochemical data from the Nutrition Canada survey which identifies nutritional problems in the British Columbia sample of pregnant women and women of childbearing years.

TABLE 11

Proportion of the Pregnant and Female Population 10-19 Years and 20-39 Years of Age in British Columbia with an Inadequate Daily Intake of Nutrients and with Moderate to High Risk Biochemical Measures, Assessed by the Nutrition Canada Survey, 1973

Nutritional Assessment Parameters		Proportion of BC Population at Nutritional Risk		
		Pregnant Women (n = 204)	Females 10-19 yr (n = 265)	Females 20-39 yr (n = 258)
		%	%	%
A. Daily Dietary Intake: Nutrient Needs				
1. Calories	≥ 1,500 kcal	21.0	21.0	34.0
2. Protein	≥ 0.75 g/kg	11.5	10.5	25.6
3. Thiamin	≥ 0.4 gm	1.4	4.0	9.6
4. Riboflavin	≥ 0.55	0.9	1.7	6.1
5. Vitamin C	≥ 40 mg	11.2	36.8	34.3
6. Vitamin A	≥ 750 RE	19.9	41.9	53.7
7. Calcium	≥ 1,200 mg	47.5	72.1	92.4
8. Vitamin D	≥ 400 IU	50.6	87.7	95.8
9. Iron	≥ 14 mg	35.6	78.9	74.8
B. Biochemical Measures: Moderate - High Risk				
1. Serum Protein		11.9	2.2	2.8
2. Urinary Thiamin		3.4	11.1	13.3
3. Urinary Riboflavin		1.5	5.7	1.3
4. Serum Vitamin C		10.0	22.8	17.7
5. Serum Vitamin A		3.2	1.2	-
6. Serum Calcium		2.2	-	0.0
7. Transferrin Saturation		31.9	26.4	25.1
8. Serum Folate		44.8	73.0	70.0

Note: According to the standards established by the Recommended Nutrient Intakes for Canadians (1983), the average daily energy requirements for pregnancy, and for females 10-19 years and 20-39 years are 2,200-2,500 kcal, 2,100-2,200 kcal and 1,900-2,100 kcal, respectively. Over 50 percent of the pregnant women and 10-39 year old females surveyed by Nutrition Canada in BC had a lower energy intake than the recommended average (50th percentile pregnancy: 2,071 kcal; 25th percentile pregnancy: 1,589 kcal; 50th and 25th percentile 10-19 year age group: 2,091 and 1,627 kcal respectively; 50th and 25th percentile 20-39 year age group: 1,661 and 1,281 kcal). Over 25 percent of the pregnant women surveyed consumed less than the average recommended intake of protein. Equal to larger proportions of women did not meet the average recommended intakes for vitamins and minerals such as Calcium, Iron, and Vitamin D.

It can be seen from this table that at least 11-21 percent of the pregnant women surveyed and 10-34 percent of the women of childbearing years had levels of protein and caloric intakes that were inadequate according to established standards (Canada, 1983; Nutrition Canada, 1973). If these survey results are indicative of the current nutritional status of the BC population, the prevalence of nutritional problems is of major public health significance. This is examined further in chapter four.

The general lack of information on the nutritional status of the BC and most other populations has created long standing problems in the evaluation of nutrition intervention strategies aimed at improving reproductive outcome (Bonham, 1983; Kotelchuck et al., 1984; Rush, 1974)

Alcohol and Reproductive Health

Observations of an association between maternal alcohol exposure and adverse productive outcome were recorded by the early Greeks, by a report to the British Parliament in the 1700s, and by a British researcher in the late 1800s (Warner & Rosett, 1975). During the early 1900s, the focus shifted from maternal exposure to social environment as the probable explanation for the disadvantaged developmental status of the children of alcoholic parents. It was not until the late 1960s and early 1970s, when Lemoine and colleagues (1968) and Jones and colleagues (1973) independently described a malformation syndrome found in offspring of female alcoholics, that alcohol was once again suspected

as a human teratogen. These clinical reports provided the stimulus for a number of major epidemiologic and experimental studies over the past 10 years—the results of which will be reviewed in this section.

The description of a distinct, although phenotypically variable syndrome, called the Fetal Alcohol Syndrome [FAS], has led to wide acceptance of the teratogenicity of alcohol. Based on this assumption, studies have focused on the mechanisms of action, clarification of critical dose and time of exposure, and the influence of other environmental or genetic factors on the teratogenic effect of alcohol.

Henderson and colleagues (1981) have recently reviewed the animal literature pertaining to the pathogenesis of FAS in terms of the factors and specific mechanisms which could influence its development. The authors extend the definition of FAS to include resorptions in utero (analogous to spontaneous abortion in humans), stillbirth and/or growth and development impairment. Mention is also made of the association between alcohol exposure and infertility in animals (i.e., decreases serum estradiol and progesterone and causes atrophy of the ovaries, uterus and fallopian tubes in females, decreases serum testosterone and produces symptoms of hypogonadism in males) which appear to be due to a direct gonadal effect and to suppression of the hypothalamic-pituitary-gonadal axis (Cicero & Badger, 1977; Kakihana & Butte, 1979; Van Thiel, Gavalier, & Lester, 1978; Van Thiel et al., 1980).

Factors known to have the potential to affect FAS expression include: ethanol and its metabolites, impaired nutrition, and other drugs (Henderson, 1981).

The investigation of the role of ethanol versus its metabolites in animals strongly suggests that ethanol per se, and most likely acetaldehyde, is toxic to the fetus. Dose dependent effects observed include resorption, significantly reduced size of offspring, and decrease in total DNA and protein content (Brown, Goulding, & Fabro, 1979; O'Shea & Kaufman, 1979). A combined toxic effect of alcohol and acetaldehyde on mitochondrial protein synthesis has been demonstrated (Burke & Rubin, 1979).

Since alcoholism is often accompanied by malnutrition, studies have examined the possible contribution of impaired nutrition to FAS. Specific nutrition deficiencies in animals have been shown to cause fetal resorption, stillbirths, impaired growth and development, and fetal malformations. Poor nutrition in alcoholics may be due to poor intake, decreased absorption, impaired tissue utilization of nutrients, and/or impaired placental transport of nutrients. While both animal and human studies suggest that alcohol causes FAS and malnutrition is not an essential component, it is likely to contribute to the syndrome (Brown, Goulding, & Fabro, 1979; Henderson et al., 1979).

Both heavy coffee consumption and cigarette smoking are also associated with excess alcohol consumption. Large doses of caffeine are teratogenic in animals (Mulvihill, 1973) but human research (re miscarriage and prematurity) is inconclusive. Caffeine metabolism, however, is significantly impaired in pregnancy (Neims, Bailey, & Aldridge, 1979) and the multiple metabolic effects of caffeine do have

the potential for influencing fetal development (Weathersbee & Lodge, 1977). The growth retarding effects of excess alcohol on the newborn can be statistically separated from those of smoking and suggest at least an additive effect. The interaction of other drugs with ethanol has been insufficiently studied.

The specific mechanisms of FAS are unknown, but those that have been most studied include: a mutagenic effect; impaired protein synthesis; hormonal changes; and abnormal neurotransmitter status (Henderson et al., 1981).

The mutagenic effect of alcohol has been reviewed by Obe and Ristow (1979) who conclude: that animal data show inconclusive evidence of a mutagenic effect of ethanol or paternal influence on fetal outcome (Obe, Ristow, & Herha, 1979; Tanaka, Suzuki, & Arima, 1982); acetaldehyde and formaldehyde are seen to be mutagenic; alcoholics have a higher rate of chromosomal aberrations compared to non-alcoholics which may be due to alcohol metabolites or other associated factors such as poor nutrition or smoking; and because alcohols and aldehydes inhibit cellular and cell-free synthesis of RNA, this could help to explain the development of malformations.

There is suggestive evidence that ethanol inhibits protein synthesis (and degradation) in various adult as well as fetal and neonatal tissues, which could explain the alcohol-related growth impairment seen in animals and children with FAS. While there are numerous problems associated with the interpretation of these studies which have yet to

be resolved, the impaired protein synthesis mechanism has the most substantial documentation (Henderson et al., 1981).

Kakihana and colleagues (1979, 1980) have published an extensive review of the various hormonal changes, including altered growth hormone homeostasis, which have been reported following alcohol intake. Causal associations are difficult to determine because of the many other influencing factors (e.g., stress, temperature, nutrition).

It has been postulated that the effects of excess acute or chronic alcohol intake and its withdrawal on brain neurotransmitters in animals (Schenker & Liéber, 1982) may help to explain the intellectual and behavioral observations in children with FAS. The evidence regarding these effects and their relevance is not yet conclusive, and confounding by nutritional impairment has not been ruled out (Henderson et al., 1981).

In humans, the Fetal Alcohol Syndrome consists of four main features: (a) distinctive, abnormal craniofacial characteristics, including microcephaly, short palpebral fissures and midfacial hypoplasia; (b) prenatal and postnatal growth retardation; (c) central nervous system dysfunction including mental retardation, physiologic depression, irritability, and hyperactivity and poor coordination during childhood; and (d) various other congenital malformations. Neugut (1981), in an epidemiological appraisal of the FAS literature, points out that because (a) all but the first of the four features are associated with other determinants (e.g., maternal age, size, pregnancy

weight gain, smoking, other drug use, etc.) and (b) criteria for many of the unusual facial characteristics which provide an important basis for FAS diagnosis are not easily standardized, that systematic study of the effects of alcohol on reproduction must endure "blind", standardized assessment of mothers and infants, and adequate control for other known antecedent factors—particularly when the full clinical syndrome is not expressed. The minimum criteria for diagnosing FAS (e.g., presence of at least one FAS feature in areas of growth, CNS function, and craniofacial appearance) (Ouelette et al., 1977) allows for considerable variation in expression of the syndrome.

Little (1981), Streissguth (1978, 1981), and Clarke (1984), as well as Neugut (1981), have recently reviewed FAS research from an epidemiologic perspective. Study designs include prospective (cohort, longitudinal, and followup) and retrospective designs with populations primarily drawn from obstetric clinics and hospital maternity units. Alcohol use was determined through interviews and questionnaires, or medical record review, both of which were based on self-reported intake.

These authors identified three key areas of concern regarding the interpretation of the results of the studies, and determination of the effects of maternal alcohol intake on reproductive outcome, which include: (a) the wide variability in the definition, measures and criteria applied to exposure; (b) lack of consistency in the definitions, measures and criteria for outcome variables; and (c) inadequate control, because of study design, data availability and/or analysis, of the many other variables known to affect reproductive outcome.

Fertility

Although the association between alcohol and fertility have not been systematically studied, recent animal studies suggest an adverse effect on fetal development (decreased litter size and decreased body weight and/or decreased cerebral weight, cerebral DNA, RNA and leucine incorporation) may be related to paternal alcoholism (Tanaka, Suzuki, & Arima, 1982). A relationship between male ethanol intake and diminished rates of testosterone synthesis accompanied by aspermatogenesis (Klassen & Persaud, 1976; Murono et al., 1980), and the induction of dominant lethal mutations (Badr & Badr, 1975) had previously been recognized. Dominant lethal mutations have been regarded as imposing no genetic hazards on man (since they result in spontaneous abortion), but the potential of a wider range of paternal-related genetic effects linked to alcohol exposure suggests that human studies should consider the pattern of paternal alcohol (as well as maternal) intake in the 4-6 months preceding conception.

Spontaneous Abortion

The findings of studies that have specifically examined the association between maternal alcohol intake and spontaneous abortions suggest that such an association exists. In the Kaiser-Permanente Birth Defects Study (Harlap & Shiono, 1980), 32,019 women of the 34,344 women in the total study (designed to examine the relationship between birth control and reproductive outcome) completed a questionnaire on alcohol use (average number of daily drinks in the first trimester) at

their first antenatal visit. Exclusions included 680 women (2 percent) whose last menstrual period date was unknown; 1,482 (4.3 percent) who were recruited in the third trimester; and 104 (0.3 percent) whose alcohol use was not reported—no further information was provided concerning the possible bias resulting from these exclusions. The overall rate of spontaneous abortions in women seen from 5 weeks was estimated, by means of life-table analysis, to be 14.4–11.8 percent in the first trimester, and 2.6 percent in the second. The percentage of women under observation at the 8th, 12th, 16th, and 20th weeks were 5 percent, 48 percent, 79 percent, and 89 percent, respectively. Drinkers tended to begin antenatal care later than non-drinkers. Expected outcomes were, therefore, calculated using woman-days of observation.

Approximately half of the women (51.7 percent) reported drinking no alcohol in early pregnancy; 44.7 percent had less than one drink daily; and 2.4, 0.4, and 0.1 percent had a daily average of 1–2, 3–5, and 6 or more drinks, respectively.

There were 1,503 spontaneous abortions, 714 in the first trimester, (5–14 weeks) and 789 in the second trimester (15–27 weeks). Regular drinkers taking one or more drinks daily had more spontaneous losses, mainly during the second trimester. Occasional drinkers differed little from non-drinkers. Life-table analysis showed that the age-adjusted relative risks of second trimester losses were 1.03 (95 percent confidence limits, 0.57–1.86) for occasional drinkers, 1.98 (1.04–3.77)

for women taking 1-2 drinks/day, and 3.53 (1.77-7.01) for women taking 3 or more drinks per day. No significant effect of alcohol on first-trimester miscarriages was found. When all drinkers were compared with non-drinkers, the relative risk was 1.10 (0.61-1.98). The authors suggest the results should not be taken to imply with certainty that alcohol has no effect in the first trimester, since it is difficult to assess whether the women who initiated antenatal care early in pregnancy could have biased the results by being at higher risk for miscarriage.

Within subgroups of other variables associated with second trimester miscarriage, regular drinkers had a consistently higher risk. Regular drinkers were more likely to be smokers and to have taken drugs in early pregnancy (penicillin, valium, librium, hypnotics, antihistamines, aspirin, and Bendectin). Smoking was found to be an independent risk factor for spontaneous abortion (significant only in the second trimester for those smoking more than 2 packs per day; RR:2.02, 1.01-4.02), but the effect of drinking was greater than that of smoking. With regression analysis, the authors calculated that about 69 (10 percent) of the 690 second-trimester abortions in the study could be attributed to the effects of drinking or smoking.

In a second study (retrospective case-control), Kline and colleagues (1980) compared the frequency of drinking alcohol among 616 women who aborted spontaneously (cases) with the frequency of drinking among 632 women who delivered after at least 28 weeks gestation (controls). Cases comprised 80 percent of a consecutive series of 1,899 spontaneous

abortions occurring to public patients at three Manhattan hospitals. Twenty percent of the cases either refused to participate or could not be traced for interview—these women were similar to the women who were interviewed except their mean age was one year older and gestational age was slightly longer (8.7 days). Controls were matched by age at last menstrual period and by hospital, and were eligible if registered for prenatal care before 22 weeks and delivered no earlier than 28 weeks. Of the 1,053 eligible controls, 909 (86 percent) agreed to be interviewed. Uninterviewed women differed slightly in age, ethnic and marital status. Only 657 case-control pairs met the study criteria of both being 15-40 years of age, contributing only one pregnancy to the series, consenting to an interview and not using heroin or methadone. Those excluded did not differ significantly from the study pairs. Controls (38 percent) were more likely to be on welfare than cases (28 percent) and were interviewed an average of 22 days later (relative to date of last menstrual period).

Information on type, frequency, and amount of alcohol consumed during and before pregnancy was obtained by interview. The relationships between alcohol use, the control variables and spontaneous abortion were examined by maximum-likelihood logistic regression methods. Cases (17. percent) were more likely than controls (8.1 percent) to drink twice a week or more. The adjusted odds ratio (adjusted for age, stage of gestation and prepregnancy drinking) was 2.62 (95 percent confidence limits: 1.62-4.24). A dose-response effect was seen. Both

drinking before pregnancy and drinking during pregnancy showed independent, statistically significant associations with spontaneous abortion but when the overlap between the two patterns of drinking was controlled for, only drinking during pregnancy remained significant. The size of the association between alcohol exposure and spontaneous abortion was not altered by controlling for any of nine potentially confounding variables (gestational age, smoking, previous spontaneous abortion, and nausea/vomiting; maternal age, race, pregravid weight, marijuana use, and caffeine use).

Each beverage (twice/week or more) was significantly associated with spontaneous abortion. The adjusted odds ratio for wine, independent of the effects of beer and spirits, was 3.15 (1.53-6.51); for beer was 1.58 (1.02-2.44) and for spirits was 2.26 (1.13-4.51). Based on the assumption that cases and controls did not substantially under report their alcohol intake/occasion, the data suggest that a dose of at least one ounce of absolute alcohol twice a week or more is the minimum threshold for producing an abortion. The data also imply that alcohol causes spontaneous abortion by acting as an acute fetotoxin (rather than as a teratogen or abortifacient), and that the fetus is highly sensitive to alcohol throughout the first and second trimesters.

The medical-record prospective cohort study of 12,127 pregnancies carried out at Cleveland Metropolitan General Hospital (Sokol, 1981), although not designed to examine spontaneous abortion in the study

pregnancy, found that women whose charts identified them as alcohol abusers were more likely to have had a history of spontaneous abortions than other study women. An increased rate of spontaneous abortion or prior history of spontaneous abortions in "drinkers" compared to "non-drinkers" has also been reported by Mau and Netter (1974) and Warburton and colleagues (1979), but not by Kaminski and colleagues (1981) or Seidenburg and Majewski (1978) or Silva and colleagues (1981).

Stillbirths and Neonatal Mortality

In a prospective study of 9,236 pregnancies in the main public hospitals of Paris, Kaminski and colleagues (1978) found a significant excess of stillbirths among the 5.5 percent of women who drank more than 40 cl of wine (or the ethanol equivalent). In a following retrospective study of 3,193 births (representative sample of a national sample, France), a similar but non-significant trend was reported. This association seems not to have been examined in most studies, with the exception of Sokol and colleagues (1981) who found no association between alcohol abuse and frequency of stillbirth in either the index pregnancy or prior pregnancy history. Likewise, an excess of neonatal deaths has not been reported with the exception of two Swedish studies—one retrospective and one prospective (Olegard et al., 1979)—which followed 40 women (70 pregnancies) identified as alcohol abusers and measured infant outcomes against reference population standards. A lack of association between moderate or heavy alcohol intake and neonatal mortality was reported by Kaminski and colleagues (1981) and Sokol and colleagues (1981).

Birthweight, Fetal Growth and Infant Development

One of the most consistent findings of studies which have examined the relationship between maternal alcohol exposure and reproductive outcome has been the negative association between alcohol and birthweight.

In Boston, Ouellette and colleagues (1977) and Rosett and colleagues (1980) conducted a prospective study of the pregnancies of 633 inner city women with differing alcohol consumption patterns. This inner city sample was primarily non-white and unmarried and represented a very high risk group. Through a questionnaire administered at the time of registration for prenatal care, information was gathered as to past and present alcohol intake, smoking habits, drug use, and previous day's food intake. Infants of women who had delivered by the time the study terminated ($n = 322$) were examined. Thirteen percent of these infants were born to mothers considered to be heavy drinkers (at least 45 drinks/month and at least 5 drinks at a time on some occasion). In the group of infants born to heavy drinkers there was an excess of both premature and postmature births, a three-fold increased risk of being small-for-gestational age (birthweight, length, and head circumference were all affected), and a significantly higher percentage of both minor and major malformations. A "blind" pediatric examination at birth revealed congenital anomalies in 9 percent of the infants of light drinkers, 14 percent of infants of moderate drinkers, and 32 percent of infants of the heavy drinkers. The diets of the majority of the women were considered poor and although nutritional status was not

seen to vary significantly between the groups, the method of assessment reported makes such a conclusion questionable. Heavy alcohol intake was associated with heavy smoking during pregnancy and prior psychoactive drug use but neither variable was controlled for in the determination of the increased risk of abnormalities. No cases of fetal alcohol syndrome were reported. Reducing alcohol intake during pregnancy decreased the risk of adverse infant outcome.

In the Cleveland cohort study (Sokol et al., 1981) mentioned above, medical record data on 12,127 pregnancies indicated that 204 (1.7 percent) of these pregnancies were complicated by maternal alcohol abuse. Data on alcohol intake were not routinely collected by hospital staff but based on the percentage distribution of drinking status reported by other hospital based studies (Kuzma & Kissinger, 1981), the identified 1.7 percent correspond to the proportions identified by others to be drinking two or more ounces of absolute alcohol per day (range:1.1-1.7 percent). A comparison of the health profile, obstetric histories, and current pregnancy of the alcohol-abusing patients with these variables in the records of the study pregnancies with no mention of alcohol abuse found the following: the obstetric histories of the drinking women were marked by excesses of previous spontaneous abortions (RR:2.3), low birthweight infants (RR:1.5) and fetal anomalies (RR:4.2); the women were more likely to smoke cigarettes and abuse other drugs; during labor, their risks of infection and of premature placental separation were increased; evidence of fetal distress during

labor and neonatal depression were more common in their infants; infant birth weights were lower by an average of 190 g, which was accounted for by a 2.7 fold increase overall in intrauterine growth retardation. The relative risk of intrauterine growth retardation associated with alcohol abuse alone was 2.4; with smoking alone was 1.8; and in association with smoking and drinking combined, was 3.9. A significant increase in congenital anomalies (38 percent) above the total sample rate of 10 percent was identified but no differences were noted in mortality rates or placental pathology. The adverse infant outcomes did not appear to be related to demographic factors, the medical care, or nutrition (measured by maternal weight, height, pregnancy gain, and anemia); nor were the congenital anomalies related to smoking. The study yields an estimate of a 2.5 percent risk for FAS from pregnancies with heavy alcohol use. Neonatologists were not blind to the maternal drinking history. The findings of the Cleveland study suggest that alcohol abuse during pregnancy constitutes a significant risk for a range of adverse perinatal outcomes in as many as 50 percent of the infants of heavy drinkers.

The Seattle longitudinal prospective study on alcohol and pregnancy (Streissguth et al., 1981) began in 1974. An unselected sample of 1,529 women (predominantly white, married, and middle class) receiving prenatal care at two large Seattle hospitals during a one-year period (1974-75) were interviewed at mid-pregnancy regarding their use of alcohol, nicotine, caffeine, drugs, etc., prior to and during pregnancy.

Fifteen percent of the eligible women did not wish to participate. A followup cohort of 500 women was selected at delivery to include about 250 at risk drinkers (an average of one or more drinks/day) and about 250 infrequent drinkers and abstainers (the control cohort). Infants were blindly assessed at birth for FAS-related features. Infants judged abnormal due to "features compatible with FAS" represented 13 percent of the infants of women averaging two or more drinks per day and only 2 percent of the infants of women drinking less than this amount. Two infants were determined to have the full FAS syndrome (prevalence: 1/750).

The focus of the Seattle study is on the correlation between moderate to heavy alcohol use and infant behavior and intelligence. Interviews, questionnaires, and infant assessments, by clinicians blind to the mother's alcohol intake, were scheduled for 8 and 18 months, and at 4 years of age. At the time of the 18-month assessment, 11 percent of the sample were lost to followup, but the proportion of heavy versus non-drinkers did not change. Multiple regression statistical tests were utilized to permit adjustment for other possibly confounding factors. The infant outcomes significantly related to increased maternal alcohol use (adjusted for other variables) include: smaller infant size (birthweight, length, and head circumference); lower Apgar scores; poorer neonatal habituation; decreased sucking pressure; increased tremulousness; decreased vigorous activity; and a higher frequency of minor dysmorphic characteristics combined with low birthweight and microcephaly. Similar correlations between infant

behavior and moderate maternal alcohol intake were reported by Landesman-Dwyer, Keller, and Streissguth (1978) in a study of naturally-occurring behaviors of newborns. Streissguth also found a drinking by smoking interaction was related to poorer newborn operant conditioning. Significantly lower mental and motor development and lower length and weight were found on followup of 468 infants at age 8 months. Other reports by the Seattle researchers have found adverse behavioral effects (e.g., poorer attending behavior) at age four in children whose mothers were moderate drinkers during pregnancy (mean = <1 drink/day) and whose home environment was considered excellent using a standardized scale.

Findings from a continuing study of drinking habits and pregnancy outcomes in women attending Charing Cross Hospital in London have been reported by Wright and colleagues (1983). The relation between alcohol intake prior to and during pregnancy and birthweight was investigated prospectively in 900 white women. Information was gathered by physician interview at first prenatal visit (8-14 weeks), by cross-check questionnaire, and by medical and lifestyle history. Women were classified as heavy drinkers (100 g alcohol/week or more), moderate drinkers (50-100 g/week) and light drinkers (<50 g/week, including non-drinkers) on the basis of their prepregnancy intake. Social class, smoking, drinking level, and birthweight were interrelated. With adjustment for social class and smoking, women drinking more than 100 g alcohol/week had more than twice the risk (RR:2.33) of delivering

a baby on or below the 10th percentile than women drinking less than 50 g/week. The effect of alcohol was synergistic with that of smoking (R:3.43). The authors interpret the data as a relationship between birthweight and drinking around the time of conception. No benefits were seen with reduced intake during pregnancy.

Little and colleagues (1980) in a case-control study of volunteer subjects (100 women with a history of alcoholism prior to conception, half of whom continued to drink during pregnancy and half abstained totally; plus control groups of non-alcoholic women who drank very little during pregnancy) also found that history of alcohol abuse had an effect on birthweight independent of maternal alcohol use in gestation. The children of abstinent alcoholic mothers weighed 258 g less than children born to controls. This difference was not due to differences in maternal height, smoking, age, race, parity, gestational age, or sex of child. Although children born to abstinent alcoholics had essentially the same mean IQ as those born to drinking alcoholics (102 versus 101, respectively), when length of abstinence before conception was considered, a 10-point increase of IQ scores was estimated for offspring of alcoholic women abstaining for a year prior to conception. It is clear that the sample population may not be representative, but these results further emphasize the need to consider the effects of a preconception history of alcohol use—and, indeed, other preconception lifestyle factors—independent of maternal alcohol use during pregnancy.

Malformations

In her detailed epidemiological appraisal of the literature on fetal alcohol syndrome in humans, Neugut (1981) states that "the consistent findings of association between heavy in utero alcohol exposure and other untoward pregnancy outcomes is somewhat more impressive than is the case for FAS . . . disentangling the causal associations . . . [from] observed associations largely remained to be accomplished" (p. 426). In the author's opinion, data which are suggestive of both the existence of FAS as a distinct syndrome and of the causation of the syndrome by maternal alcohol include: (a) the congruence between the initial case reports of Jones and Smith (1973) and the anecdotal description of Lemoine and colleagues (1968) given the lack of awareness of each other's work until after the 1973 paper was published; (b) the scattered instances of blind diagnosis of FAS; (c) the photographic similarities of FAS children; and (d) the results of the studies of Hanson (1978) and Olegard et al. (1979).

In British Columbia, the incidence of fetal alcohol syndrome is estimated to be 1/1,000 live births (MacLeod, 1981) which represents approximately 40 new cases per year. The Native populations have been identified as a high risk group (Asante, 1981).

Prevalence of Alcohol Use in the Population

The most recent prevalence data for alcohol use in the Canadian population was collected as part of the Canada Health Survey, 1978-79 (see previous discussion of sample design, pp. 117-118) (Ottawa, 1981).

The information on alcohol consumption was collected from persons 15 years of age and over on a self-administered, confidential questionnaire. A response rate of 84 percent was achieved for the alcohol consumption section of the survey. Fourteen percent of the non-respondents did not answer any of the survey questionnaire—this type of non-response was distributed proportionately across the response categories and the population estimates were adjusted accordingly. For the remainder of the non-respondents who did not answer one or more of the questions in the alcohol section but completed other sections, the non-response is reported as unknown for each category.

Survey results show substantial variations by age and sex in alcohol consumption patterns as measured by "type of drinker" and "weekly volume of alcohol consumed." Most adults (65 percent) drink alcoholic beverages at least once a month. The proportions of current drinkers (drink alcohol at least once a month) were highest for 20-24 year olds (79 percent) and 25-44 year olds (73 percent). Men who were current drinkers outnumber female current drinkers by 25-42 percent (under 45 years-over 45 years) and are more likely to be heavy drinkers (14 or more drinks per week). In the 20-24 year old age group, 31 percent of men and 8 percent of women have 14 or more drinks per week. Alcohol consumption patterns show marked variation by major activity (occupation) and region. Working people are more likely to be current drinkers and heavy drinkers regardless of age and sex group. The proportion of current drinkers in the population increases steadily

from east to west in Canada—ranging from 55 percent in the Atlantic provinces to 73 percent in British Columbia—and the proportion of heavy drinkers shows the same pattern (15 percent in Atlantic provinces to 23 percent in British Columbia). The proportion of daily drinkers ranges from a low of 11 percent in smaller communities (under 100,000) to a high of 20 percent in urban centres of at least one million population.

The prevalence of regular alcohol consumption tends to increase with occupational status, with higher levels of education, and with higher income levels.

(Note: 14 or more drinks per week is not considered to be a hazardous level of consumption for the general population. Only very high levels of consumption—40 or more drinks per week—are unequivocally hazardous to health. The lower level would be considered a risk level for pregnancy, however.)

Table 12 below provides data from the Canada Health Survey, 1978-79 for drinking status and quantity of alcohol consumption by age and sex in Canada and in total, for British Columbia.

The prevalence of daily drinkers, estimated to range from 14-33 percent in the British Columbia population of childbearing years, is seen to be of public health significance. The implication of this level of lifestyle-risk exposure is discussed in the following chapter.

TABLE 12

Population 15 Years and Over by Type of Drinker and Weekly Volume of Alcohol Consumed, by Age and Sex, Canada and by Total Population, BC, 1978-79

Type of Drinker	BC		Canadian Population by Age Groups				
	15+	Total 15+	15-19	20-24	25-44	45-65	65+
	N	N	N	N	N	N	N
Total M & F	1,918	17,492	2,333	2,214	6,472	4,473	2,019
Male	N/A	8,584	1,187	1,106	3,230	2,174	887
Female		8,907	1,146	1,108	3,242	2,279	1,132
	%	%	%	%	%	%	%
Never Drank	8.4	11.5	18.3	5.3	5.9	12.8	25.5
Male		6.8	15.3	3.4	3.4	5.6	14.3
Female		16.0	20.8	7.2	8.3	19.7	34.2
Former Drinker	4.4	3.7	2.2	2.3	3.2	4.7	6.6
Male		4.4	1.3	2.1	3.5	6.2	10.0
Female		3.1	3.1	2.6	2.8	3.2	4.0
Occasional Drinker	10.5	15.1	16.1	11.3	16.0	13.7	18.2
Male		9.8	13.7	5.7	9.8	8.1	13.8
Female		20.2	18.5	16.9	22.2	19.2	21.6
Current Drinker	73.3	65.3	56.5	79.2	72.6	63.5	40.1
Male		75.2	60.7	87.2	81.3	76.5	53.9
Female		55.7	52.1	71.1	63.9	51.5	29.3
# drinks/week							
<1	7.7	7.7	9.6	10.3	7.8	6.2	5.8
Male		6.8	10.1	7.3	5.8	6.0	6.7
Female		8.7	9.1	13.2	9.8	6.4	5.0
1-6	25.5	26.2	23.1	31.0	31.2	24.7	11.9
Male		24.9	22.5	25.5	28.2	25.5	13.9
Female		27.5	23.7	36.4	34.1	24.1	10.4
7-13	16.7	13.2	10.6	16.3	15.2	12.7	7.3
Male		17.1	11.2	20.8	19.4	17.1	11.9
Female		9.4	10.2	11.8	10.9	8.6	3.7
14+	16.8	12.0	9.1	19.6	13.3	10.8	5.1
Male		19.4	12.6	31.0	21.6	18.0	9.6
Female		4.8	5.5	8.1	5.0	4.1	1.6
Unknown	-	6.2	4.0	2.1	5.2	9.1	10.0
Type of Drinker Unknown	3.5	4.4	6.9	1.9	2.3	4.9	9.6

Source: Adapted from Canada Health Survey, Table 1 and 2, pp. 28-30 (Ottawa, 1981).

CHAPTER IV: THE PREVENTABLE PORTION OF REPRODUCTIVE CASUALTIES

The preceding two chapters have provided a detailed examination of (a) the outcome measures of reproductive performance that, as a composite, can provide a meaningful description or profile of the level of reproductive health in a community; and (b) the evidence that paternal and maternal lifestyle habits affect these reproductive health outcomes and, thus, play a role in determining the level of reproductive health in a community.

This chapter will assess the evidence presented in chapter three against established criteria for causal association; will discuss the implications of this assessment for health planning in British Columbia; will recommend methods for improving health information and surveillance techniques as they pertain to reproductive health in the province; and will identify the benefits likely to be associated with these recommendations. In doing so, the chapter will focus on a number of specific questions that, for practical purposes, require answers: Is the evidence sound enough to warrant the current health promotion message? Is the evidence sound enough to warrant action beyond a health promotion message? Is it possible to estimate a preventable portion of reproductive casualties based on lifestyle change? Do we have enough information to estimate the "preventable portion" for British Columbia?

The Effect of Lifestyle: Review of Evidence

The literature on reproductive health and lifestyle, of which only a representative portion could be presented in this study, leaves the reader with little doubt that an association exists between these two factors. Whether the association is causal, however, is not so easily determined. Even in applying the relatively straightforward "germ theory" (single cause, single effect) one recognizes that although the presence of a specific germ is a prerequisite for a specific disease (e.g., tubercle bacillus for active tuberculosis), factors such as host resistance and nutritional status can determine whether the disease will or will not occur. Because of this, causal associations must inevitably be assessed in relative terms—at some point, the evidence is considered strong enough to entail action.

The accepted criteria for assessing causal association, based on the original work of A. Bradford Hill (1971), requires a review of the evidence in terms of the following: experimental confirmation; the strength of the association between suspected "cause" and the outcome(s) of interest; consistency of observed evidence; temporality of the relationship; demonstration of dose-response; biological plausibility; specificity of the relationship; and coherence of the evidence (Gehlbach, 1983). An explanation of these criteria and an assessment of the causal association between lifestyle factors (e.g., smoking, nutrition, alcohol, drugs, stress) and reproductive health

outcomes using these criteria is presented in the following section. Studies to be used as evidence in this type of assessment have been critiqued in terms of meeting standards for reliability and validity of exposure and outcome measures, and in terms of how the research design and implementation meets criteria for internal validity (Campbell & Stanley, 1966; Shortell & Richardson, 1978; Weiss, 1972). Issues of reliability and validity associated with lifestyle and reproductive health studies are discussed in chapters two and three.

Criteria for Assessing a Causal Association

1. Experimental evidence in humans. By this criterion, the strength of the evidence is determined by the experimental method used in studies appropriately designed for the setting and hypothesis. In descending order of strength, the best evidence comes from a randomized control trial, a prospective cohort study, a retrospective cohort study, a case-control study, a quasi-experimental design study which lacks a control group and the weakest evidence from case studies. Only two randomized control studies were found for review—the diet supplement study conducted by Rush and colleagues (1974) and a recently published smoking intervention study by Sexton and Hebel (1984). Unfortunately (from the perspective of assessing causal association), randomization of lifestyle variables is seldom feasible, and where feasible, is generally considered unethical.

Prospective cohort studies provide evidence of an association between each lifestyle and reproductive health variable selected for review, with the exception of nutrition and infertility where the cohort study (Stein et al., 1975) was a retrospective analysis of prospectively collected data. Without the benefit of evidence from randomized trials, it is particularly important that the design or analysis of cohort studies adequately control for confounding variables. In general, variables known to affect reproductive outcome were controlled by analysis. Potential interaction or intercorrelation between lifestyle variables remains an unresolved issue that has not been adequately studied.

2. Strength of the association. By this criterion, strength of association is measured by the level of risk associated with exposure. In the case of randomized trials or cohort studies, this can be calculated directly by comparing outcome rates in the exposed and nonexposed populations. For case-control studies risk can only be estimated by indirect methods (relative odds) since the study groups are not represented in relation to their prevalence in the total population. The relative risks reported for the reviewed cohort studies are summarized in Tables 13, 14, and 15. Where relative risks are not reported, relative odds or statistical measures of significance are provided in the summary tables. Each of the lifestyle factors is similar in that the relative risk of any specific reproductive casualty with exposure is fairly low (on average, RR:1.6-3.0) but appears to be a true risk (i.e., 95 percent confidence limits do not include 1.0).

3. Consistency of the observed evidence. By this criterion, consistency is high when an association between exposure and outcome is repeatedly demonstrated by different investigators, in different studies, different populations and settings. The most striking aspect of the lifestyle and reproductive health literature is the consistency with which small, but independent associations between each of the lifestyle factors and each of the reproductive health outcomes are reported. This repeated demonstration of a lifestyle effect provides one of the strongest arguments for a causal association.

4. Temporality of relationship. The test of temporality is that the exposure is known to occur prior to the outcome. In the case of reproductive outcomes where there tends to be a sequence of related events leading to the measurable outcomes, it is not always possible to identify the beginning of the sequence (i.e., is the outcome related to the preconception period, embryogenesis, or mid-pregnancy development). The test of temporality is most easily applied in situations where lifestyle patterns are reasonably consistent over the period of reproductive function under investigation. For example, a sequence of events related to a chronically inadequate dietary intake rather than short term nutrient imbalance, or a regular daily alcohol abuse pattern as opposed to binge drinking, is more readily assessed in terms of temporality. Given our current understanding of individual lifestyle patterns, the association between population lifestyle patterns and sociodemographic variables (e.g., social class, economic status, level

of education), and the fit between the timing of lifestyle changes and the type of reproductive outcome changes that result (e.g., a mid-pregnancy change in lifestyle can be expected to modify third trimester fetal growth but not abnormal embryonic development that has already occurred), the temporal relationship seems appropriate.

5. Dose-response. The dose-response criterion requires demonstration of increasing risk or severity of outcome associated with increased amount (dose) or duration of exposure. In a number of ways, the lifestyle-reproductive health association appears to meet this criterion. First, increased risk is seen to occur at increased levels of exposure (e.g., the risk of low birthweight is increased with heavy smoking compared to moderate smoking, or in association with a very poor diet versus a moderately inadequate diet), once a minimal level of exposure (or threshold) has been exceeded. Where a significant dose-response association is not demonstrated, a trend is usually reported. Second, decreased risk is seen to occur with decreased levels of exposure. Third, increased risk is associated with increased exposure in terms of the total number of different lifestyle variables involved. And in a more speculative vein, there appears to be an association between level and duration of exposure in the population and the degree of impairment of reproductive function per se (i.e., reflected by the number of different reproductive outcomes that are adversely affected). Thus, at various different levels of investigation, a dose-response gradient characterizes the association between lifestyle and reproductive outcomes.

6. Biological plausibility. By this criterion, current biological knowledge (i.e., current understanding of the responses of cells, tissues, organs, and organisms to stimuli) must be reconcilable with the notion of causal association. The McMaster Series (1981) suggests this is the yardstick against which nonhuman experimental data should be measured.

A cause and effect relationship between each of the specific lifestyle variables and each measure of reproductive function has been demonstrated in animal research under precisely controlled conditions. The causal association pertains to both male and female animals, and effects include impairment of the reproductive system, mutagenesis, chromosomal aberrations, fetal absorptions, stillbirths, fetal growth retardation, reduced litter size, birth defects, neonatal death, growth and development disorders, and impairment of reproductive function in subsequent generations. Summary reviews of this research, and/or the implication of the results of this research for the human population, are numerous (see e.g., Abdul-Karim, 1981; Bora, Douglas, & Nestmann, 1982; Council on Environmental Quality, 1981; Klingberg & Weatherall, 1979; Obe, 1984; Rechcigal, 1981; Schwartz & Yaffee, 1979; Wilson & Fraser, 1977; Wynn & Wynn, 1981). It is precisely because of the evidence that such wide ranging and long reaching effects on reproductive health in animals could be attributed to nutrient deficiencies, stress, drugs and chemicals, nicotine and alcohol that an understanding of the lifestyle effect on human reproduction is considered so important. Plausibility is enhanced by the observation that a similar range of

reproductive casualties can occur in human populations when levels of exposure are high (e.g., famine and starvation).

Animal and human pathology studies provide evidence of the manner in which fetal growth or placental function is adversely affected by lifestyle variables (see, e.g., Beaconsfield & Birdwood, 1982; Naeye, Kissane, & Kaufman, 1981). Studies of human and animal cell and tissue cultures provide evidence of alteration and limitation of cell replication which continue to help in the determination of plausible mechanisms of action (see, e.g., Chandra, 1980; Fehr & Kalant, 1983; Metcalf, 1981).

The test of biological plausibility based on animal and "in vivo" research appears to be met without difficulty. It is the degree to which inferences about human reproduction may be drawn from the results of animal or "in vitro" studies (or from studies where levels of exposure are thought to differ significantly from those in the average population) that has not been fully clarified.

7. Specificity of the relationship. To meet this criterion, a single cause-single effect association must be demonstrated. However, it is clear from animal research (where the causal variables are controlled) that a wide variety of different lifestyle factors can cause a similar range of specific reproductive casualties—as can "biological" or genetic factors and environmental toxins. Evidence from human studies demonstrates the same lack of specificity at these levels of outcome measurement, including lack of specificity in terms

of the magnitude of the association. As well, it is known that adverse effects of lifestyle factors are not limited to reproductive health outcomes and that factors other than lifestyle effect reproductive health. The McMaster Series (1981) suggests the test is "only moderately useful—and, even then, only when (the) illness is present." "The weakness of this test," say the authors, "is underscored when you consider that teratogens commonly have multiple effects in several organ systems" (p. 989). Hill (1971) states: "We must not, however, over-emphasize the importance of the characteristic" and must "keep in mind that diseases may have more than one cause" (p. 317). It may be that the test of specificity is inappropriate in this situation or it may be that specificity will be recognized at a more precise level of measurement, perhaps associated cellular function, or by cause of mortality or type of fetal growth retardation if appropriate data are collected. Support for the possibility that specificity might be elucidated through the use of more precise and detailed outcome measures than those chosen for this thesis is provided by studies of the effects of lifestyle factors on fetal growth parameters (see, e.g., Miller & Merritt, 1979) and on maternal weight gain, placental development, and neonatal physical and behavioral characteristics (Picone, Allen, & Olsen, 1982; Picone, Allen, & Schramm, 1982).

8. Coherence of the evidence. Hill (1971) explained coherence by saying the cause and effect interpretation should not seriously conflict with the generally known facts of the natural history and

biology of the disease (outcome). Another way to consider this criterion is to determine if the interpretation makes epidemiological sense (McMaster Series, 1982)—i.e., is in agreement with current understanding of the distributions of causes and outcomes in humans. In general terms, coherence requires supporting evidence from different levels of organization—i.e., ecological evidence as well as evidence from clinical and cohort studies.

Since variation in reproductive outcome can be attributed to changes in other factors besides lifestyle, the assessment of coherence is dependent on adequate knowledge of the other confounding factors and the potential for ecologic fallacy. Most attempts to assess coherence from an historical perspective or by comparisons between different countries or populations must be based on some degree of assumption that is open to the challenge of an alternate interpretation. For example, the proportion of low birthweight infants (weighing less than 2,500 g) in Finland has recently dropped from a plateau around 5 percent of annual live births to 3.7 percent in 1983, the lowest reported national low birthweight statistic in the world (Leppo, 1984). It is the opinion of the Director of Planning of the Finnish National Board of Health that the recent reduction in low birthweight infants reflects the fact that the earliest recipients of a comprehensive health promotion program for youth are now of childbearing age and, thus, he attributes the improvements in reproductive outcome to improved lifestyle habits and level of health of the younger parents. If corroborated, this occurrence would provide an excellent illustration

of coherence. Support for the Finnish interpretation will increase if low birthweight continues to fall in relation to an increase in the proportion of new parents who have participated in the health program for youths, and if no alternate explanations seem more appropriate.

Generally speaking, when sufficient information on lifestyle patterns, reproductive outcome, and other variables known to affect these outcomes is available, the causal interpretation has coherence. A typical example would be the positive relationship between improved reproductive outcome and improved standard of living (which implies improved nutrition and health) whether it be a time trend or a between-country analysis. Beaton and Bengoa (1976), in discussing the association between malnutrition and mortality throughout the world, distinguish between the effect of a change in factors which "precipitate" acute malnutrition (e.g., diarrhoea and infectious diseases superimposed on chronic undernutrition) versus a change in factors that "condition" malnutrition (agricultural policy, geographical conditions, biological nature of a population's staplefoods). A decrease in mortality may be achieved by a reduction in either the factors which "precipitate" malnutrition or "condition" it or both, but for each type of change different community parameters may be observed. The 50 percent decline in mortality that occurred 50-100 years ago in the now developed countries took a century to accomplish, was largely attributed to the improvements in living conditions and nutritional status, and was associated with improved health status of the surviving population.

The 50 percent decline in mortality recently achieved in developing countries in 1/10th-1/5th the time span has been largely attributed to improved health care services, but because real improvements in standard of living or nutritional status have not occurred, increased survival has not been accomplished by increased levels of health or by improved physical and mental potential (Bengoa, 1972). This is an analogous situation to the effects of different methods employed in reducing infant mortality (i.e., improved perinatal care of very small infants compared to increased birthweight through improved maternal health). If the lifestyle habits of a population are factors which "condition" reproductive performance, lifestyle modification should affect a broad spectrum of reproductive health outcomes as is indicated by the research literature.

Rating the Evidence

An attempt has been made in Tables 13, 14, and 15 to introduce a standardized method of rating the evidence of a causal association between nutrition, smoking, alcohol, and the specific reproductive health variables reviewed for this study, using the above set of criteria. This seemed a necessary step given the volume of literature to be considered and the difficulty of maintaining a consistent approach to assessment if specific guidelines were not identified. The method uses deliberately conservative (although at times admittedly arbitrary) guidelines as the best means of ensuring the legitimacy of an interpretation of causation. The rationale for the rating method and scoring system is described in detail below, followed by summary tables

of lifestyle and reproductive health associations using this rating method and an assessment of the effect of alternate choices of inclusion and weighting of criterion.

1. Inclusion and weighting of criteria categories. Three references (Gehlbach, 1983; Hill, 1971; McMaster Series, 1982) were used to determine the criteria considered most important to accepting a causal association. Strength of association and consistency of evidence were highly ranked by all three and because of this, both were considered essential criteria. An evaluation of the quality of experimental evidence from human studies was considered by the McMaster article to be a prerequisite to including specific study results in a causal association assessment (i.e., how the results were derived determine their value as evidence) and a means of ranking the results from included (i.e., well designed) studies. By this rationale, meeting the test of experimental design was considered essential. Biological plausibility was ranked highly by Gehlbach, but not demanded by Hill and McMaster if biological knowledge was inadequate. Since in this case, biological knowledge is adequate and non-human research has been conducted with the specific intent of clarifying issues that cannot be researched in humans (i.e., exposure to toxins, imposed nutrient deficiencies), biological plausibility was considered essential.

Two other criteria—dose response and coherence—were rated as supportive, in that they added further clarification to the assessment of strength of association and biological plausibility, respectively.

The lifestyle-reproductive health associations were evaluated for specificity and temporality and, without exception, temporality was sufficiently demonstrated and specificity was not. Since the scores for these two criteria, also considered to be "supportive", would cancel one another out using this rating method, they are not included in the summary table. The effect of including or not including them will be considered.

2. Scoring between criteria categories. Maximum scores of 5 were assigned to each of the four criteria considered to be essential to the determination of causal association—experimental design, strength of association, consistency of observation, and biological plausibility. The "supportive" criteria—i.e., dose-response and coherence—were assigned a score of 2. Since there is a noticeable difference in the amount of research attention given to some lifestyle-reproductive outcome relationships compared to others, 1 point is subtracted from the score in areas where bias may be introduced because of the limited number of studies available for review.

3. Scoring within criteria categories. The within-category scoring was designed to identify differences in the degree to which the evidence supports a causal association. Since there is no known precedent for assigning such scores, and because the rationale for assigning a score differs for each criterion, the guidelines are detailed below:

(a) Experimental design. A decision was made, based on the argument of the McMaster Series, that a maximum score of 5 would not

be assigned unless a randomized trial, supporting a causal association, had been carried out. To clearly discriminate between this level of evidence and that of a cohort design or a case-control study, 2 points separate these two levels. Therefore, if the strongest evidence is provided by a prospective cohort design, the score given is 3; if the strongest evidence comes from case-control studies, the score given is 2; and if the strongest evidence comes from quasi-experimental design studies, the score given is 1. This evidence must be supported by a number of studies of the same ranking and at a lower ranking—where the extent of this support is limited by number of studies this is recognized by reducing the score by 1 point prior to tally and where the support is limited due to consistency of observation, this is recognized by the scoring within that category. No points are given if the strongest evidence is provided by case studies.

(b) Strength of association. Maximum points (5) are given in this category if a substantial "real" difference is seen in cohort or randomized trial studies as demonstrated by a relative risk greater than 4 and 95 percent confidence limits that do not include 1.0; 3 points are given when this difference provides a relative risk between 2 and 4; 2 points are given for a relative risk of less than 2; and 1 point is given if a statistically significant difference is reported (e.g., $p < 0.01$) without relative risk (and there is insufficient data to make this calculation).

(c) Consistency of observation. Maximum points (5) are given in

this category if all major studies support an association between lifestyle and a reproductive outcome; 3 points if the majority of studies report an association but at least one well designed study (and highly ranked in terms of experimental design) shows no association, and 0 points if well designed studies report mixed results. Since both the research design and the conceptual design are considered when selecting the studies to be "rated", it is recognized that the consistency of observation scoring may be biased by the interpretation of a "well designed" study.

(d) Dose-response gradient. Two points are given in this category when a dose-response relationship has been studied and demonstrated, and 0 points where this relationship has not been studied or is not demonstrated.

(e) Biological plausibility. Maximum points (5) are given in this category if a broad range of studies (e.g., animal, cell, tissue, organ) have been conducted which support the association (i.e., provide rationale or a potential mechanism of action) between the lifestyle factor and the reproductive outcome of interest; 3 points are given where biological explanations for causal association are reported but in a limited range of studies; and 0 points given if biological support for the association has not been demonstrated.

(f) Coherence. Coherence is rated either good (2 points) or not (0 points). If there seemed to be insufficient information to allow an assessment of coherence, this is noted.

4. Summary score and rating category. Five summary categories were developed to identify subtle differences in the strength of evidence for a causal association. For example, the score indicating the strongest evidence for causal association could not be reached without maximum points in 3 of the 4 essential criteria. Since randomized trials have not been carried out and relative risks are low to moderate in all outcome categories, the highest rating could not be achieved. The rating scheme allows for three other categories in which the strength of evidence is perceived to be sufficient to merit attention as a potential causal association. In these categories, the degree of support is indicated by the descriptors—probable, suggestive, and possible—which relate to the total scores assigned to the evidence for a causal association and percent of total achievable score. A threshold score of 60 percent of the total achievable score was arbitrarily established below which it was considered there was insufficient evidence to support a causal association. These lower scores seem mainly to reflect the limited investigation of the particular lifestyle-reproductive health association in human populations and, thus, do not in themselves rule out a causal association. The summary categories and scores (out of a total of 25 points) were assigned as follows:

23-25 points (90-100% of total)	Causal Association
20-22 points (80- 90% of total)	Causal Association, probable
18-19 points (70- 79% of total)	Causal Association, suggestive
15-17 points (60- 69% of total)	Causal Association, possible
<15 points (<60% of total)	Evidence lacking for Causal Association

This rating scheme is illustrated in Tables 13, 14, and 15 below.

TABLE 13

Smoking and Reproductive Health—Summary of Evidence for Causal Association Between
Smoking Exposure and Seven Reproductive Health Outcomes, Based on Seven Criteria

Criteria for Causal Association	Infertility	Spontaneous Abortion	Stillbirth	Infant Mortality	Fetal Growth Birthweight FGR	Congenital Anomalies	Morbidity:Growth & Development
1. Experimental Design (Strongest Evidence)	5 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies
2. Strength of Association (Relative Risk Range)	5 Significant RR:1.6-2.3	3 Significant RR:1.8-2.0	2 Significant RR:1.2-1.6	2 Significant RR:1.2-1.6	3 Significant decrease RR:1.8-2.0 130-300g	1 Significant (p value only)	1 Significant (p value only)
3. Consistency of Evidence	5 Good	3 Fair	3 Fair	3 Fair	5 Good	0 Poor	5 Good
4. Dose-Response Gradient	3 Yes	2 Yes	2 Yes	2 Yes	2 Yes	0 No	1 Yes
5. Biological Plausibility	5 High	5 High	5 High	5 High	5 High	3 Moderate	5 High
6. Coherence	2 Good	2 Good	2 Good	2 Good	2 Good	1 Information Limited	2 Good
7. Limited Number of Studies	-1	-1				-1	-1
8. Summary Score Percentage Rating Category of Causal Association	19/25 76% Probable	17/25 68% Suggestive	17/25 68% Suggestive	17/25 68% Suggestive	20/25 80% Probable	7/25 28% Evidence Lacking	16/25 64% Suggestive

TABLE 14

Nutrition and Reproductive Health—Summary of Evidence for Causal Association Between Exposure to Poor Nutrition and Seven Reproductive Health Outcomes, Based on Seven Criteria

Criteria for Causal Association	Infertility	Spontaneous Abortion	Stillbirth	Infant Mortality	Fetal Growth Birthweight FGR	Congenital Anomalies	Morbidity:Growth & Development
1. Experimental Design (Strongest Evidence)	5 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies	3 Prospective Cohort Studies
2. Strength of Association (Relative Risk Range)	5 Significant (r value only)	1 Significant (RO:7.9)	3 Significant RR:1.7-3.9 (RO:8.9)	3 Significant RR:1.8-2.1	3 Significant decrease RR:1.6 50-300 g LBW-RR:1.9-2.5	1 Significant (RO:8.7)	1 Significant (p value only)
3. Consistency of Evidence	5 Good	5 Fair	3 Fair	5 Good	3 Fair	0 Poor	3 Fair
4. Dose-Response Gradient	3 Yes	2 Yes	2 Yes	3 Yes	3 Yes	0 No	2 Yes
5. Biological Plausibility	5 High	5 High	5 High	5 High	5 High	5 High	5 High
6. Coherence	2 Good	2 Good	2 Good	2 Good	2 Good	1 Information Limited	2 Good
7. Limited Number of Studies	-1	-1	-1			-1	
8. Summary Score Percentage Rating Category of Causal Association	17/25 68% Suggestive	15/25 60% Possible	17/25 68% Suggestive	21/25 84% Probable	19/25 76% Probable	9/25 36% Evidence Lacking	16/25 64% Suggestive

TABLE 15

Alcohol and Reproductive Health—Summary of Evidence for Causal Association Between Exposure to Alcohol and Seven Reproductive Health Outcomes, Based on Seven Criteria

Criteria for Causal Association	Infertility	Spontaneous Abortion	Stillbirth	Infant Mortality	Fetal Growth Birthweight FGR	Congenital Anomalies	Morbidity:Growth & Development
1. Experimental Design (Strongest Evidence) 5	Case-Control Studies 1	Prospective Cohort Studies 3	Prospective Cohort Studies 3	Prospective Cohort Studies 3	Prospective Cohort Studies 3	Prospective Cohort Studies 3	Prospective Cohort Studies 3
2. Strength of Association (Relative Risk Range) 5	Significant (p value only) 1	Significant RR:1.9-3.5 3	Significant (p value only) 1	Significant (p value only) 1	Significant decrease RR:2.3-3.0 60-190g LBW-RR:1.5 3	Significant RR:4.2 5	Significant (p value only) 1
3. Consistency of Evidence 5	Good 5	Fair 3	Fair 3	Fair 3	Good 5	Good 5	Good 5
4. Dose-Response Gradient 3	Yes 2	Yes 2	- 0	- 0	Yes 2	Yes 2	Yes 2
5. Biological Plausibility 5	High 5	High 5	High 5	High 5	High 5	High 5	High 5
6. Coherence 2	Good 2	Good 2	Good 2	Good 2	Good 2	Good 2	Good 2
7. Limited Number of Studies	-1		-1	-1			
8. Summary Score Percentage Rating Category of Causal Association	15/25 60% Possible	18/25 72% Suggestive	13/25 52% Evidence Lacking	13/25 52% Evidence Lacking	20/25 80% Probable	22/25 88% Probable	18/25 72% Suggestive

What can be concluded from the summaries outlined in the above tables? If one views scientific experimentation as the means by which one probes proposed theories, models or hypotheses to determine which will escape being rejected or displaced by alternate hypotheses, these summaries indicate that the working hypothesis of this thesis (i.e., the level of reproductive health in a population which determines the degree to which reproductive casualties occur, is determined in part by lifestyle factors) should not be rejected. The purpose of developing a quantified rating scheme was to determine, in as objective a manner as possible, whether sufficient probing of the hypothesis had been carried out to assume it provides a reasonable basis for decision-making.

The results of this criterion-based rating method suggest that in 5-6 of the 7 reproductive outcome categories, there is sufficient evidence to merit further attention to a potential causal association between these outcomes and exposure to the lifestyle risks of smoking, alcohol, and poor nutrition; and to merit continuing attention be paid to the effect of lifestyle on reproductive health per se. An important observation, from the perspective of investigating possible preventive action to reduce risk exposure, is the fact that these lifestyle-reproductive health associations include the preconception as well as the prenatal period.

Before determining whether this summary provides sufficient evidence to warrant specific action, it is necessary to examine in what way the

rating of evidence might be changed by other choices to include or exclude studies or criterion, or to establish between-criteria scoring?

1. The effect of choice of studies to be included. The review of evidence for this thesis for all criteria except biological plausibility, has been confined to studies of human populations using randomized control trials, cohort or case control designs which best met established standards for good research design (Campbell & Stanley, 1966; Shortell & Richardson, 1978; Weiss, 1972). A representative selection of the included studies is reviewed in chapter three allowing the reader an opportunity to assess whether the selection of studies as evidence appears suitable. In general, an attempt was made to err on the conservative side in selecting studies to be included. However, this does not preclude the possibility that a more experienced reviewer (e.g., an epidemiologist, statistician, or researcher knowledgeable in the area of reproductive health) might alter the selection of studies used as evidence. A smaller number of studies might be considered well designed, thereby increasing the frequency of "evidence lacking" ratings.

Equally, a larger number of studies might be considered appropriate for inclusion. Campbell and Stanley (1966) state:

We may assume an ecology for our science in which the number of potential positive hypotheses very greatly exceeds the number of hypotheses that will in the long run prove to be compatible with our observations. The task of theory-testing data collection is, therefore, predominantly one of rejecting inadequate hypotheses. In executing this task, any arrangement of observations for which certain outcomes would disconfirm theory will be useful, including quasi-experimental designs of less efficiency than true experiments. (p. 35)

The authors have established standards for quasi-experimental research designs that they believe to be sufficiently probing and "worth employing where more efficient probes are unavailable." In discussing consolidation of evidence, as attempted in this thesis, Campbell and Stanley (1966) state "the more numerous and independent the ways in which the experimental effect is demonstrated, the less numerous and less plausible any single rival invalidating hypothesis becomes" (p. 36). Campbell and Stanley assert that the collective experience from the literature can be used to rule out rival hypothesis (which are likely to differ from study to study) even though research design problems may be identified on an individual study basis. This expanded approach could help to clarify issues of consistency and cohesiveness of results which may occur in areas where a limited number of true experiments have been (or can be) conducted. It is likely that the inclusion of a greater number of studies (particularly the inclusion of studies with small samples but very detailed investigation and quasi-experimental designs) as consolidated evidence would enhance the support for causal association between lifestyle factors and reproductive health. This mode of inference, however, should be the domain of an expert, multi-disciplinary group.

2. The effect of the choice of inclusion and weighting of criterion. A comparison of rating categories and percent of total achievable scores was made between (a) the rating schemes described in summary tables 13, 14, and 15; (b) a rating scheme which includes

specificity and temporality as criteria (given 2 points for a positive test); and (c) one which rates each criterion equally (maximum 5 points each). Adding the two additional criteria did not alter rating categories but produced a slight convergence in the range of percent of total achievable scores from the 60-88 percent in the original scheme to 61-86 percent. When equal scores were assigned to each criterion category, a more pronounced convergence occurred (range of 68-78 percent of total achievable score) which had the effect of increasing the lower scores, decreasing the higher scores and removing any lifestyle-reproductive health associations from the "probable" causal association category. No category change occurred for the associations where evidence was considered lacking with either modification.

3. The effect of altering within-criterion scoring. The most plausible within-criterion scoring changes are seen to be (a) the accommodation of consolidated evidence which includes quasi-experimental design without the demand for randomized control trial design under experimental evidence; (b) a demand for greater strength of association (e.g., Relative Risk of 30 or more as reported for the association between smoking and lung cancer); and (c) a requirement for biological evidence primarily from human studies. Change (a) is likely to increase scores to a maximum of 2 points, change (b) to decrease the scores to a maximum of 2 points, and change (c) will either have no effect or decrease scores by about 2 points. The overall effect could be a change in category for four associations which scored 15-16 total points from "possible" causal association to "evidence lacking".

The requirement that maximum scoring within the biological plausibility criterion be based primarily on human research is seen to have the greatest negative effect on the rating of evidence. Even if this were incorporated into the rating scheme, the majority of the reproductive health outcome associations investigated for each lifestyle factor would still be rated as "possible" to "suggestive" causal associations and would still have implications for lifestyle exposure in both the preconception and prenatal period. Thus, it seems reasonable to conclude that the potential effect of lifestyle habits on reproductive health merits attention at both the clinical and community level. Given that the evidence of a causal association may be sufficient to warrant action, what other information should influence decision-making?

The BC Population at Risk

It is obvious that it is important to know whether a significant proportion of the population of reproductive age is at risk because of their lifestyle habits. Lifestyle prevalence data for British Columbia were reported in chapter three. Clearly these data need updating, but they provide the most current information available for a representative sample of the population. If one summarizes the available data on smoking and alcohol prevalence in relation to levels of exposure that are reported to effect reproductive outcome, the following profile develops: (a) approximately 31 percent of all women and 38 percent of men in BC smoke daily (1978-79 Canada Health Survey), and of those,

two-thirds or 20 percent of the total population smoke heavily enough to be considered "at risk" for reproductive health problems (13 or more cigarettes/day); (b) 56 percent of Canadian women and 75 percent of Canadian men currently drink alcohol, 14 percent of women and 36 percent of men drink sufficient amounts to be "at risk" (7 or more drinks/week or an average of one ounce of alcohol/day), and 5 percent of women and 19 percent of men are "high risk" drinkers (2 drinks/day or more) (1978-79 Canada Health Survey). Alcohol intake in BC was generally higher than the Canadian average and in 1978-79, 73 percent of the BC population were current drinkers, 33 percent were "at risk" and 17 percent were heavy drinkers which would be considered "high risk".

A dietary profile is provided by the one and only population survey of dietary intake and nutritional status, conducted in 1972-74. In BC the caloric intake of the sample of pregnant women showed that (a) 21 percent were consuming 1,500 calories or less (the threshold level for the Dutch Famine study) and (b) close to 50 percent were consuming less than an adequate amount of calories for pregnancy (Ottawa, 1983). Just over 11 percent were at "high risk" because of poor protein intake and 25 percent ate less than 60 g protein/day while pregnant. The proportion of pregnant women having inadequate amounts of specific vitamins or minerals in their diets reached 50 percent for some nutrients (see Table 11, chapter three). Because the pregnant women were selected from prenatal class attendees, it is

assumed that this sample presents a more positive picture of dietary intake than would a non-selected group.

Since women tend to make some additions to their usual dietary intake once they are aware of their pregnancy, it is also important to have information about the diets of those who may become pregnant. A representative sample of BC women aged 10-19 and 20-39 years were surveyed and their diets provide the best available profile of the population's dietary intake around the time of conception and during embryogenesis. In the group of adolescents, 21 percent consumed 1,550 calories or less/day; 10 percent were at risk because of low protein intake; and specific nutrient inadequacies were found in up to 79 percent of the diets. In the 20-39 year old women, 25 percent were consuming less than 1,300 calories/day, 34 percent less than 1,500 calories, and 50 percent less than 1,700 calories/day; over 25 percent were at risk for protein intake (25th percentile: 45 g/day); and specific vitamin or mineral inadequacies were found in up to 96 percent of the diets. The diets of the Native Indian and Eskimo women were less adequate than those reported above.

Health promotion programs aimed at improving nutrition and decreasing smoking and alcohol consumption may have achieved a reduction in the proportion of the population at risk for these lifestyle factors since the above surveys were conducted. Until such information is available, it is prudent to assume the data presented above are appropriate estimates of prevalence. On this assumption, there is

sufficient reason to believe that a significant proportion of the BC population are "at risk" because of at least these lifestyle habits.

The Preventable Portion of Reproductive Casualties

It is also important to have some understanding of the proportion of the reproductive problems that might be prevented given that (a) lifestyle factors are causal agents and (b) these lifestyle factors can be successfully modified to a "no risk" status.

Morgenstern and Bursic (1982) have proposed a method for using epidemiologic data to estimate the potential impact of an intervention involving risk factor modification on the health status of a target population. The authors describe a quantitative measure, which they call the "potential impact fraction", that can be used to estimate the proportion of expected new cases that may be prevented via intervention programs of varying success. The measure is derived from (a) the distribution in the population of the risk factor that is to be modified (prevalence of levels of exposure of interest), and (b) the magnitude of the association (relative risk) between the risk factor and the "disease" outcome in the population. With knowledge of the incidence of the outcomes of interest in the population, the resulting impact estimates can then be used to assess the potential efficacy, effectiveness, adequacy, and efficiency of planned intervention strategies (see Morgenstern & Bursic, 1982, for formulae and methods). The terms used to describe this measure in the epidemiology literature include: attributable fraction (Ouellet, Romeder, & Lance, 1979), attributable

risk (Levin, 1953), population attributable risk percent (Cole & MacMahon, 1971) or etiologic fraction (Miettinen, 1974). Morgenstern and Bursic have advanced the practical application of this measure for the benefit of health planners by allowing one to select the level of expected shift in population risk that might realistically result from risk factor intervention. However, since the aim at this time is to quantify the impact of lifestyle factors on reproductive outcome rather than the impact of intervention strategies, the "optimal condition" of the "potential impact fraction" (i.e., all lifestyle risks removed) is more appropriate for this study. This is identical to the formula used for calculating etiologic fraction and because it is a more widely recognized term, the measure will be referred to as the etiologic fraction. The equation for calculating the etiologic fraction is as follows:

$$(Lamda) \text{ ETIOLOGIC FRACTION} = Pe (R-1) / [Pe(R-1) + 1]$$

where Pe is the population exposed to the causal agent
 R is the relative risk if exposed, and
 the fraction derived represents the proportion of disease in the target population that would not have occurred had the risk factor been absent.

Table 16 provides an estimate of the preventable portion of reproductive casualties in BC if lifestyle risks for diet, smoking, and alcohol intake were removed. In each case, the relative risk "R" has been obtained from the results of cohort studies reviewed in chapter three.

The incidence of stillbirths, infant mortality, and low birthweight ($<2,500$ g) are for British Columbia, 1983 (Division of Vital Statistics, BC). The "incidence" of spontaneous abortion is an estimate using 1983 data but based on an interpretation of the findings of Rowe (1973) in his study of pregnancy loss among BC mothers and the results of the NSFG survey (Mosher & Pratt, 1982) discussed in chapter two. The "incidence" of infertility is derived from the findings of the NSFG survey (Mosher & Pratt, 1982) that infertility occurred in 10-14 percent of married couples aged 18-45 years, and 1981 Census data for BC (Statistics Canada, 1983) reporting 411,117 married couples between the ages of 15-45 years. The incidence of congenital malformations is based on the 1981 report of the Health Surveillance Registry (Division of Vital Statistics, BC) that an average rate of 4.7 cases/100 livebirths was reported for BC over the previous nine-year period. Information regarding the number of surviving infants who are affected by impaired mental, physical, or behavioral growth and development is not available for the BC population.

The proportion of exposed individuals in the population experiencing reproductive problems is estimated from the lifestyle prevalence data discussed above and in chapter three. The specific proportions used are as follows: a range of 11-21 percent of the target population were assessed to be nutritionally "at risk" during pregnancy and exposure level was used in the calculation of the etiologic fraction for all reproductive health outcomes; 25-34 percent of the population were

considered to have been nutritionally "at risk" around the time of conception and this exposure level was used to determine the upper range of the etiologic fraction for infertility, spontaneous abortion and stillbirths. The proportion at risk due to smoking habits was set at 20 percent (those smoking 13 or more cigarettes/day). The proportion at risk because of alcohol consumption was established at 14 percent (those consuming one or more drinks/day)—4.8 percent of the population are classified as heavy drinkers (two or more drinks/day). Where relative risk information was not available, this is noted as "not quantified".

An estimate of the preventable portion of reproductive casualties occurring in BC is outlined in Tables 16 and 17 below.

TABLE 16

An Estimate of the Preventable Portion (Etiologic Fraction) of Adverse Reproductive Health Outcomes in British Columbia, 1983. A. Calculation of the Etiologic Fraction for Single Lifestyle Factors

Reproductive Health Outcomes	Lifestyle Risk Factor	Prevalence of Risk ¹	Relative Risk of Reproductive Casualty ²	Etiologic Fraction ³
Infertility	Smoking	20%	1.6-2.3	.107-.206
	Diet	25-34%	N/A	?
	Alcohol	14%	N/A	?
Spontaneous Abortion	Smoking	20%	1.8-2.0	.160-.167
	Diet	25-34%	(RO:7.9)	.633-.701
	Alcohol	14%	1.9-3.5	.113-.262
Stillbirth	Smoking	20%	1.2-1.6	.038-.107
	Diet	11-25%	1.7-3.9	.071-.420
	Alcohol	14%	N/A	?
Infant Mortality	Smoking	20%	1.2-1.6	.038-.107
	Diet	11-25%	1.8-2.1	.081-.188
	Alcohol	14%	N/A	?
Congenital Malformation	Smoking	20%	N/A	?
	Diet	25-34%	(RO:8.7)	.658-.724
	Alcohol	14%	4.2	.133-.309
Fetal Growth: Low Birthweight	Smoking	20%	1.8	.160
	Diet	11-25%	1.9-2.5	.090-.240
	Alcohol	14%	2.0	.123
Fetal Growth Retardation	Smoking	20%	1.8-2.0	.160-.167
	Diet	11-25%	1.6	.062
	Alcohol	14%	2.3	.154
Morbidity: Growth & Development	Smoking	20%	N/A	?
	Diet	11-25%	N/A	?
	Alcohol	14%	N/A	?

Notes:

1. Prevalence of lifestyle exposure in BC female population at levels considered in literature to be "at risk". For smoking this is 13 cigarettes or more per day (Source: Canada Health Survey 1978-79); for alcohol, at least 1 ounce of alcohol per day (Source: Canada Health Survey, 1978-79); and for dietary intake, less than 1,500 calories per day or 60 g protein per day while pregnant (or less than 1,500 calories per day in the preconception period in the case of risk for infertility, spontaneous abortion and congenital malformation) (Source: Nutrition Canada, 1972-74).
2. Relative Risk as reported in literature for prospective cohort studies (see chapter three) or relative odds ratio (RO) as calculated from case control studies.
3. Etiologic fraction calculated as per following equation:

$$a = Pe(R-1) / [Pe(R-1) + 1]$$
 where Pe = BC population exposed to lifestyle risk
 R = relative risk if exposed.
 The fraction derived represents the proportion of disease in the BC population that would not have occurred had the single risk factor (smoking, alcohol, diet) been absent.

TABLE 17

An Estimate of the Preventable Portion (Etiologic Fraction) of Adverse Reproductive Health Outcomes in British Columbia, 1983. B. Estimates of the Minimum Number of Preventable Reproductive Casualties Given the Etiologic Fraction Reported in Table 16

Reproductive Health Outcomes	Number or Estimate of Number Affected, 1983 ¹	Lifestyle Risk Factor	Preventable Portion of Reproductive Casualties ²	Estimate: Minimum Number Preventable Casualties ³
Infertility	41,117 (estimate)	Smoking Diet Alcohol	10.7-20.6% ? ?	4,399-8,470
Spontaneous Abortion	4,089-4,305 (estimate)	Smoking Diet Alcohol	16.0-16.7% (63.3-70.1%) 11.3-26.2%	462-1,128
Stillbirth	312	Smoking Diet Alcohol	3.8-10.7% 7.1-42.0% ?	12-131
Infant Mortality	374	Smoking Diet Alcohol	3.8-10.7% 8.1-18.8% ?	14-70
Congenital Malformation	1,722	Smoking Diet Alcohol	? (65.8-72.4%) 13.3-30.9%	229-532
Fetal Growth: Low Birthweight	2,158	Smoking Diet Alcohol	16% 9.0-24.0% 12.3%	194-518
Fetal Growth Retardation	626	Smoking Diet Alcohol	16.0-16.7% 6.2% 15.4%	39-104
Morbidity: Growth & Development	N/A	Smoking Diet Alcohol	? ? ?	?

Notes:

1. Incidence reported for stillbirth, infant mortality low birthweight (2,500 g or less), fetal growth retardation (-2SD, Usher) and congenital malformations (average 9 year rate, 1971-1980) for BC population, 1983 (Source: Province of BC, Division of Vital Statistics). Estimate of incidence reported for infertility based on Mosher (1982) as 10% of married couples in BC, 1981; and for spontaneous abortion, based on Rowe (1973) and Mosher (1982).
2. Etiologic fraction calculated for single lifestyle risk factors as per Table 16, converted to percentage proportion of preventable reproductive casualties. The low to high range used for estimate of preventable numbers of casualties is underlined.
3. Estimate of number of preventable reproductive casualties for BC, 1983 calculated as number affected (i.e., number of reproductive casualties) X the preventable portion (etiologic fraction) for a single lifestyle risk. Since more than one lifestyle risk factor is prevalent in the population, this estimate represents the minimum number of preventable casualties rather than an estimate of the total preventable number.

British Columbia's Preventable Portion of Reproductive

Casualties: The Problem of Missing Data

It can be seen from Tables 16 and 17 that the removal of any one lifestyle risk could be expected to reduce the incidence of infertility, spontaneous abortion, stillbirth, infant mortality, congenital malformations, low birthweight, and fetal growth retardation by between 10 and 20 percent. Can it be argued that with the removal of the three lifestyle risks the preventable portion would reach 30-60 percent? Perhaps, but an investigation of this assumption strongly suggests that BC-specific data for exposure and outcome is required before an estimate of the total etiologic fraction related to lifestyle risk can be made.

If, for example, it is assumed that etiologic fractions are additive, does this have the effect of double counting the adverse outcomes of those exposed to two or three lifestyle risks? If, on the other hand, one assumes an increased relative risk with exposure to more than one lifestyle factor, how would this alter the etiologic fraction for the population? Table 18 shows that summing the etiologic fractions associated with lifestyle risks is the more conservative estimate because the prevalence of exposure remains the same in both assumptions while the relative risk of a proportion of the population is increased when the exposure "dose" is taken into account.

TABLE 18

Alternate Methods¹ to Estimate the Preventable Portion of
Low Birthweight from Removing Exposure
to Two Lifestyle Risk Factors

Reproductive Health Outcome ²	Lifestyle Risk Factor ³	Prevalence of Risk ⁴	Relative Risk of Reproductive Casualty ⁵	Etiologic Fraction	Preventable Portion ⁶ (N)
A. Low Birthweight (N=2,158) 5% of total births, BC population, 1983 (N=43,047)	Smoking N=4,571	26.1%	1.8	.173	37.4% (807 LBW)
	Drinking N=4,398	25.1%	2.0	+	
				.201	
	(N=8,969)			.374	
B.	Smoking only N=2,820	16.1%	1.8	.114	46.4% (1,001 LBW)
	Drinking only N=2,647	15.1%	2.0	.131	
	Smoking and Drinking N=1,751	10.0%	3.8 (1.8 + 2.0)	.219	
	(N=7,219)			.464	

Notes:

1. This table shows the difference between the estimate of the preventable portion of low birthweight when the calculation is based on (A) the prevalence of two different lifestyle risk factors in the population without recognition of the population exposed to both risks and (B) the prevalence of single but different lifestyle risk factors and the prevalence of two risk factors occurring together. For B, the etiologic fraction is larger because of the increased relative risk associated with multiple risk exposure.
2. Number affected by low birthweight in the BC population, 1983 (Source: Province of BC, Division of Vital Statistics).
3. Numbers of smokers and drinkers at "at risk" levels in the Canadian population (Source: Canada Health Survey, 1978-79). When the prevalence of multiple risk was not identified as in A, a number of individuals (1,751) were doubled counted—thus, in A, there is an N of 8,969 and in B, an N of 7,219 (the actual number of individuals exposed).
4. Prevalence of "at risk" smoking and drinking in the Canadian population 1978-79 (Source: Canada Health Survey).
5. Relative Risk of exposure as reported in Table 16 for single lifestyle factors. Relative risk of exposure to 2 risk factors (B. Smoking and drinking) is assumed to be additive.
6. If exposure to the two lifestyle risk factors smoking and drinking were removed, the percent low birthweight for the population would be expected to be 3.1% (135/43,047) by calculation A, and 2.7% (1,157/43,047) by calculation B.

However, the precise nature of the shift in relative risk (or etiologic fraction) with increased exposure per se, with different combinations of exposures or with variations in degrees of exposure cannot yet be determined from current studies or available data. It may be discovered that multiple low risk exposure levels are equivalent to a single moderate-high risk exposure level in terms of impact on reproductive health. It is quite possible that the relative risk of multiple exposure will be seen to demonstrate a synergistic rather than additive effect on reproductive health. Information is required to clarify whether there is a lifestyle interactive effect on reproduction outcome—if not, the relative risks can be assumed to be additive. .

It is also likely that a relationship between the preventable portion of different reproductive casualties will be seen when any one or more lifestyle risks are removed. Without adequate data to provide (a) expected reproductive outcomes for a healthy reference population, and (b) variations in outcomes associated with different levels, types and combinations of lifestyle risk exposure, it is not possible to provide the public with cogent health promotion messages or clinical advice during their reproductive years.

Morgenstern & Bursic (1982) have suggested that one way to estimate the impact of two or more risk factors is to calculate the relative risk of the combined exposures based on the experience of a reference group without exposure to any of these factors. Although data to derive lifestyle-related relative risk is not available for BC., Miller and

Merritt (1979) followed this basic approach in their study of the impact of "behavioral conditions" on fetal growth. This study was described in chapter two under the category of fetal growth. Table 19 identifies the preventable portion of low birthweight for the researchers' Kansas population according to the number of behavioral conditions present.

The Kansas data can also be used to demonstrate the potential value of having such information available when decisions are to be made regarding intervention strategies. Where resources are limited, it is often assumed that the most significant impact is realized when these resources are directed toward the high risk target group. The above data allows one to assess and compare the potential impact of successful intervention programs aimed at specific target groups in the population. In Table 20 below, the study group with no behavioral risks provides a reference population (no risk), and the study groups with one, two, and three or more behavioral risks are categorized as low, moderate, and high risk groups, respectively. It can be seen that although the high risk group has the highest proportion of reproductive casualties the potential impact of removing their behavioral risks has a smaller effect on the "incidence" of low birthweight (i.e., potential to prevent 6 LBW outcomes versus 23 LBW outcomes) in the total population than the potential impact of removing the single behavioral factor of the low risk group.

TABLE 19

An Estimate of the Preventable Portion of Low
Birthweight in the Kansas Study¹ Population

Actual LBW Outcomes (Kansas Study)		Level of Lifestyle Risk	Prevalence of Risk	Relative Risk of Reproductive Casualty	Etiologic Fraction	Preventable Portion LBW		Potential LBW Outcome	
#	%		%			%	#	#	%
6	1.0	<u>No Risk Group</u> No Lifestyle Risk Condition (N=624)	46.5	1.0	.00	-	-	6	1.0
34	6.7	<u>Low Risk Group</u> 1 Lifestyle Risk Condition (N=506)	37.7	6.9	.690	69.0	23	11	2.2
17	10.1	<u>Moderate Risk Group</u> 2 Lifestyle Risk Conditions (N=168)	12.5	10.4	.540	54.0	9	8	4.8
13	28.9	<u>High Risk Group</u> 3 or more Lifestyle Risk Conditions (N=45)	3.3	29.7	.486	48.6	6	7	15.6
70	5.2								
N = 1,343									

Note: 1. Reference: Miller, H. C., & Merritt, T. A. (1979).

TABLE 20

An Estimate of the Potential Impact of a Successful
Lifestyle Intervention Program on Low Birthweight
in the Population when Risk Groups are Selectively
Targeted, Based on Data from the Kansas Study¹

Target Risk Group	Actual LBW/ Target Group		Potential Impact of Intervention on Target Group LBW		Potential Impact of Target Group Intervention on Population LBW	
	#LBW/ Livebirths	% LBW	#Preventable LBW	% LBW	#LBW/ Livebirths	% LBW
No Risk	6/634	1.0	0	1.0	70/1,343	5.2
Low Risk (1 Lifestyle Risk)	34/506	6.7	23	2.2	47/1,343	3.5
Moderate Risk (2 Lifestyle Risks)	17/168	10.1	9	4.8	61/1,343	4.5
High Risk (3 or more Lifestyle Risks)	13/45	28.9	6	15.6	64/1,343	4.8
Total Population (Includes No Risk Population)	70/1,343	5.2	38	2.4	32/1,343	2.4

Note:

1. Reference: Miller, H. C., & Merritt, T. A. (1979).

The potential impact of targeting intervention resources may vary from community to community, or region, depending upon the proportion of the population in each of the risk group categories. The cost-effectiveness of intervention strategies cannot be estimated by calculation of potential impact alone, but must incorporate, for example, the variations in cost and efficacy of different intervention methods, and variations in resources needs to reach and effect change in different target groups. If the longterm impact on the growth and development of surviving infants varies with different degrees of maternal or paternal risk exposure, this must be considered. The extent to which benefits of lifestyle intervention can be realized beyond reproductive health should be considered so that the program benefits are not underestimated.

This study suggests that real improvements in reproductive health outcomes can be achieved with successful lifestyle intervention programs. Others have examined the economic issues of prevention (Editorial, 1980; Kristein, 1977; Scheffler & Paringer, 1980) and suggest such improvements can lead to economic benefits. Methods have been devised to allow rational decision-making by health planners and policy makers in the area of primary prevention (for example, Morgenstern & Bursic, 1982). Progress in clarifying realistic estimates of the preventable portion of reproductive casualties for BC (or any specific population) and the ability to evaluate the actual impact of intervention strategies on these outcomes is data limited. The

following and final chapter examines the type of data required for planned improvements in reproductive health and discusses some of the issues related to intervention decisions at the clinical and community level.

CHAPTER V: A REPRODUCTIVE HEALTH INDEX

Chapters three and four presented evidence of the causal link between reproductive casualties and adverse lifestyle habits. A method for quantifying the preventable portion of lifestyle-related reproductive casualties was described in chapter four. Based on the assumption that the prevalence data for lifestyle factors and the incidence data for reproductive casualties provide reasonable estimates of exposure and outcome for the British Columbia population of reproductive years, it can be calculated that a significant proportion of these reproductive casualties could be prevented by applying the current level of knowledge and skills.

It was pointed out that more substantive population data is required by health planners and policy makers if they are to be able to estimate the potential impact of a planned intervention, to select the most appropriate cost-effective strategies for intervention, and to monitor or evaluate program-related improvements in reproductive health. This final chapter describes the type of data which would provide support to researchers and planners in the reproductive health area, based on literature reviewed for chapters two and three, and outlines the possible incremental development of a reproductive health data base for British Columbia. Recognition is given to the fact that a data base such as this will only affect practices which lead to improved reproductive health if the information derived from it complements or enhances information currently used by the practitioner or public to make clinical or personal decisions. The chapter concludes with a

summary of the study objectives and the extent to which they were met, and an assessment of the implication of the study results for the scientific, health promotion and planning communities in improving reproductive health outcomes.

The Benefits of a Reproductive Health Data Base

It is readily apparent when conducting a review of the large volume of literature on lifestyle and reproductive health that much of the research work with human populations suffers from the lack of a suitable comparison or reference group. This is an inherent problem which stems from a number of legitimate reasons; however, it is a serious problem because the results of this research cannot be used as "evidence" and provide weak predictions at best. The overall effect is the need for an extravagant amount of repetitive study, a substantial loss of benefit from research dollars, and a time lag of approximately 10-20 years before the "evidence" evokes a public health or clinical response.

Thus, the benefits to the research community of having a population data base are substantial. Specific benefits have been reviewed by Roos & Nichol (1981) which include: (a) wide coverage to facilitate generalizability; (b) a large enough N to permit a number of simultaneous controls in data analysis; (c) a long enough time-series of data to allow analysis before and after a particular intervention; and (d) the potential for combining files to aid the research design. Data bank simulations can be used to further explore published results of quasi-experimental studies (Maltz, 1980) and could provide an important (and

less expensive) alternative to the randomized trials that are generally not feasible or ethical in lifestyle-pregnancy studies. Population data banks are suitable for studying the longterm effects of intervention (or the lack of intervention) and, in the case of reproductive health, the longterm effects of reproductive casualties (i.e., the effects of fetal growth retardation on later growth and development) and the multiple effects of lifestyle risk exposure on reproductive outcome (i.e., a history of poor reproductive performance due to poor nutrition may be identified by different combinations of reproductive casualties, such as repeated low birthweight, or stillbirth plus growth retardation in a livebirth). The potential for examining the effect of prenatal or preconception exposure on the reproductive performance of the second generation with a linked data base can be seen as a benefit of extreme importance, given our more recent animal-based understanding of mutagenic substances and their mode of action, and the more general understanding that lifestyle in one generation may become human biology in the second. The value of linked data systems which support sibling and twin studies for total populations needs no explanation.

The provision for identification of data for individuals and families, for institutions and by area, will allow all research benefits to accrue to the clinical, community health, and health promotion communities. Advancements in the area of applied research and program evaluation have been severely limited by problems of inadequate reference and comparison populations. Moreover, two additional benefits are

likely to result from adequate support to the applied research efforts of practitioners in the reproductive health field—(a) the quality of the data base should be enhanced by efforts to provide clinically relevant information, since any population data collection system is dependent upon the individual practitioner's motivation and ability to accurately and consistently report the needed information (a similar case is made for the individual client in providing accurate personal information); (b) a greater interest in incorporating an applied research component into treatment or service-oriented programs should result from efforts to ensure the results will be meaningful.

The benefits to the planning community have already been identified. In order to be able to estimate the potential impact of an intervention on the health status of a target population, and to use this estimate to assess the potential efficacy, effectiveness, adequacy and efficiency of planned intervention strategies, the distribution of the risk factor to be modified, the magnitude of the association between risk factor and outcome of interest, and the total risk of the outcome in the population are required. Having this data available should allow planners to maximize the benefits in improved reproductive health outcomes for each level of resource allocation.

It is beyond the scope of this study to examine the overall cost-benefits of establishing a comprehensive reproductive data base for British Columbia, but the following considerations should be included in such an assessment: (a) the value of improved reproductive health

outcomes and the value of improved health per se, from both a short-term and long-term perspective; (b) the value of increased cohesiveness and interaction between the research, clinical, public health, and health promotion communities; (c) the value of increasing the cost-effectiveness of research dollars and the increased applicability of both compulsory and voluntary data collection; (d) the value of a more informed public; (e) the value of integrating reproductive health data from inter-related but currently independent data collection systems within each of the health communities; (f) the value of lifestyle-related reproductive health data to improving the knowledge base in other lifestyle-related health outcome fields of study; (g) the value of a long-term data perspective that cannot be realized by any other means; (h) the potential for using the same information system to examine the impact of the environment, human biology, and the health care system in addition to that of lifestyle.

The anticipated benefits from an expanded reproductive health data base are important enough to warrant an examination of the feasibility of establishing a comprehensive data collection and surveillance system for the BC population. In part, the feasibility will depend on the type and quantity of data required and the ease of collecting quality data.

Reproductive Health Index Variables

For this study the data focus is specific to lifestyle-related reproductive casualties, yet in reality, data should attend to each

of the four contributing aspects—environment, lifestyle, human biology, and the system of health care organization. Dever (1980, 1984) has developed an epidemiological model for health policy analysis which recognizes the important interaction of each of these four elements. Dever (1984) defines the four elements as follows: (a) Lifestyle—self-created risks described as leisure activity risks (i.e., degree of fitness), consumption patterns (i.e., dietary components, alcohol, smoking, drugs), and employment/occupational risks (i.e., work stress, driving patterns); (b) Environment—physical, social and psychological events external to the body over which the individual has little or no control (i.e., air pollution, rapid societal change, decision stress); (c) Human Biology—concerned with genetic inheritance and health outcomes determined by individual basic biologic and organic makeup (i.e., genetic disorders); and (d) System of Medical Care Organization—the availability, quality, and quantity of resources to provide health care for curative, restorative, and preventive medicine. A specific application of this model requires more data than is available; however, an example of this approach can be provided, in general terms, using infant mortality as a focus. Given the objective of reducing infant mortality by a certain amount within a particular time frame, how would this model help to (a) determine the best strategies to accomplish the objective and (b) assess the ability of the health system to support these strategies. The application of the model from a policy perspective would involve (a) identifying by rank order the

causes of infant mortality; (b) determining to what degree (i.e., what proportion or percentage) lifestyle, environment, human biology, and system of medical care are contributing factors to infant mortality in general, and to specific causes of infant mortality (e.g., congenital anomalies, SIDS) in particular; (c) determining the proportionate allocation of total health expenditures to the four elements of the model; and (d) assessing the difference in proportions between (b) and (c).

The lack of epidemiologic-based cause of death reporting in BC is a limiting factor in applying this model as described. If appropriate data were available to identify and rank causes of infant mortality etiologically but not to establish the percent contribution of each of the four elements, Dever suggests that agencies can derive reasonable estimates from surveys of experienced professionals cross-checked against estimates reported in the literature. For example, percentage allocations derived by professional survey have been reported for mortality due to congenital anomalies (9 percent lifestyle; 6 percent environment; 79 percent human biology; 6 percent health system) and birth injuries and other diseases of early infancy (30 percent lifestyle; 15 percent environment; 28 percent human biology; 27 percent health system) (Dever, 1976).

Even in the absence of comprehensive data, the application of the model to available data can be informative. For example, since BC data shows that the risk of infant mortality is directly proportionate

to birthweight and that 60-70 percent of all perinatal deaths and 45-50 percent of infant deaths occur to infants weighing less than 2,500 g at birth (see Table 6), low birthweight could be considered in the same manner as a specific cause of death (step one). In this study, lifestyle has been shown to contribute significantly to low birthweight. Using the method of calculating potential impact (etiologic fraction) for more than one lifestyle exposure (see Table 16), the percentage allocation of low birthweight to lifestyle would be 64 percent if the effect of poor diet along with smoking and alcohol were considered. Thus, if over 50 percent of the neonatal deaths occur to low birthweight infants and over 60 percent of the low birthweight is associated with lifestyle exposure, any strategy to reduce infant mortality, if it is to be effective, must emphasize the prevention of low birthweight and the reduction of lifestyle risk.

Even without data-derived allocations of the contribution to low birthweight of human biology, environment and system of health care, one can examine the allocation of health expenditures for reducing infant mortality—and within this component, the allocation for reducing low birthweight—to each of the four elements. The premise of this model is that the proportionate allocation of health expenditures to lifestyle, environment, human biology, and the system of health care for reducing mortality, and preventing low birthweight, should approximate the proportionate contribution of these elements to mortality (or low birthweight). This premise is, of course, theoretical in nature.

There has been no practical application of the approach for the purpose of evaluating outcome. However, given the example cited by Dever (1976) and the US Department of Health, Education, and Welfare (1978) of the contributing factors to premature mortality (prior to 65 years of age) by the ten leading causes of death (average: lifestyle, 53.1 percent; environment, 21.7 percent; human biology, 16.8 percent; and health system, 9.8 percent for the US population, 1975) compared to Federal health expenditures (average: lifestyle, 1.2 percent; environment, 1.5 percent; human biology, 6.9 percent; and health system, 90.6 percent for US in 1974-76), it is clear that health expenditures are not necessarily rationalized with health goals.

The categories of health expenditures appropriate to each of the four elements of the model have been determined by Dever (1976) as follows: (a) Lifestyle—disease prevention and control; (b) Environment—environmental control and consumer safety; (c) Human biology—health research; (d) System of medical care organization—training and education, construction of health care facilities, improving organization and delivery, and the provision of hospital and medical services. More explicit guidelines would be needed to develop a BC profile since no details are provided as to the way specific types of services or programs should be categorized—for example, how to classify preventive medical services (e.g., antenatal risk screening) or health surveillance systems. The process of review required to determine such guidelines can, in

itself, be useful if it provides a forum for discussion as to the cost-effectiveness and implications of the present distribution of expenditures.

Although the epidemiological model proposed by Dever requires further refinement and evaluation, the basic approach which requires an assessment of whether the established balance of resources and expenditures is rational, given specific health problems and an understanding of contributing factors, is to be recommended.

Haro (1979) identifies two distinct types of planning—goal attainment and control-oriented models—according to the type of information required for the planning process. The goal-attainment model makes use of epidemiological data in determining the effectiveness of health care programs, and the control-oriented model makes use of financial, manpower and service information in determining the efficiency of existing programs. This study has been developed around the goal-attainment or problem solving planning model. In terms of data collection this means that the primary focus is on measures of health status and the solution of defined health problems (i.e., health workers, administrators and agencies throughout the health services system share the common goal of preventing reproductive casualties and promoting optimal reproductive health) and the type of financial, manpower and service information required is determined within the context of monitoring effectiveness. To be useful, data must be able to be tailored to fit the needs of each level and type of user, and in total, provide a comprehensive information system suitable to the planning needs of the overall health sector (Cerkovnij et al., 1979).

In general, the type of data which is needed for all levels includes: demographic data which identifies risk groups in the population and serves as denominators for constructing rates and making comparisons; measures of death, disease and disability; measures of the use of services which describe morbidity as seen by the health and social agencies; and measures of health hazards which determine mortality and morbidity.

To specifically examine the impact of lifestyle on reproductive health, decision makers at all levels should be provided with enough information (a) to clearly identify the extent to which there are reproductive health problems in the community (as discussed in chapter two); (b) to describe the prevalence of exposure to each lifestyle risk for the population of reproductive years (as discussed in chapter three); (c) to assess the short-term and long-term variation in reproductive outcome with and without exposure to lifestyle risk; and (d) to identify the population with reproductive health problems in a way that more detailed assessment of the etiology of the problem can be carried out, and/or intervention strategies can be planned and evaluated. This common set of data has been referred to earlier in the study as the "reproductive health index". The review of recommended data variables will be limited to this broad province-wide level of data collection since an appropriate review at the more specialized levels is sufficiently complex to require an independent study.

At other levels of decision making one should expect differences

in content, scope, specificity, timing and frequency of information required, as well as differences in perspective or focus of concern. An example of how data collected for a province-wide "reproductive health index" might be used to identify problems at the regional or community level has been described by King and Ross (1981). The authors selected perinatal mortality as an indicator of both the quality of the obstetric/ paediatric services and maternal health in a community. From a review of the literature (see, e.g., Car & Wolfe, 1976; Dever, 1980; Holland, Ipsen, & Kostrzewski, 1979; Jazair, 1976; Kessner & Kalk, 1973; Kisch et al., 1978; Mallet & Knox, 1979; Wynn & Wynn, 1979) they determined that the effect of these two contributing factors in different regions of the province could be independently assessed by examining the inter-regional differences in (a) birthweight-standardized perinatal mortality rates as a measure of the quality of health services, and (b) low birthweight, a major predeterminant of perinatal mortality, as a measure of maternal health. One of the results reported by King and Ross was a significant inter-regional difference ($\chi^2 = 24$, $p < .001$) in the relative risk of mortality for infants weighing 3,501-4,500 g at birth—the most optimal birthweight range in terms of perinatal health (see chapter two, Table 6). This type of problem identification is an important feature of an information system at the provincial level. Further analysis of the problem would then be required at the regional, community, or institutional level (e.g., case reports reviewed, opinions of obstetric personnel sought, inter-community comparisons examined) and

once the potential contributing conditions had been identified, comparison of these conditions in the regions with the lowest mortality could provide clues as to the most suitable condition(s) to change and evaluate.

Similar inter-regional differences might be seen in the proportion of infants weighing less than 2,501 g. In this case further analysis might focus on potential contributing conditions such as higher prevalence of lifestyle risk exposure, risk screening and referral mechanisms, availability of resources for risk intervention, etc.

The data set for the different communities, institutions, agencies or research groups should be planned so as to provide important supplementary information—therefore, an essential feature of the comprehensive information system is the predetermination of the level-specific "reproductive health index" and the ability to integrate this data for use at all levels. Although reproductive health data is currently collected at most levels, seldom is it reported in detail or in a format that can be readily integrated at the provincial level. In most cases the basis for determining data collection is administrative or statutory and the information is not useful for epidemiological problem solving. The DH3 and MB3 series of the OPCS Monitor (Office of Population Censuses & Surveys, London) are excellent examples of the type of data review that can be provided.

Variables considered important for the provincial reproductive health index are as follows:

A. Identification Variables

1. A unique identification number for mother and infant that will allow for linking of all reproductive health records for an individual (i.e., it should be possible to identify the type and number of prior reproductive health problems associated with each new reproductive outcome), and for long term followup of growth, development and, where possible, subsequent reproductive performance of each infant (i.e., it should be possible to examine the long term implications associated with specific outcome measures and/or with exposure to specific risks). This ID number should be able to be accurately and independently generated by each level of the health care system.

2. Reference group identifiers (such as area of residence and institution providing labor and delivery services) that will allow for comparative analysis of data collected at each level of research or service.

B. Reproductive Health Outcome Variables (Annual Incidence)

1. Clinically recognized infertility in males, females, and couples of reproductive age; (baseline and interval incidence of secondary amenorrhea in the female population).

2. Clinically recognized spontaneous abortion, gestational age of abortuses and classification as to embryo or fetus (e.g. pathology reports as to normal/abnormal karyotyping should be available at the institutional level of the data collection system).

3. Stillbirths and livebirths described by birthweight, birth length, and head circumference; sex of infant; and number and type of birth defects present. Etiologic reports regarding congenital anomalies, and placental pathologies, should be available at a different level of the data collection system. Diagnostic reports of birth defects, subsequent to the submission of livebirth registration, should be used for an annual update of the birth cohort. Thus, the Health Surveillance Registry, which currently collects this data, and the Reproductive Health Index systems must be readily compatible. "Cause of Death" reporting for stillbirths should include an etiologic focus designed to support intervention research.

4. Infant mortality, accompanied by "cause of death" reporting designed to support etiologic and intervention research. Infant mortality rate should be automatically integrated into the reproductive health index at the provincial level.

C. Exposure to Lifestyle Risk Variables (Prevalence/Outcome)

1. Degree of exposure to the lifestyle risks of malnutrition, tobacco and cannabis, alcohol, drugs and chemicals, psychological and physical stress should be reported for the preconception and mid-pregnancy period. Accompanying descriptive data should include: maternal age, weight and height at diagnosis of infertility or pregnancy; total pregnancy weight gain; major infection or medical conditions treated during the pregnancy; and obstetric complications of labour or delivery. Although details of medical and obstetric complications need

not be reported at the provincial level, indication of occurrence is required in order to correctly identify the "healthy" reference population and induced versus precipitous preterm deliveries.

D. Utilization of Services (Supplementary Data: Discretionary)

Although service use data does not contribute to the assessment of lifestyle impact on reproductive outcome, it can provide important information to help determine feasible intervention strategies (i.e., what proportion of the population attend prenatal education classes or well baby clinics, what proportion attend family planning clinics, have early ultrasound examinations or receive genetic counselling, etc.); or to determine the cost of lack of successful intervention (i.e., what proportion of infants need support from the infant development clinic, require intensive care after birth, require longterm institutional and/or medical support, or require special education services). Once baseline data has been established, this type of information can be examined at regular intervals and would be readily available from appropriate institutions and agencies if the data systems were integrated.

The Feasibility of a British Columbia Index

Table 21 provides a summary of the variables recommended for a provincial reproductive health index according to whether the data is currently available for the population of British Columbia.

TABLE 21

Current Availability of Data for the Recommended
Reproductive Health Index, BC Population, 1984

Reproductive Health Index Variables	Currently Available, BC
A. Identification Variables	
Unique ID - mother & infants	No
Reference group ID	Possible
B. Outcome Variables	
Infertility	No*
Spontaneous Abortions	No*
Stillbirths & Livebirths	Yes
Birthweight	Yes
Birth length	No*
Head circumference	No*
Sex of infant	Yes
Birth defects (diagnosed at birth)	Yes
(diagnosed subsequently)	Yes, but not integrated
Cause of death, Stillbirth	Yes, but not etiologic
Infant Mortality	Yes, but not integrated and not etiologic
C. Lifestyle Risk Variables	
Malnutrition	No
Tobacco & Cannabis	No*
Alcohol	No*
Drugs & Chemicals	No*
Psychological & Physical Stress	No
Age	Yes
Maternal weight	No*
Maternal height	No*
Total pregnancy gain	No*
Medical conditions/infections	Yes, but quality poor
Obstetric complications	Yes, but quality poor
D. Utilization of Services	
	No*

* Data generally collected by physicians, or agencies in British Columbia.

Table 21 shows that although data for more than half (14/25) of the recommended reproductive health index variables are not available at the provincial level, 80 percent (11/14) of the non-available variables represent data collected at some other level of the health care system, for example, by physicians, hospitals, or community health agencies. Five of these variables—pregravid weight, maternal height, pregnancy gain, infant birth length and head circumference—could be incorporated into present reporting forms, would cause minimal inconvenience to reporters, and are of sufficient significance to pregnancy outcome and the measurement of fetal growth retardation that province-wide data collection should be instituted immediately. Pregravid weight for height and pregnancy weight gain, for example, are two of the maternal variables required by the clinician in determining whether a woman requires a referral to a nutritionist for intervention support (Ministry of Health, 1984). Birth length and head circumference, as well as birthweight, are required for the clinician's assessment of whether fetal growth retardation has occurred and whether a specialist referral is indicated for either mother or infant.

Outcome variables for infertility, including secondary amenorrhea, and spontaneous abortion are collected on a case by case basis at the clinical and hospital level. Since there is sufficient evidence to suggest that (a) those with a prior history of infertility or spontaneous abortion are at increased risk for subsequent reproductive problems and (b) that a significant proportion of the problems can be prevented,

this group represents an important target group for planned intervention programs. Since intervention strategies cannot be evaluated without adequate knowledge of the population at risk, there is reasonable justification for considering this data to be valuable component of the provincial level reproductive health index and for taking steps to determine acceptable reporting mechanisms. Physicians working in these areas would provide the most suitable advisory group to determine the most efficient and accurate means of reporting this data. Physician acceptance of additional "paperwork" may pose the greatest constraint to feasibility in this case.

Table 21 also shows the disparity between the availability of outcome versus input (risk) variables. Although the majority of the selected reproductive health index "outcome" variables are reported at the provincial level, almost no risk variables are reported and because of this, there is insufficient data to support a problem solving approach to reproductive health issues.

Survey techniques for collecting lifestyle data have now developed to a stage where high quality data can be anticipated. The standardized perinatal record used by BC physicians recognizes the need for lifestyle assessment but unfortunately lifestyle screening is not common practice.

From the perspective of the reproductive health index, exposure data for smoking should include (a) whether the individual is a current smoker; if no, whether they have ever smoked, and if so, how long ago did they quit;—and for smokers: (b) the average number of cigarettes smoked daily during the preconception period; (c) the total number of

years the individual has been smoking; (d) the average number of cigarettes smoked during the first, the second, and the third trimester (or around the 10th, the 20th, and the 30th week of gestation); (e) whether smoking cessation advice (or counselling) was given,—if so, when (i.e., what trimester), and what change was observed (no change, reduced exposure, quit). These provincial level data requirements for lifestyle risk exposure are similar to the clinician's requirement for risk screening. In addition to the above information, the clinician needs to know the level of exposure which constitutes a risk, whether a referral for smoking cessation support is indicated, and what intervention services are available. Data collection at the provincial level will generate sufficient information to determine the relative risk of different exposure levels and to help characterize the individuals who would benefit from intervention programs (i.e., Sexton & Hebel, 1984, suggest that women who have not stopped smoking by the second trimester do not change their pattern of smoking without smoking cessation support). Information required by planners to evaluate the effectiveness of intervention programs can also be useful to the clinician, particularly if collected in a way that it can be integrated at any level of reproductive health index data collection.

Similar sets of specific information about other lifestyle risk variables in the preconception and prenatal period are required for the reproductive health index and for initial risk assessment and management by the physician. Thus, it seems appropriate to consider

revisions to the current perinatal record so that the data collected would adequately support both these needs.

Efforts need to be directed toward developing standardized risk assessment measures and referral mechanisms that require a minimum of the clinician's time. In the short term, self-report lifestyle data forms to be completed at initial infertility or pregnancy confirmation (preconception period) and 20 week prenatal physician visits (mid-pregnancy period) could be validated in a designated community and used to test an integrated information system. The integrated system should include data derived from in-depth lifestyle risk assessment. Professionals working in the area of lifestyle assessment and management (e.g., Nutritionists, Psychologists, Community Health Nurses, Drug and Alcohol Counsellors, Family Practice Physicians) should be called upon to develop suitable tools for collecting quality lifestyle data and/or for screening for lifestyle risk at each level of investigations. A mandate to develop nutrition screening measures for pregnancy has already been established at the Federal-Provincial level.. Consideration should be given to the feasibility of adopting already-established provincial programs, such as the Saskatchewan Drug Utilization Surveillance Program (Saskatchewan Joint Committee on Drug Utilization, 1979 & 1984).

For the most part, the recommended data collection changes are a refinement of established policy within the Division of Vital Statistics —i.e., an extension of the current set of outcome variables and

outcome-associated variables in order to improve the ability of the health care system to determine appropriate action. At present it is possible to identify health problems, but not the reasons for the problems. Lifestyle-adjusted rates or pregravid weight-adjusted rates provide clear direction for action in a way that rates adjusted for ethnic origin, or even parental age, cannot. The recommendation that reproductive health-related data be integrated within and between levels of measurement and decision-making, and linked across a mother's overall reproductive experience or an infant's period of growth and development by using identifier variables has obvious policy implications. However, the benefits (detailed previously) of this type of comprehensive surveillance system are sufficiently cogent to warrant a feasibility study.

In summary, the potential for collecting additional reproductive health data for BC at the provincial level varies from good to unknown depending on the extent to which the information is required (and has been standardized) at other levels within the health system. For "unknown" areas, feasibility studies are considered justifiable because of the potential value to be derived from having the data available.

Study Conclusions

The objectives of this thesis were:

1. To review the evidence linking maternal or paternal lifestyle habits around the time of conception, and maternal lifestyle habits during pregnancy to adverse reproductive and pregnancy outcomes.

2. To determine what proportion of reproductive casualties can be attributed to lifestyle and, therefore, are amenable to prevention, or what information is required to determine if there is a preventable portion attributable to lifestyle factors.

3. To examine a method for surveillance of lifestyle-related reproductive health outcomes in a community.

Within the limitations of available research and data, these objectives have been met. As a means of managing the size of the study report, only a representative set of lifestyles and research literature was reported in detail, although a comprehensive review of the evidence linking each of the lifestyle variables to reproductive outcome was in fact conducted. It should not be assumed that only the lifestyle variables reviewed for this report affect reproductive health, for there is ample evidence to implicate drugs, chemicals and other toxins, as well as physical and psychological stress (Chenier, 1982; Council on Environmental Quality, 1981; Naeye, Kissane, & Kaufman, 1981; Obe, 1984; Rechcigl, 1981; Schwarz & Yaffe, 1980; Wilson & Fraser, 1977; Wynn & Wynn, 1981). Nor should it be assumed that only those studies which were reported or referenced are important to the determination of a causal relationship between a specific lifestyle variable and a specific reproductive outcome. However, the fact that the study's conclusion—that evidence suggests a "cause and effect" relationship—is based on conservative criteria and an extensive review of the literature, suggests it is reasonable to assume this conclusion will be substantiated by future research.

The etiologic (potential impact) fraction was used to estimate that at least 10 percent of reproductive casualties in British Columbia were preventable with the elimination of any one lifestyle risk factor and that under conditions of multiple risk, the preventable portion of reproductive casualties could be as great as 50 percent. The calculation of the etiologic fraction for lifestyle-related reproductive casualties requires knowledge of (a) the incidence of each reproductive casualty, (b) the prevalence of lifestyle risks, and (c) the relative risk of poor reproductive outcome associated with the presence of single or multiple lifestyle factors. To derive an estimate of the preventable reproductive casualties for the British Columbia population in 1983, it was necessary to assume rates of infertility and spontaneous abortion from surveys of other populations; to assume lifestyle risk prevalence from earlier studies; and to assume relative risk from the research literature experience because the required BC data were not available.

Surveillance of any health problem in a community requires accurate up-to-date information about the extent of the problem. The data requirements of a Reproductive Health Index that provides the means for adequate surveillance of reproductive problems in the population—as well as a means to estimate the preventable portion and determine appropriate intervention strategies—were described. The Reproductive Health Index was also designed to support applied research efforts in the health community by providing appropriate reference population

data. A comprehensive information data base, which would support reproductive health research, planning, and evaluation needs at all levels of the health care system, and which could be established through the design of an integrated data collection system was discussed.

The study supports the following conclusions:

1. There is sufficient evidence to suggest a causal relationship between exposure to adverse lifestyle factors and a range of reproductive casualties which include infertility, spontaneous abortion, stillbirth, low birthweight and fetal growth retardation, infant mortality, birth defects and problems of postnatal growth and development. The effect of exposure during the preconception period (as compared to exposure during pregnancy) has received insufficient attention given the serious and longterm nature of the potential impact. It is concluded that lifestyle factors affect reproductive health per se and for this reason, preventive health measures should address the broad aspect of reproductive health status. Preventive action at the clinical level is considered warranted.

2. It is possible to estimate the preventable portion of lifestyle-related reproductive casualties occurring in a community given the incidence of reproductive casualties and the prevalence of exposure to lifestyle risks—in British Columbia, the preventable portion may be in the range of 10-50 percent. This potential to improve reproductive health is significant enough to warrant action at the community level.

3. A more extensive set of population data for British Columbia is required to determine an accurate estimate of the lifestyle-related preventable portion of reproductive casualties, to plan cost-effective intervention strategies, to monitor improvements in reproductive health, and to support applied research initiatives.

IT IS THEREFORE RECOMMENDED THAT THE NEED FOR A MORE COMPREHENSIVE REPRODUCTIVE HEALTH INFORMATION SYSTEM IN BRITISH COLUMBIA BE CONSIDERED A HIGH PRIORITY AND BE ACTIVELY SOUGHT BY GOVERNMENT, AS WELL AS INSTITUTIONS, AGENCIES AND INDIVIDUALS WORKING TO IMPROVE REPRODUCTIVE HEALTH OUTCOMES. The benefits to be derived from an improved data base are substantial and have been outlined in this chapter. With recent advances in computer technology and the current evolution of information management systems, an investigation of the feasibility of an integrated, linked data base seems timely for each level of health care organization.

Preventive Measures: What Action Should be Taken?

The recommendation that an integrated, comprehensive reproductive health information system be developed and the conclusion that preventive action is warranted at both the clinical and community level, raises an issue that has policy, planning and data collection implications—what new preventive action, if any, should be taken by whom, for whom, and on what basis should these decisions be made?

At a minimum, the action should entail informing parents-to-be of the reproductive health risks associated with poor lifestyle habits.

Lifestyle and other health information for pregnancy, but not preconception, is provided by the Provincial Ministry of Health for all couples in British Columbia through contact with their physician or public health unit. Providing such information is an issue of public trust and requires no outcome evaluation apart from assurance that the information is as accurate and up-to-date as current understanding will allow, that it is readily available to all and is widely known to be available. (On the other hand, providing information that is inaccurate is an abuse of the public trust. Although providing accurate, up-to-date information is also the responsibility of each health professional who delivers reproductive health services, practically speaking, this responsibility cannot be met without the support of government and expert committees. The literature is too voluminous and diverse to assume the average clinician has the time or varied skills to review and interpret it appropriately.)

Action beyond the provision of information, however, is designed to effect a reaction and it is essential, wherever possible, to determine whether planned preventive action produces intended or unintended results. This type of evaluation is required not only to assess the cost-effectiveness of a particular preventive measure compared to other options, but to ensure that no unintended, unexpected harm occurs to the public as a result of advice or intervention.

A task force report on theory, practice and application of prevention in personal health services, and quality control and

evaluation of preventive health services (Fogarty International Center & American College of Preventive Medicine, 1976), provides an excellent reference for assessing suitable preventive measures and includes for example, criteria for evaluating preventive services, criteria for evaluating screening procedures, methods to evaluate the health education components of preventive health programs, and recommended goals of preventive services for the mother and neonate. The report states, in summary:

It is of the utmost importance that evaluation and quality control be built into all preventive efforts so that their value may be objectively and precisely measured, thus providing a basis for comparison in setting priorities for health programs at every level and for providing feedback to delivery systems for improvement of services. Without such efforts, decisions about prevention treatment, cure, and care can only be made on a philosophic basis, clearly inadequate to serve the purposes of policy making in the health care field—at every level. A public commitment by (the federal health department) supported by policies, funding, and staff is necessary to achieve these objectives. (p. 143)

This statement is clearly as pertinent to British Columbia and Canada as it is to the United States, and as pertinent to treatment services as to prevention services.

The purpose of this statement was not to discourage the introduction of comprehensive preventive health procedures and programs, for clearly the task force felt that a concerted effort to incorporate specific preventive packages (i.e., recommended preventive procedures for the mother and fetus, which included lifestyle counselling) as part of accepted health service provision was justified. It is simply a recognition of the fact that there must be the means to differentiate

between effective and ineffective procedures and programs if the goal to improve reproductive health is to be achieved.

In a recent article, Bryce and Enkin (1984) suggest that advice alone on nutrition, alcohol, and smoking in pregnancy has not been demonstrated to improve outcome. However, these authors point out that when appropriate advice is accompanied by a program of social support, beneficial effects in terms of behavior change and reproductive outcome are reported. Most successful intervention programs have been designed and conducted by highly skilled professionals (i.e., dietitian-nutritionists and health educators who have specialized in reproductive health, experienced lifestyle and drug abuse counsellors) and the same degree of success may not be achieved with different personnel. Intervention strategies may be effective for some individuals or groups and not for others. Thus, evaluation must be designed to help determine what intervention strategies, by whom, and for whom are most effective.

The following scenario was described in the introduction to this thesis: Consensus had been reached by government that improvements in infant health could be realized by improving the lifestyle habits of expectant parents and that health promotion and prevention strategies were to be encouraged. Health promotion required a clear, unequivocal message and the scientific community, which perceived the knowledge base to be inadequate, viewed such health promotion attempts with skepticism. Thus, there seemed an implicit need for action that would establish the cooperative role of government, planners, researchers and health professionals in confirming or rejecting the validity of

the health promotion messages and in determining ways to improve reproductive health. Having now completed this study, the need for a planned cooperative approach to improving reproductive health and increasing our knowledge base seems even more critical. Too much time and money has been wasted in the past because studies lacked the support of population reference data and were not generalizable, or because important confounding variables were not considered or measurement tools were inappropriate.

The fact is that the issues involved in improving reproductive health are complex and require a comprehensive understanding of the multiple factors that contribute to reproductive health status or to poor reproductive performance—there are problems of measurement in determining both outcome and exposure to risk, and there are system constraints to quality data collection and problem-solving approaches to data analysis. No one individual or professional group has sufficient knowledge to examine the issues in a comprehensive manner. A broad spectrum of expertise and active support from government and the research, planning and health care communities is needed for the development of an effective and mutually beneficial plan to improve and monitor reproductive health in the community.

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Chapter II

Fertility and Impaired Fecundity

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Chapter III

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APPENDIX

Maternal and infant health records routinely used by
clinicians, institutions and government agencies in
British Columbia (Source: Province of British
Columbia, Ministry of Health, Victoria, B.C.).

PRENATAL RECORD

PART I

HOSPITAL																																																																																																												
1. NAME					RACIAL ORIGIN																																																																																																							
ADDRESS					TELEPHONE NUMBER																																																																																																							
MOTHER'S DATE OF BIRTH AGE			OCCUPATION		MARITAL STATUS			DOCTOR'S NAME																																																																																																				
FATHER'S NAME					RACIAL ORIGIN																																																																																																							
FATHER'S AGE			FATHER'S OCCUPATION		M.S.P. NUMBER			DOCTOR'S PHONE NUMBER																																																																																																				
2. OBSTETRICAL HISTORY INCLUDING ABORTIONS																																																																																																												
<table border="1" style="width:100%; border-collapse: collapse;"> <thead> <tr> <th style="width:10%;">DATE</th> <th style="width:20%;">PLACE OF CONFINEMENT OR ABORTION</th> <th style="width:10%;">DUR. PREG.</th> <th style="width:10%;">HOURS OF LABOUR</th> <th style="width:20%;">TYPE OF DELIVERY</th> <th style="width:20%;">COMPLICATIONS MOTHER AND/OR INFANT</th> <th style="width:10%;">SEX</th> <th style="width:10%;">BIRTH WEIGHT</th> <th style="width:10%;">PRESENT HEALTH</th> </tr> </thead> <tbody> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr> </tbody> </table>										DATE	PLACE OF CONFINEMENT OR ABORTION	DUR. PREG.	HOURS OF LABOUR	TYPE OF DELIVERY	COMPLICATIONS MOTHER AND/OR INFANT	SEX	BIRTH WEIGHT	PRESENT HEALTH																																																																																										
DATE	PLACE OF CONFINEMENT OR ABORTION	DUR. PREG.	HOURS OF LABOUR	TYPE OF DELIVERY	COMPLICATIONS MOTHER AND/OR INFANT	SEX	BIRTH WEIGHT	PRESENT HEALTH																																																																																																				
3. RISK ASSESSMENT Reproductive History <input type="checkbox"/> Age - less than 15, greater than 35 <input type="checkbox"/> Parity 5+ <input type="checkbox"/> Weight - less than 45, greater than 90kg (<100, >200 lbs) <input type="checkbox"/> Habitual Abortion <input type="checkbox"/> Stillborn/Neonatal Death <input type="checkbox"/> Fetal Anomalies <input type="checkbox"/> Labour Premature <input type="checkbox"/> Labour Prolonged <input type="checkbox"/> Labour precocious (<3 hours) <input type="checkbox"/> Difficult Delivery <input type="checkbox"/> Post p. Hemorrhage Manual Removal <input type="checkbox"/> Preeclampsia/Hypertension					4. HISTORY OF PRESENT PREGNANCY (Specify) NO YES <input type="checkbox"/> BLEEDING (Date) <input type="checkbox"/> _____ <input type="checkbox"/> PYREXIA (Date) <input type="checkbox"/> _____ <input type="checkbox"/> RADIATION (Date) <input type="checkbox"/> _____ <input type="checkbox"/> NAUSEA <input type="checkbox"/> _____ <input type="checkbox"/> SMOKING (Query pattern of usage) <input type="checkbox"/> _____ <input type="checkbox"/> ALCOHOL, DRUGS (Query pattern of usage) <input type="checkbox"/> _____ <input type="checkbox"/> OCCUPATIONAL <input type="checkbox"/> _____ NUTRITION (24 hour recall) GOOD <input type="checkbox"/> FAIR <input type="checkbox"/> POOR <input type="checkbox"/>					7. MENSTRUAL HISTORY L.M.P. (Date) _____ E.D.C. _____ IF UNSURE, CONSIDER EARLY ULTRASOUND MENSTRUAL CYCLE _____ 8. METHOD OF CONTRACEPTION (Specify) _____ DATE OF DISCONTINUANCE _____ 9. CURRENT MEDICATIONS _____ _____ _____ _____ _____ _____ _____ _____ _____ _____																																																																																																		
Associated Hi Risk Conditions <input type="checkbox"/> Uterine Surgery or Malformations C-section, Cone Biopsy, Cervical Suture, etc. <input type="checkbox"/> Chronic Renal Disease <input type="checkbox"/> Diabetes (incl. Gest.) <input type="checkbox"/> Cardiac Disease & Hypertension <input type="checkbox"/> Serious Medical, Surgical or Psychiatric Disorders					5. PAST ILLNESS (Specify) NO YES <input type="checkbox"/> RENAL <input type="checkbox"/> _____ <input type="checkbox"/> CARDIAC <input type="checkbox"/> _____ <input type="checkbox"/> INFECTIONS <input type="checkbox"/> _____ <input type="checkbox"/> RUBELLA <input type="checkbox"/> _____ <input type="checkbox"/> VENEREAL <input type="checkbox"/> _____ <input type="checkbox"/> ALLERGIES <input type="checkbox"/> _____ <input type="checkbox"/> OPERATIONS <input type="checkbox"/> _____ <input type="checkbox"/> TRANSFUSIONS <input type="checkbox"/> _____ <input type="checkbox"/> OTHERS <input type="checkbox"/> _____ 6. FAMILY HISTORY (Specify) NO YES <input type="checkbox"/> DIABETES <input type="checkbox"/> _____ <input type="checkbox"/> CARDIAC <input type="checkbox"/> _____ <input type="checkbox"/> HYPERTENSION <input type="checkbox"/> _____ <input type="checkbox"/> TUBERCULOSIS <input type="checkbox"/> _____ <input type="checkbox"/> TWINS <input type="checkbox"/> _____ <input type="checkbox"/> MALFORMATIONS <input type="checkbox"/> _____ <input type="checkbox"/> OTHERS <input type="checkbox"/> _____					10. EXAMINATION DATE _____ GENERAL CONDITION _____ HEAD & NECK: _____ mm Hg BREAST & LYMPH NODES: _____ HEART & LUNGS: _____ ABDOMEN: _____ SPINE: _____ MUCOSAE & SKIN: _____ PELVIS NORMAL, ABNORMAL (Describe): _____ CERVIX CYTOLOGY (Class No.): _____ OTHER OBSERVATIONS: _____ SIGNATURE _____ MD _____					11. TOPICS FOR DISCUSSION AND ADVICE <table border="0" style="width:100%;"> <tr> <td style="vertical-align: top;"> Alternate Physician(s) Genetic Counseling Prenatal Course & Classes Nutrition Supplements Wt. Control Exercise Hosp. Adm. Procedures Arrival at Hospital Anaes. & Analg. Cordus </td> <td style="vertical-align: top;"> Bowels Baths Clothes Books Breast Care Breast Feeding Baby Care Labour Stages Rest Smoking Alcohol Medications </td> </tr> </table>					Alternate Physician(s) Genetic Counseling Prenatal Course & Classes Nutrition Supplements Wt. Control Exercise Hosp. Adm. Procedures Arrival at Hospital Anaes. & Analg. Cordus	Bowels Baths Clothes Books Breast Care Breast Feeding Baby Care Labour Stages Rest Smoking Alcohol Medications																																																																																							
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 HLTH 1582
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 Prepared by THE PERINATAL PROGRAM OF BRITISH COLUMBIA
 WHITE COPY - MOTHER'S CHART

YELLOW COPY - INFANT'S CHART

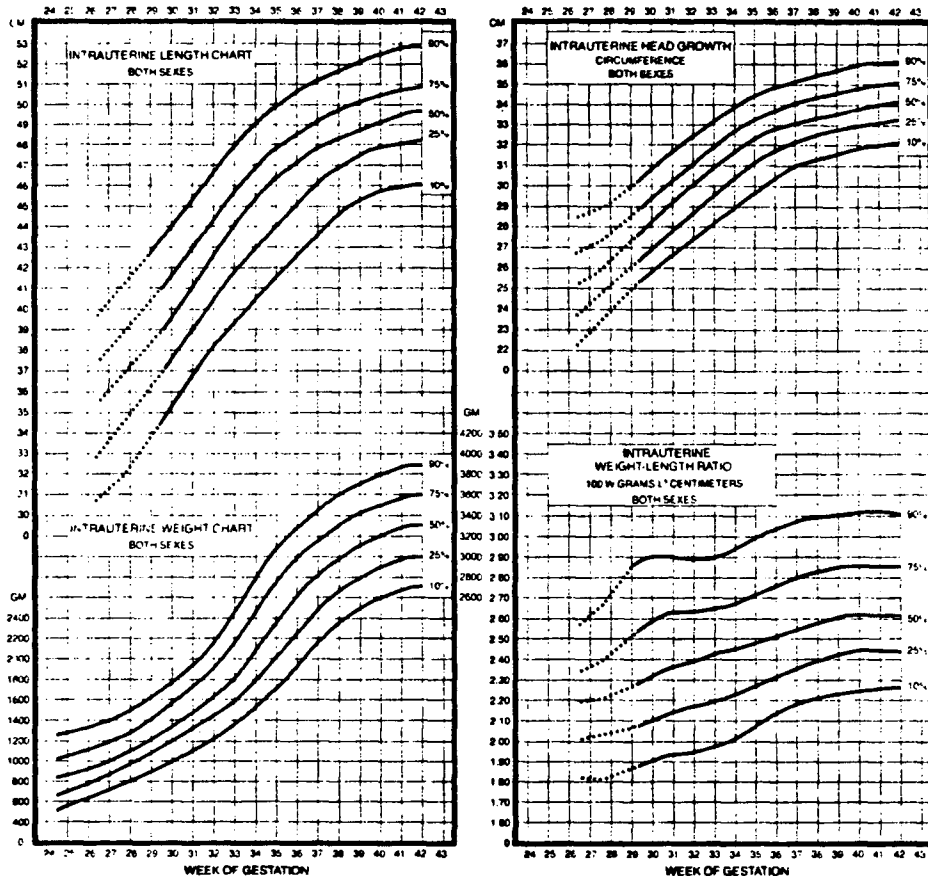
 Vancouver, B.C.
 PINK COPY - PHYSICIAN'S

PRENATAL RECORD

PART II

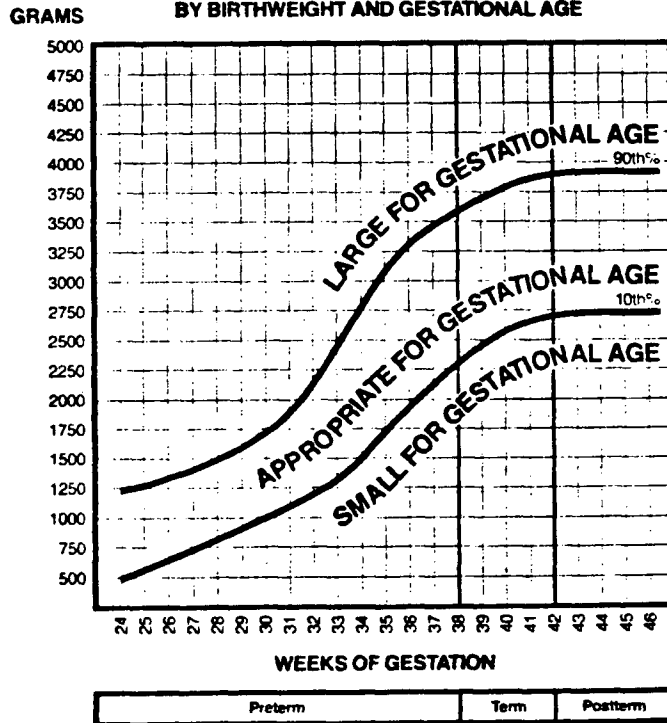
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INTRAUTERINE GROWTH CHART



LUBCHENCO L.O., MARESHMAN C., and BOYD E.: Pediatrics 57:403, 1956

CLASSIFICATION OF NEWBORNS BY BIRTHWEIGHT AND GESTATIONAL AGE



BATTAGLIA F.C., LUBCHENCO L.O.: Pediatrics 71:161, 1967
Copyright American Academy of Pediatrics 1966 and 1967

LABOUR SUMMARY AND DELIVERY RECORD PART I

HOSPITAL

1. GRAVIDA PARA ABORTIONS LIVING L.M.P. E.D.C.

WEEKS OF GESTATION BLOOD GROUP & TYPE Hbg ON ADMISSION ☐ HEPATITIS CARRIER?**2. RISK FACTORS BEFORE LABOUR**

TIME OF ADMISSION TO LABOUR AREA:

In Multiple Pregnancy

SPECIFY WHETHER BABY A, B, C.

3. RISK FACTORS DURING LABOUR**4. LABOUR**

- ☐ NONE
☐ SPONTANEOUS
☐ INDUCED
☐ AUGMENTED

METHOD OF INDUCTION OR AUGMENTATION:

- ☐ A.R.M. ☐ OXYTOCIN
☐ OTHER - SPECIFY

INDICATIONS AND COMMENTS:

5. FETAL MONITORING

TYPE	✓	NORMAL	ABNORMAL
AUSCULTATION			
EXT. MONITOR			
SCALP ELECTRODE			
INT. UTERINE PRESSURE CATHETER			

FETAL BLOOD SAMPLING

F & B SAMPLE NO. OF TIMES	
LOWEST pH	
CORD BLOOD GASSES UAPM	
MECONIUM AT DELIVERY?	YES NO

TIME SUMMARY

MEMBRANES RUPTURED
 1st STAGE STARTED
 2nd STAGE STARTED
 BABY DELIVERED
 PLACENTA DELIVERED

HR	DAY	MONTH	YEAR

DURATION

	HOURS	MIN
1st STAGE		
2nd STAGE		
3rd STAGE		
DURATION OF RUPTURED MEMBRANES		

6. CONSULTATION

OBSTETRIC

PAEDIATRIC

7. BABY

WEIGHT (g)

SEX

PAEDIATRIC

☐ STILLBORN

IDENTIFICATION #

HOSPITAL #

CONGENITAL MALFORMATIONS

UMBILICAL CORD COMPLICATIONS ABNORMALITIES

2 VESSELS

3 VESSELS

PLACENTA

WEIGHT grams

ABNORMALITIES

	0	1	2	1 MIN	5 MIN	10 MIN
HEART RATE	ABSENT	BELOW 100	ABOVE 100			
RESP. EFFORT	ABSENT	SLOW IRREG.	GOOD CRYING			
MUSCLE TONE	FLIMP	SOME FLEXION	ACTIVE MOTION			
REFLEX IRRITABILITY	NONE	GRIMACE	COUGH OR SNEEZE			
COLOUR	BLUE PALE	BODY PINK BLUE EXTREM	ALL PINK			
APGAR SCORE TOTAL						

8. ANALGESIA/ANAESTHESIA

LABOUR

DELIVERY

ADDITIONAL COMMENTS ON LABOUR

NARCOTIC		
OTHER ANALGESIC/SEDATIVE		
ENTONOX		
REGIONAL BLOCK (EPIDURAL/SPUDENDAL)		
LOCAL INFILTRATION		
GENERAL		
OTHER		
NIL		

DOCTORS PRESENT

DELIVERED BY

NURSES PRESENT

SIGNATURE

OTHERS PRESENT (SUPPORT PERSON ETC.)

Prepared by THE PERINATAL PROGRAM OF BRITISH COLUMBIA
WHITE COPY - MOTHER'S CHART

YELLOW COPY - INFANT'S CHART

R.N.
Vancouver, B.C.
PINK COPY - PHYSICIAN

LABOUR SUMMARY AND DELIVERY RECORD PART II

HOSPITAL

9. MEDICATION

IV/IM	DOSE	TIME	DATE	NURSE'S SIGN

SHADED SECTION IS TO BE COMPLETED BY PHYSICIAN

10. DELIVERY

PRESENTATION & POSITION		DURING LABOUR		AT DELIVERY	
Type	Spontaneous Vaginal <input type="checkbox"/>	Ventouse Extraction <input type="checkbox"/>	Shoulder Dystocia <input type="checkbox"/>		
	Low <input type="checkbox"/>	Low Mid <input type="checkbox"/>	Mid <input type="checkbox"/>		
Forceps	Traction Mild to Mod <input type="checkbox"/>	Traction Mod to Severe <input type="checkbox"/>			
	Trial Successful <input type="checkbox"/>	Trial Failed <input type="checkbox"/>			
Rotation	Manual & Spontaneous Delivery <input type="checkbox"/>	Forceps Rotation & Spontaneous Delivery <input type="checkbox"/>			
	Manual & Forceps Delivery <input type="checkbox"/>	Forceps Rotation & Forceps Delivery <input type="checkbox"/>			
Breech	Easy <input type="checkbox"/>	Moderately Difficult <input type="checkbox"/>	Difficult <input type="checkbox"/>		
	Internal Version <input type="checkbox"/>	Breech Extraction <input type="checkbox"/>	Forceps to after coming head <input type="checkbox"/>		
Caesarean Section	Pfannenstiel Incision <input type="checkbox"/>	Vertical Midline Incision <input type="checkbox"/>	Tubal ligation <input type="checkbox"/>		
	Low Segment Transverse Incision <input type="checkbox"/>	Low Segment Vertical Incision <input type="checkbox"/>	Classical <input type="checkbox"/>	Inverted-T <input type="checkbox"/>	
Birth Injury	Cephalhematoma <input type="checkbox"/>	Fracture <input type="checkbox"/>	Nerve Paralysis <input type="checkbox"/>		
Third Stage	Complications, Manual Removal, etc.				

11. ADDITIONAL COMMENTS AND OPERATIVE FINDINGS

ATTENDING PHYSICIAN

DATE

X

MD.

19

12. BLOOD LOSS

MINIMAL

MODERATE

EXCESSIVE

☐ ESTIMATED☐ MEASURED

CC'S

13. PERINEUM EPISIOTOMY

☐ MEDIAN☐ MEDIOLATERAL☐ EXTENSION - SPECIFY

VAGINAL/CERVICAL LACERATION

☐

LACERATION

☐ 1st Degree - Skin and/or Mucosa only☐ 2nd Degree - Plus Deeper Perineal Structures☐ 3rd Degree - Plus Rectal Sphincter☐ 4th Degree - Plus Rectal Mucosa

SUTURED BY

BLOOD TRANSFUSION

NO. OF UNITS

14. OPERATIVE DELIVERY

LIST INDICATION IN
ORDER OF PRIORITY

15. PUERPERIUM

☐ NORMAL☐ COMPLICATIONS - SPECIFY

Anti - D

Rubella Titre

Vaccine needed?

P.P. Hgb

☐ INFECTION - SPECIFY

OTHER COMMENTS

Breast feeding

Sterilization

X

DISCHARGE AUTHORIZATION

DATE

19

Prepared by THE PERINATAL PROGRAM OF BRITISH COLUMBIA
WHITE COPY - MOTHER'S CHART

YELLOW COPY - INFANT'S CHART

Vancouver, B.C.
PINK COPY - PHYSICIAN'S

NEWBORN RECORD

PART I

1. MOTHER'S NAME				AGE	
FATHER'S NAME				AGE	
MOTHER'S UNIT NO	PARA	E.D.C.	BLD. GROUP	Rh Antibodies?	
RISK FACTORS FOR INFANT					
GENERAL CONDITION AT BIRTH				MECONIUM AT DELIVERY? <input type="checkbox"/> YES <input type="checkbox"/> NO	

2.		0	1	2	1 MIN	5 MIN	10 MIN	3. RESUSCITATION		Spontaneous breathing by: _____ Mins		
HEART RATE	ABSENT	BELOW 100	ABOVE 100					<input type="checkbox"/> None				
RESP EFFORT	ABSENT	SLOW IRREG	GOOD CRYING					<input type="checkbox"/> Oxygen				
MUSCLE TONE	LIMP	SOME FLEXION	ACTIVE MOTION					<input type="checkbox"/> Mask & Pressure				
REFLEX IRRITABILITY	NONE	GRIMACE	COUGH OR SNEEZE					<input type="checkbox"/> Endotracheal Tube				
COLOUR	BLUE PALE	BODY PINK BLUE EXTREM	ALL PINK					<input type="checkbox"/> Tracheal Aspiration				
APGAR SCORE TOTAL								<input type="checkbox"/> Cardiac Massage				
4. DELIVERY ROOM				TIME				6. PHYSICAL EXAMINATION (INCLUDING STILL BIRTHS)				MD.
BIRTHDATE DAY MONTH YEAR								BY DATES		BY EXAM		SEX
METHOD OF DELIVERY								1. GESTATIONAL AGE: _____ WKS		_____ WKS		Male
UNIT NUMBER								NORMAL		ABNORMAL		Female
HOSPITAL NUMBER								2. GENERAL APPEARANCE		<input type="checkbox"/>		Ambiguous
IDENTIFIED BY _____ Signature								3. SKIN		<input type="checkbox"/>		
EYE PROPHYLAXIS <input type="checkbox"/> OTHER SPECIFY _____								4. HEAD		<input type="checkbox"/>		
CORD BLOOD <input type="checkbox"/> Rh <input type="checkbox"/> A R.T. <input type="checkbox"/> OTHER <input type="checkbox"/> RESERVE								5. ENT		<input type="checkbox"/>		
VONDED? <input type="checkbox"/> YES <input type="checkbox"/> NO				PASSED MECONIUM? <input type="checkbox"/> YES <input type="checkbox"/> NO				6. RESPIRATORY		<input type="checkbox"/>		
5. NURSERY ADMISSION				TEMP				7. CARDIOVASCULAR		<input type="checkbox"/>		
HEART				RESP RATE				8. ABDOMEN		<input type="checkbox"/>		
ROUTINE PROCEDURES <input type="checkbox"/> CORD CARE SPECIFY _____				<input type="checkbox"/> VITAMIN K				9. UMBILICAL CORD		<input type="checkbox"/>		
FEEDING PLAN <input type="checkbox"/> BREAST <input type="checkbox"/> BOTTLE								10. EXTREMITIES		<input type="checkbox"/>		
GENERAL CONDITION								11. GEN. RECTAL		<input type="checkbox"/>		
								12. CNS		<input type="checkbox"/>		
								13. OTHER		<input type="checkbox"/>		
								DATE		TIME SIGNATURE		MD.
PHYSICIAN IN CHARGE:				TIME NOTIFIED		BY						
7. EVALUATION OF DEVELOPMENT				(growth curve and chart on reverse)								
<input type="checkbox"/> PRE TERM												
<input type="checkbox"/> TERM												
<input type="checkbox"/> POST TERM												
BIRTH WEIGHT				LENGTH		HEAD CIRCUMFERENCE						
gms				cms		cms						
%				%		%						

Prepared by THE PERINATAL PROGRAM OF BRITISH COLUMBIA
WHITE COPY - INFANT'S CHART

YELLOW COPY - MOTHER'S CHART

Vancouver, B.C.
PINK COPY - PHYSICIAN'S

NEWBORN RECORD

PART II

8. CONSULTANT (If Applicable) <input type="checkbox"/> CONTINUING CARE		_____ _____ _____ _____	
9. SCREENING TESTS <input type="checkbox"/> Pts & T4 <input type="checkbox"/> URINALYSIS		_____ _____ _____	
HIP SCREEN <input type="checkbox"/> NORMAL <input type="checkbox"/> ABNORMAL <input type="checkbox"/> NOT DONE		_____ _____	
10. DATE	PROBLEM LIST	DATE RESOLVED	
11.	PROGRESS NOTES		
12.	CIRCUMCISION		SIGNATURE
	<small>METHOD</small>		<small>MD</small>
13. DISCHARGE EXAMINATION			
<small>GENERAL APPEARANCE</small>	<small>NORMAL</small> <input type="checkbox"/>	<small>ABNORMAL (Specify)</small> _____	<small>ABDOMEN</small> <input type="checkbox"/>
<small>HEAD</small>	<input type="checkbox"/>	_____	<small>SKELETAL</small> <input type="checkbox"/>
<small>ENT</small>	<input type="checkbox"/>	_____	<small>EXTREMITIES</small> <input type="checkbox"/>
<small>RESP</small>	<input type="checkbox"/>	_____	<small>GEN. RECTAL</small> <input type="checkbox"/>
<small>CARDIO VASC.</small>	<input type="checkbox"/>	_____	<small>CNS</small> <input type="checkbox"/>
<small>SKIN</small>	<input type="checkbox"/>	_____	<small>OTHER</small> _____
14. DISCHARGE INFORMATION		15. FINAL DISCHARGE DIAGNOSIS	16. FOLLOW UP PROBLEMS
<small>WEIGHT</small> _____ <small>gms</small>	<small>HEAD CIRCUMFERENCE</small> _____ <small>cms</small>		
DISCHARGED TO:			
<input type="checkbox"/> HOME			
<input type="checkbox"/> FOSTER HOME			
<input type="checkbox"/> OTHER HOSPITAL (Specify) _____			
<input type="checkbox"/> NEONATAL DEATH		<input type="checkbox"/> BREAST FEED <input type="checkbox"/> FORMULA	FOLLOW UP BY: <input type="checkbox"/> PRIVATE PHYSICIAN <input type="checkbox"/> EXAMINER <input type="checkbox"/> OTHER, M.D. (Specify) _____ <input type="checkbox"/> PUBLIC HEALTH NURSE <input type="checkbox"/> DEPT. OF HUMAN RESOURCES
<input type="checkbox"/> AUTOPSY PERFORMED		<input type="checkbox"/> VITAMINS <input type="checkbox"/> IRON <input type="checkbox"/> FLUORIDE	
		MEDICATIONS	
DATE _____		SIGNATURE _____	
		<small>MD</small>	

FORM 4A.

PROVINCE OF
BRITISH COLUMBIA (Canada)
DEPARTMENT OF HEALTH
Division of Vital Statistics

REGISTRATION OF
STILLBIRTH

Registration No.
(Department use only)

SEE REVERSE FOR MEDICAL CERTIFICATE AND INSTRUCTIONS
IMPORTANT: Any change or correction made in the completion of this form must be initialed by the person certifying the original information.

CHILD	1. Surname (print or type)			
	Given names (if any)			2. SEX
DATE OF BIRTH	3. Month (by name), day, year of birth		4. KIND OF BIRTH—State whether single, twin, triplet	
	5. If twin, triplet, state whether this child was born 1st, 2nd, 3rd			
PLACE OF BIRTH	6. Name of hospital (If not in hospital give exact location where birth occurred)			
	City, town or other place (by name)			Inside municipal limits? (State Yes or No)
USUAL RESIDENCE OF MOTHER	7. Complete street address. If rural give exact location, not Post Office or Rural Route address			
	City, town or other place (by name)			Province (or country)
OTHER BIRTH PARTICULARS	8. Duration of pregnancy (in completed weeks)		9. Children ever born to this mother (including this birth)	
	10. Weight of child at birth		11. Are the parents married to each other? (State Yes or No)	
	12. If the parents are not married to each other state whether mother is single, married, widowed, or divorced		Number Liveborn (after 20 weeks pregnancy)	
	13. (OR) 14. grams		15. oz.	
PARENTS	FATHER		MOTHER	
	13. Surname of child's father (print or type)		18. Maiden surname of child's mother (print or type)	
	All given names in full		All given names in full	
	14. City, town or other place of birth (by name)		19. City, town or other place of birth (by name)	
BIRTHPLACE	Province (or country if outside Canada)		Province (or country if outside Canada)	
	15. Month (by name), day, year of birth		16. AGE (at time of this birth)	
BIRTHDATE	17. Native Indian? If "yes" give name of band		22. Native Indian? If "yes" give name of band	
	Yes <input type="checkbox"/> No <input type="checkbox"/>		Yes <input type="checkbox"/> No <input type="checkbox"/>	
ATTENDANT	23. Name and address of attending physician (or other attendant)			
	24. Complete mailing address (if different from item 7); If rural give Post Office or Rural Route address			
CERTIFICATION OF PARENT	25. I certify the foregoing to be true and correct to the best of my knowledge and belief: X		26. Date signed — Month (by name), day, year	
	Signature of parent		B.C.	
DISPOSITION	27. Burial, cremation or other disposition (specify)		28. Date of burial or disposition (month, day, year)	
	29. Name and address of cemetery, crematorium or place of disposition			
FUNERAL DIRECTOR	30. Name and address of funeral director (or person in charge of remains) (print or type)			
	DO NOT WRITE BELOW THIS LINE — OFFICE USE ONLY			
Notations:				
CERTIFICATION OF DISTRICT REGISTRAR	I certify this return, including the medical certificate of Stillbirth, on reverse, was accepted by me on this date at —			
	District Registration No.		Signature of District Registrar	

MEDICAL CERTIFICATE OF STILLBIRTH

CAUSE OF STILLBIRTH	31. Part I Immediate cause - Foetal disease or condition directly leading to stillbirth		(a)..... due to (or as a consequence of)		Check Foetal (F) or Maternal (M)	F	M
	Antecedent causes - Foetal and/or maternal conditions, if any, giving rise to the im- mediate cause (a) above, stating the underlying cause last		(b)..... due to (or as a consequence of)				
			(c).....				
	Part II Other significant conditions of foetus or mother which may have contributed to the stillbirth but were not causally related to the immediate cause (a) above						
AUTOPSY PARTI- CULARS	32. Autopsy being held?	Yes <input type="checkbox"/> No <input type="checkbox"/>	33. Does the cause of stillbirth stated above take account of autopsy finding?	Yes <input type="checkbox"/> No <input type="checkbox"/>	34. May further information relating to the cause of stillbirth be available later?	Yes <input type="checkbox"/> No <input type="checkbox"/>	
DELIVERY AND LABOUR	35. Manipulative, instrumental or other operative procedure for delivery?		Yes <input type="checkbox"/> No <input type="checkbox"/>	Was foetus dead before such procedure?		Yes <input type="checkbox"/> No <input type="checkbox"/>	
	36. Nature of procedure (low, middle or high forceps, version and extraction, caesarian section, craniotomy, etc.)						
	37. Did death occur before labour?	Yes <input type="checkbox"/> No <input type="checkbox"/>	During labour?	Yes <input type="checkbox"/> No <input type="checkbox"/>	Labour induced?	Yes <input type="checkbox"/> No <input type="checkbox"/>	(If "yes" specify method(s))
CERTIFI- CATION (attending physician, coroner, etc.)	38. I certify that the state- ments herein are true and correct to the best of my knowledge and belief		Signature (attending physician, coroner, etc.)				
			Attending physician <input type="checkbox"/> Physician examining body after death <input type="checkbox"/> Coroner <input type="checkbox"/>				
	39. Name of physician or coroner (print or type)						
		Address		Date certified: Month, day, year			

NOTES FOR THE CERTIFYING PHYSICIAN OR CORONER

A "stillbirth" is defined for purposes of registration under the British Columbia Vital Statistics Act as follows:

"Stillbirth" means the complete expulsion or extraction from its mother, after at least twenty weeks' pregnancy, of a product of conception, in which, after such expulsion or extraction, there is no breathing, beating of the heart, pulsation of the umbilical cord, or unmistakable movement of voluntary muscle.

Physician's Statement of Cause of Stillbirth: The morbid conditions relating to stillbirth in the Medical Certificate of Stillbirth are divided into two groups. In Group I are those related to the "Immediate cause", i.e., "the foetal disease or condition directly leading to stillbirth," and the "Antecedent causes", and in Group II, "Other significant conditions" in the foetus or the mother which contributed to the death of the foetus but which were not causally related to the immediate cause. In most cases a statement of cause under Group I will suffice. In many cases a single cause will adequately describe the case (see Example 1); however, where it is necessary to record more than one cause it is important that these be stated in etiological sequence and in the position provided on the form so as to indicate their mutual relationship. Information is sought in this organized fashion so that the selection of the "cause" of stillbirth for tabulation purposes (as described below) may be made in the light of the certifier's viewpoint.

Cause of Stillbirth Assignment - The "cause" selected for coding and tabulation of the official "cause-of-stillbirth" statistics is the "underlying cause", that is, "the disease or injury which initiated the train of events leading to the death of the foetus". This "cause" will ordinarily be the last condition mentioned in Part I of the Certificate.

Foetal or Maternal Diseases or Conditions - Conditions which may be reported as Antecedent cause(s) (Part I) or Contributory cause(s) may, of course, relate to either the foetus or the mother. It is therefore important to indicate whether the reported condition was, in fact, a "foetal" (F) or "maternal" (M) condition by checking off (F) or (M) in the appropriate box as illustrated in the examples below.

Autopsy and Autopsy Findings - An indication of whether or not an autopsy is being held and whether the certified causes of stillbirth take account of autopsy findings is valuable in assessing the reliability of cause-of-stillbirth statistics. Where an autopsy is being held and the recorded statement of cause of stillbirth does not take account of the autopsy findings, a supplementary enquiry of the certifying physician may be initiated by the Director of Vital Statistics.

Item 34, Further Information - If there is an indication that "further information relating to the cause of stillbirth may be available later" - from autopsy or other findings - the Director will initiate a supplementary enquiry of the certifying physician or coroner.

The following examples illustrate the essential principles in completing the cause of stillbirth certificate:

Part I	Example 1	Example 2	Example 3
	F M	F M	F M
Immediate cause	(a) Anencephaly due to (or as a consequence of)	Anoxia	Intra-ventricular hemorrhage
Antecedent causes	(b)..... due to (or as a consequence of)	Premature separation of placenta	Dystocia with cranial compression
	(c).....	Severe pre-eclampsia	Congenital hydrocephalus
	Part II Other significant conditions	Diaphragmatic hernia (massive)	Chronic nephritis
Part I	Example 4	Example 5	Example 6
	F M	F M	F M
Immediate cause	Compression of prolonged cord (a)..... due to (or as a consequence of)	Exsanguinating hemorrhage	Anoxia (foetal distress)
Antecedent causes	(b) Breech presentation due to (or as a consequence of)	Ruptured uterus and placental vessels	Severe intra-uterine growth retardation
	(c) Premature onset of labour (incompetent cervical os)	Automobile accident injuring mother	Small placenta with multiple infarcts (placental insufficiency)
	Part II Other significant conditions		

Form 4.

PROVINCE OF
BRITISH COLUMBIA (Canada)
DEPARTMENT OF HEALTH SERVICES
AND HOSPITAL INSURANCE
Division of Vital Statistics

REGISTRATION OF
LIVE BIRTH

Registration No.
(Department use only)

THIS IS A PERMANENT LEGAL RECORD
TYPE OR WRITE PLAINLY AND COMPLETE ALL ITEMS

(See reverse for instructions and legal requirements under the Vital Statistics Act)

NAME OF CHILD	1. Surname of child (print or type)		
	All given names in full (print or type)		
DATE OF BIRTH	3. Month (by name), day, year of birth	4. KIND OF BIRTH - State whether single, twin, triplet	5. If twin, triplet, state whether this child was born 1st, 2nd, 3rd
PLACE OF BIRTH	6. Name of hospital (If not in hospital give exact location where birth occurred)		
	City, town or other place (by name)		
USUAL RESIDENCE OF MOTHER	7. Complete street address. If rural give exact location, not Post Office or Rural Route address		
	City, town or other place (by name)		
OTHER BIRTH PARTICULARS	8. Duration of pregnancy (in completed weeks)	9. Children ever born to this mother (including this birth)	10. Weight of child at birth (lb. oz. (OR) grams)
	11. Are the parents married to each other? (State Yes or No)	12. If the parents are not married to each other state whether mother is single, married, widowed, or divorced	
PARENTS	FATHER		MOTHER
NAME	13. Surname of child's father (print or type)		17. Maiden surname of child's mother (print or type)
	All given names in full		All given names in full
BIRTHPLACE	14. City, town or other place of birth (by name)		18. City, town or other place of birth (by name)
	Province (or country if outside Canada)		Province (or country if outside Canada)
BIRTHDATE	15. Month (by name), day, year of birth	16. AGE (at time of this birth)	19. Month (by name), day, year of birth
	20. AGE (at time of this birth)		
ATTENDANT	21. Name and address of attending physician (or other attendant)		
MAILING ADDRESS OF MOTHER	22. Complete mailing address (if different from item 7) If rural give Post Office or Rural Route address		
CERTIFICATION OF PARENT	23. I certify the foregoing to be true and correct to the best of my knowledge and belief: X		24. Date signed - Month (by name), day, year

DO NOT WRITE BELOW THIS LINE - OFFICE USE ONLY

Notations:

CERTIFICATION OF DISTRICT REGISTRAR	I certify this return was accepted by me on this date at -	
	District Registration No.	Date: Month (by name), day, year
		Signature of District Registrar

Do not use



Province of
British Columbia
MINISTRY OF HEALTH -
DIVISION OF VITAL STATISTICS

PHYSICIAN'S NOTICE OF A LIVE BIRTH OR STILLBIRTH

Do not use

NAME OF FATHER (Surname)				(Given names)		If parents legally married to each other, is father non Indian <input type="checkbox"/> or registered Indian <input type="checkbox"/>			
NAME OF MOTHER (Maiden surname)				(Given names)		AGE		If parents <u>not</u> legally married to each other, is mother non Indian <input type="checkbox"/> or registered Indian <input type="checkbox"/>	
PERMANENT ADDRESS OF MOTHER				(House No.) (Street)		(City or Municipality)		Postal Code	Was child born alive? <input type="checkbox"/> Yes <input type="checkbox"/> No
PLACE OF BIRTH				(Name of Institution)		(Location)		Office Use Only	
DATE OF BIRTH		Hour a.m. <input type="checkbox"/> p.m. <input type="checkbox"/>	Day <input type="checkbox"/>	Month <input type="checkbox"/>	Year 19 <input type="checkbox"/>	Male <input type="checkbox"/>	Female <input type="checkbox"/>	Apgar Score at: 1 min. <input type="checkbox"/> 5 min. <input type="checkbox"/>	Single <input type="checkbox"/> Twin <input type="checkbox"/> Triplets <input type="checkbox"/>
BIRTH WEIGHT		grams <input type="checkbox"/>	Gestation period weeks <input type="checkbox"/>		Total pregnancies <input type="checkbox"/>	Total live births <input type="checkbox"/>	Total stillbirths <input type="checkbox"/>	Total abortions (Spont. & induced) <input type="checkbox"/>	
What special measures (if any) were taken to promote respiration?							If stillborn, did death occur before labour <input type="checkbox"/> or during labour <input type="checkbox"/>		
Mode of delivery: Spontaneous vertex <input type="checkbox"/> Forceps vertex <input type="checkbox"/> Breech <input type="checkbox"/> Caesarean 1st <input type="checkbox"/> 2nd + <input type="checkbox"/>					Other operative procedure (specify): _____				
Abnormality (major or minor) or pathology of infant:			No <input type="checkbox"/>	If yes, describe: _____					
Complications of pregnancy, labour or delivery:			No <input type="checkbox"/>	If yes, describe: _____					
Physician's signature				Physician's address				Date:	

PLEASE REMOVE CARBON BEFORE MAILING

FORM V.S. 3

THIS REPORT TO BE SENT WITHIN 48 HOURS TO THE DISTRICT REGISTRAR OF BIRTHS, DEATHS AND MARRIAGES
VITAL STATISTICS ACT SEC. 3

Province of
British ColumbiaMinistry of
Health

HEALTH SURVEILLANCE REGISTRY
828 WEST 10th AVENUE VANCOUVER, B C V6Z 1L8

9

3

3 SURNAME

4 GIVEN NAMES

5. BIRTH DATE (Y/M/D)

6 ADDRESS											7 REG																	
											8 CUR																	
9 SEX M F													10 BIRTH SINGLE OR MULTIPLE				SGL TWI TRI OTH				11 CITY AND/OR COUNTRY OF BIRTH				12 PL		13 V.S. REG NUMBER	
14 ETHNIC ORIGIN IF KNOWN											15 BIRTH SURNAME IF DIFFERENT FROM ABOVE				16 OTHER RELATIVES REGISTERED		17 CURRENT PARTNER'S NAME											
18 PARENT S/GUARDIANS NAMES											19 MOTHER'S BIRTH SURNAME																	
20 HOSPITALS ATTENDED																												
21 FAMILY PHYSICIAN											22 DATE OF DEATH (Y/M/D)				23 DEATH REG NO.		CAUSE OF DEATH											
															341		342											
25 SOURCE NUMBERS																												
REGISTERED BY																												

ETIOLOGY: INDICATE ANY CLUES AS TO THE CAUSE OF THIS CONDITION, SUCH AS MATERNAL INFECTION, BIRTH TRAUMA, HEREDITARY, POST-NATAL TRAUMA OR INFECTION (E.G. MENINGITIS ETC)

[illegible]

COMMENTS INDICATE ANY SOCIAL OR EMOTIONAL PROBLEMS IN PATIENT AND OR FAMILY WHO ARE HANDICAPPED ETC

[illegible]

FORM 6

- 18 -

PROVINCE OF
BRITISH COLUMBIA (Canada)
DEPARTMENT OF HEALTH
Division of Vital Statistics

**REGISTRATION OF
DEATH**

Registration No.
(Department use only)

NAME OF DECEASED	1. Surname of deceased (print or type)		2. SEX	
PLACE OF DEATH	3. Name of hospital or institution (otherwise give exact location where death occurred)			
	City, town or other place (by name)		Inside municipal limits? (State Yes or No)	
USUAL RESIDENCE	4. Complete street address: If rural give exact location (not Post Office or Rural Route address)			
	City, town or other place (by name)		Inside municipal limits? (State Yes or No)	Province (or country)
MARITAL STATUS	5. Single, married, widowed, or divorced (Specify)		6. If married, widowed, or divorced, give full name of husband or full maiden name of wife	
OCCUPATION	7. Kind of work done during most of working life		8. Kind of business or industry in which worked	
BIRTHDATE	9. Month (by name), day, year of birth		10. AGE (years) (Months) (Days) (Hours) (Minutes)	
			If under 1 year: If under 1 day:	
BIRTHPLACE	11. City or place Province (or country) of birth		12. Native Indian? Yes No If "yes" state name of band	
FATHER	13. Surname and given names of father (print or type)		14. BIRTHPLACE - City or place, Province (or country)	
MOTHER	15. Maiden surname and given names of mother (print or type)		16. BIRTHPLACE - City or place, Province (or country)	
INFORMANT	17. Signature of informant		18. Relationship to deceased	
	19. Address of informant		20. Date signed - Month, day, year	
DISPOSITION	21. Burial, cremation or other disposition (specify)		22. Date of burial or disposition (month, day, year)	
	23. Name and address of cemetery, crematorium or place of disposition			
FUNERAL DIRECTOR	24. Name and address of funeral director (or person in charge of remains) (print or type)			

MEDICAL CERTIFICATE OF DEATH

DATE OF DEATH	25. Month (by name), day, year of death		Approx. interval between onset & death	
CAUSE OF DEATH	26. Part I Immediate cause of death (a) due to, or as a consequence of Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the underlying cause last (b) due to, or as a consequence of (c)			
	Part II Other significant conditions contributing to the death but not causally related to the immediate cause (a) above			
	AUTOPSY PARTICULARS	27. Autopsy held? Yes No	28. Does the cause of death stated above take account of autopsy findings? Yes No	29. May further information relating to the cause of death be available later? Yes No
ACCIDENT OR VIOLENCE (if applicable)	30. If accident, suicide, homicide or undetermined (specify)		32. Date of injury (Month (by name), day, year)	
	33. How did injury occur? (describe circumstances)			
SURGICAL OPERATION	34. If there was a recent surgical operation give date of operation		35. State operative findings	
CERTIFICATION (attending physician, coroner, etc.)	36. I certify that to the best of my knowledge and belief the above-named person died on the date and from the causes stated herein: Signature (attending physician, coroner, etc.)		Attending physician <input type="checkbox"/> Physician examining body after death <input type="checkbox"/> Coroner <input type="checkbox"/>	
	37. Name of physician or coroner (print or type)		Date: Month, day, year	

DO NOT WRITE BELOW THIS LINE - OFFICE USE ONLY

Notations:

CERTIFICATION OF DISTRICT REGISTRAR	I certify this return was accepted by me on this date at - District Registration No. _____ Date: Month (by name), day, year _____ Signature _____	
--------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------	--

626-88 110-2087-1

See Reverse for Instructions

IMPORTANT: Any change or correction made in the completion of this form must be initialed by the person certifying the original information.

INSTRUCTIONS

1. Under Item 7 the trade, profession or kind of work in which the deceased was occupied during most of his (her) working life is to be inserted, for example, physician, stenographer, sales clerk, office clerk, elevator operator, salesman, labourer, carpenter, et cetera. If deceased was a housewife in her own home, state "housewife".
2. Under Item 8 the type of industry or business in which the deceased was occupied during most of his (her) working life is to be inserted, for example, law office, department store, insurance, banking, clothing factory, newspaper, et cetera. If deceased was a housewife in her own home, state "At home".

Notes for the Certifying Physician or Coroner

Physician's Statement of Cause of Death.—The morbid conditions relating to death on the Medical Certificate of Death are divided into two groups. In Group I are the "Immediate cause" and the "Antecedent causes", and in Group II "Other significant conditions" contributing to the death but not causally related to the "Immediate cause". In most cases a statement of cause under Group I will suffice. The entry of a single cause is preferable where this adequately describes the case (see Example 1). Where the physician finds it necessary to record more than one cause it is important that these be stated in the position provided on the form which is indicative of their mutual relationship. Information is sought in this organized fashion so that the selection of the cause for tabulation may be made in the light of the certifier's viewpoint.

- a) Purpose of medical certification of death.—The principal purposes are to establish the fact and date of death, and to provide the basis for reliable mortality statistics.
- b) Cause-of-death assignment.—For statistical purposes the cause selected for coding and tabulation of the official cause-of-death statistics is the "underlying cause" of death, i.e. "the disease or injury which initiated the train of events leading to death". This cause ordinarily will be the last condition which is mentioned in Part I of the Cause of Death section of the form.
- c) Approximate interval between onset and death.—This is often of great value in selecting the underlying cause for statistical purposes (as described above). Where these intervals are not known or are uncertain, an estimate should be recorded.
- d) Maternal deaths.—Qualify all diseases resulting from pregnancy, abortion, miscarriage, or childbirth, e.g. "puerperal septicaemia", "eclampsia, arising during pregnancy". Distinguish between septicaemia associated with abortion and that associated with childbirth.
- e) Cancer.—In all cases the organ or part FIRST affected, i.e. the primary site of the neoplasm, should be specified.
- f) Items 27, 28, Autopsy and autopsy findings.—An indication of whether or not an autopsy is being held and whether the cause of death stated takes account of autopsy findings is valuable in assessing the reliability of cause-of-death statistics. Where an autopsy is being held and the recorded statement of cause of death does not take account of autopsy findings, a supplementary enquiry of the certifying physician may be initiated by the Director of Vital Statistics.
- g) Item 29, Further information.—If there is an indication that "further information relating to the cause of death may be available later"—from autopsy or other findings—the Director will initiate a supplementary enquiry of the certifying physician or coroner.

The following examples illustrate the essential principles in completing the cause of death certificate—

	Example 1	Example 2	Example 3	Example 4	Example 5
CAUSE OF DEATH					
Part I					
Immediate cause of death	Labor (a pneumonia)	Acute peritonitis	Cancer of lung (metastatic)	Coronary thrombosis	Hypostatic pneumonia
	due to, or as a consequence of				
Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the underlying cause last	<div> <div>1b.....</div> <div>due to, or as a consequence of</div> <div>1c.....</div> </div>	Acute appendicitis	Cancer of breast		Fracture of hip
					Fall on stairs
Part II					
Other significant conditions contributing to death but not causally related to the immediate cause (a) above		Diabetes		Cancer of breast	

Confidentiality—The Vital Statistics Act specifically protects the confidentiality of the physician's medical certification as follows:

Sec. (6) No certificate issued in respect of the registration of a death shall be issued in such a manner as to disclose the cause of death as certified on the medical certificate, except:

- (a) upon the authority in writing of the Deputy Minister; or
- (b) upon the order of a Judge of a Court.

STILLBIRTH

The special stillbirth registration form must be used in registering a stillbirth