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# Cancer and Work in Canada with particular reference to occupational risk factors in breast cancer patients in one community and related selected research methods used to investigate those factors.

## Volume 1

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" Some circumstantial evidence is very strong,
as when you find a trout in the milk."

- Henry David Thoreau, 19th century American philosopher

"My basic sense of it has always been to get people to understand that in the long run they themselves are the only protection they have against violence or injustice.... People have to be made to understand that they cannot look for salvation anywhere but to themselves."

- Ella Baker, 20th century American civil rights advocate

**Abstract**

Cancer represents a major cause of human morbidity and mortality. There is no scientific consensus regarding cancer causality or prevention. Occupational exposure potentially remains a major contributor to the incidence of this group of diseases, but the data to assess its impact continues to elude researchers and public health advocates. Among women in industrialised countries, breast cancer is the most prevalent cancer. The known or suspected risk factors, including family history and lifetime oestrogen load, can account for less than 50 percent of the cases. New hypotheses about the role of xenoestrogens and endocrine disrupting compounds are challenging the previous scientific precepts regarding cancer causality.

Within this context, the extent to which a community-based occupational history data collection initiative can contribute to advancing our scientific understanding of associations between cancer and work is explored. The possibility that occupational histories data can find associations missed in conventional breast cancer research that ignore occupation is also explored. More specifically, the extent to which data derived from an occupational history questionnaire can provide insight into the potential association between breast cancer risk and farming is examined. Occupational histories of cancer patients contain data that could help to elucidate and inform our understanding of cancer aetiology and prevention.

In the community of Windsor, Ontario, Canada a local cancer treatment centre responded to community concerns by cooperating in a collaborative research project to collect the occupational histories of cancer patients. *Computerised Record of Occupation Made Easy (CROME)* was an innovative method that allowed individual

patients to document their lifetime work histories. This data collection process represented the first time a local Canadian cancer treatment center had undertaken such an initiative.

Based on the hypothesis generated by CROME, a new research study was launched – *Lifetime Occupational History Record (LOHR).* Over a two-and-a-half year period, all female patients at the Windsor Regional Cancer Centre with new incident breast cancer were invited to participate in a population-based case-control study along with an equivalent number of randomly selected community controls. A comprehensive lifetime history questionnaire was administered to subjects by interview. Data gathered included known or suspected risk factors along with a complete occupational history of all jobs ever worked. An occupational history of farming alone produced an Odds Ratio (OR) = 2.8 (CI, 95%, 1.6- 4.8).

These findings are important for our understanding of cancer causality with implications for resolving the current scientific conflict regarding the role of occupationally caused carcinogenesis. Such collaborative, community-based studies also demonstrate the importance of community participation in the scientific research process.

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Andrew Watterson has unselfishly acted as supervisor, mentor and academic advisor throughout the process. Andrew is one of the few intellectuals that have remained committed to the radical democratic ideals of worker-centred occupational health and I acknowledge his contribution to forming and presenting my ideas within this dissertation and beyond into my day to day work in occupational health. Michael Gilbertson, one of my academic advisors, is also a good friend and mentor. Michael also gave me an opportunity to participate with him in examining the health of Windsor in a way that enriched and changed my understanding particularly of environmental exposures (*see Appendix A*). I also wish to acknowledge Alan Sears, who is the head of Labour Studies at the University of Windsor and my other academic advisor, for his advice and political insights.

A number of people have read drafts and offered their ideas. Rory O'Neill first suggested that I consider working with Andrew Watterson on an academic degree. His passion and commitment to workers' rights remains an inspiration. Abraham Reinhartz is an exceptional occupational physician. He participated in this research process from the very first day. It could never have advanced without him. Michael Lax, another exceptional occupational physician, read a number of chapters and gave me political criticism about how I was situating the conflict of

occupational cancer in the capitalist economy. His writings were influenced in my own understanding of why preventable cancer is still being tolerated. Kathy Mayville, a colleague at the Occupational Health Clinic for Ontario Workers in Windsor and co-investigator in several collaborative undertakings, proofread the manuscript. Marion Keith, family member and friend, generously read the final drafts offering encouragement and suggestions for improvements. I am forever grateful to all of these friends and colleagues for their willingness to assist me in this laborious task.

**Declaration of association**

The author of this dissertation is employed as executive director of the co-sponsoring Occupational Health Clinics for Ontario Workers (OHCOW) Sarnia-Lambton. While on a leave of absence in 2002 from the clinic, the author was employed as a research associate by the University of Windsor (the host institution) for a period of one year during the LOHR study. The author has no financial interest in these research studies.

**Two Case Studies**

There were numerous people and organisations involved in the two collaborative research projects that constitute the cases studies within this dissertation - *Computerised Record of Occupation Made Easy (CROME)* (Brophy, 1999; Brophy and Keith, 1998; Brophy, 1994a, 1994b, 1993) *and the Lifetime Occupational History Record (LOHR)* (Brophy et al., 2004, 2002, 2000a; Brophy and Keith, 2002a, 2002b, 2001a, 2000c, 2000b; Brophy, 2002c, 2002d, 2001b, 2000d, 1999a, 1999b).

An elaboration of the individuals involved in these research projects and the research funding sources are contained in *Appendices B, C, and D* including information about the new breast cancer case control study, *Lifetime Occupational and Environmental History Record, LOEHR.*

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# CHAPTER 1: INTRODUCTION

## 1.1 Introduction

This dissertation examines the increasing incidence of cancer globally. It further elucidates the debates surrounding the aetiology of that increase and links this discussion of the potential contribution of occupational exposure to toxic substances. The global analysis is followed by an assessment specific to Canada and then to the area of Windsor, Ontario with special attention -to breast cancer.

The scientific debates in the last two decades have focused mainly on the role of lifestyle factors versus exogenous, (for example, external occupational and environmental) exposures. The dissertation argues that increasing exposures to exogenous carcinogens in the environment and in the workplace have contributed to the increased incidence of cancer. There is not only a lack of scientific consensus but also a lack of political will in addressing these causal risk factors. This conflict has particular significance for populations at risk, such as industrial workers and women, who are often left without adequate protection against potential exposures to hazardous substances. These differing perspectives on cancer causality are reflective of deeper political divisions within society over the power to control matters of health and prevent diseases (Watterson, 1999).

In order to explore the subject both rigorously and thoroughly, the thesis draws on a range of methods. The first part of the thesis uses the normal techniques provided by systematic reviews and policy analysis to identify and explain ~~what~~ the dominant view of cancer causation and discuss the role of occupational exposures as a possible aetiologic factor. It therefore provides an analysis of the current state of knowledge and locates the literature within a framework of international, national, and regional Canadian policy. Without this analysis, which underpins the thesis, it would not be possible to identify and pursue the research questions in the second part of the thesis. The second part employs bespoke techniques developed to explore links between occupation and specific diseases. These particular tailored methods are discussed in detail in the case study chapters.

The dissertation therefore contains a critical review of the traditional epidemiological methods, their limitations, and the implications for policy and public health. The contextualisation of the scientific issues surrounding cancer causality appear in the chapters -preceding that review in order to understand the barriers that tend to prevent critical examination of the links between exogenous exposures and cancer incidence. To help identify the role of workplace exposures, a collaborative, action-based community research project was launched in Windsor, Ontario, Canada. *These studies resulted in the identification of elevated breast cancer risk among women engaged in agriculture.* The findings and lessons of this undertaking are described in two case studies found herein.

**1.2 Research Questions**

This dissertation is centred on the following interrelated research questions:

> What is the dominant medical/scientific view of cancer causation, particularly the contribution of occupation to cancer, and how and why has this affected public health policy and practice in Canada?

What recognised alternative views on cancer causation linked to occupation exist and why?

Can a community-based occupational history data collection initiative contribute to advancing our scientific understanding of associations between cancer and work and more specifically, breast cancer and work?

And finally, can data derived from an occupational history questionnaire provide insight into the potential association between breast cancer risk and farming?

## 1.3 Objectives

The research questions will be addressed through various means to meet a series of objectives. These objectives are interconnected. They provide a coherent means to move from the larger to the smaller picture and begin to provide a valid method of exploring the research questions at a local level with data readily available to the researcher.

This dissertation will:

1. Review the current overall cancer statistics with particular emphasis on breast cancer incidence - globally, nationally, provincially, and locally;

2. Critically evaluate the different paradigms for understanding cancer causality, especially the scientific debate surrounding the issue of lifestyle versus environmental aetiology;

3. Critically review the current state of knowledge on female breast cancer incidence with a bearing on possible occupational and environmental factors;

4. Critically review Canadian occupational cancer studies and reports with respect to their perspective on work-related cancer;

5. Contextualise the occupational and environmental health studies specific to the community of Windsor, Ontario, Canada;

6. Present and evaluate the methods developed collaboratively in a local setting to identify possible populations at risk arising from occupational factors;

7. Explore how a local occupational cancer research initiative can provide insight into the potential association between breast cancer risk and farming;

8. Evaluate the strengths and limitations of the methods employed to explore occupational risk factors for cancer and their relevance to cancer prevention.

## 1.4 Background

Cancer is a largely preventable group of diseases that continues to adversely affect ever larger numbers of people throughout the globe (Parkin et al., 2001). While there have been improvements in treatment that have reduced mortality for some cancers and significant advances made in understanding the mechanisms of carcinogenesis, there have been no widely accepted new hypotheses regarding the reasons behind the increases in cancer incidence. Furthermore, for the majority of cancers, life expectancy has not been significantly increased (Epstein, 1998a).

The history of cancer research and intervention during the past thirty years has been dominated by a deep-seated intellectual conflict concerning the avoidable causes of risk. There is a debate as to whether causal factors are more related to genetics, lifestyle and voluntary exposures to carcinogenic agents (such as tobacco) or more related to involuntary exposures to carcinogenic chemicals in the workplace and in the general environment. Some epidemiologists such as Sir Richard Doll and Sir Richard Peto are generally associated with the lifestyle side of the cancer conflict: while toxicologists and physicians such as Dr. Samuel Epstein represent an alternative perspective that assigns greater weight to involuntary exposures to synthetic chemicals. Because the identification of risk factors may implicate particular human activities that have both personal and economic values, the motives of the researchers, the interests of their funding sources, and their relationships to powerful vested interests can frame their research and the results (Rosenstock and Lee, 2002). This conflict provides the intellectual context for the organisation of this dissertation in that it demonstrates that questionnaire surveys of risk factors for cancer patients must include consideration of all the known and suspected activities and agents, whether related to genetics, lifestyle, environment, or occupation.

For most of the twentieth century, industrial workers employed in industries that used or produced cancer-causing substances were recognised as bearing an elevated risk of developing cancer (World Health Organisation, 1999a; Landrigan, 1996; Landrigan and Markowitz, 1989). The elevated cancer risk for millions of workers due to asbestos exposure is but one example of such a phenomenon (LaDou, 2004; Landrigan, 2004; Peto et al., 1999).

The dissertation attempts to explore whether or not cancer is part of the "accepted" epidemic of occupationally related diseases in capitalist societies (Watterson, 1999, 109-11). Epidemic refers to "the occurrence in a community of a group of illnesses of similar nature, clearly in excess of normal expectation" (MacMahon et al., 1960, p.4). By such a definition, it will be argued that cancer, occupational cancer, and breast cancer can all be classified as *silent* epidemics, that is, they are not generally accepted by mainstream science and medicine as being epidemics, and yet, their incidence is in excess of normal expectations. Further, it will be argued that the major institutions that administer cancer treatment, research, and prevention allocate minimal resources towards the detection of risk factors related to occupationally related cancer (Epstein, 2003).

Change, however, does not come solely from the availability of scientific information, but requires the involvement and advocacy of the affected community. Cancer prevention will require the social mobilisation of the populations at risk and a reorientation of the power relations in society to allow for democratic decision-making and the implementation of the precautionary principle (Toronto Cancer Prevention Coalition, 2001).

Several observers have suggested that epidemiology, and particularly cancer epidemiology, is in crisis because there are few new significant risk factors that have been recently identified (Susser and Susser, 1996a; 1996b; Pearce, 1996). They have recommended that advances in our understanding of cancer causality will occur when population epidemiology links with molecular epidemiology;

reconnects to public health and the resulting science is placed within a social, economic and political context.

There is increasing use and respect for community-based research as a method to overcome the "institutional biases" that prevent the detection of health problems (Gills, 2001, p.12). In public health settings, community-based research examines "social, structural, and physical environmental inequities through active involvement of community members, organisational representatives, and researchers in all aspects of the research process" (Israel et al., 1998, p. 173). This method incorporates the concerns, needs, and knowledge of the populations at risk and, in the process, helps empower them to alter their conditions (Giachello et al., 2001).

The occupational cancer research that is examined in this dissertation initially involved, amongst other groups, the trade unions associated with the automotive industry in Windsor, Ontario, with a view to empowering them to bring about change in workplace conditions and reductions in exposures to chemicals. With the initial collection of information on cancer patients at the Windsor Regional Cancer Centre (WRCC), serving Windsor and Essex County, it became apparent that there were female breast cancer patients who wanted to participate in this project and whose occupational histories were available for analysis. These patients have become not only the focus of the studies reported in the dissertation, but also are a part of the community that can potentially bring about change in cancer policy. The breast cancer movement has become one of the strongest women's health movements, particularly in industrialised countries, and is forcefully challenging the power and control of the "cancer establishment" (Epstein, 2002) to define treatment, research and prevention and, more broadly, the very question of health (Myhre, 2004, 1999).

Women employed in numerous occupations, like their male industrial worker counterparts, also bear an elevated risk of cancer due to occupational exposures to carcinogens. In the United States, for example, it is estimated that over 1 million women are potentially exposed at work to breast carcinogens as identified in animal bioassays (Epstein, 1997, p. 274). Primary prevention would entail the removal of these carcinogenic substances from the workplace. The idea of breast cancer prevention is, however, generally confined to secondary prevention strategies such as early detection through self-examination and mammography.

## 1.5 Dissertation outline

The dissertation examines the conflicts between those who espouse the lifestyle aetiologies versus those who favour environmental aetiologies. Themes of discussion include the inertia in recognising the occupational contribution to cancer with particular emphasis on breast cancer aetiology, and the difficulties that populations at risk have in identifying and preventing cancer arising from their respective work environments. The focus of each of the Chapters 2 through 11 is described below.

Chapter 2 first examines cancer morbidity and mortality in a global, national, regional and local context, and then, focuses on breast cancer. These statistical findings help to contextualise the scientific debate on the avoidable causes of cancer and the public health crisis posed by increasing incidence.

Chapter 3 explores the scientific conflict over cancer aetiology and its political and social ramifications. There is an intertwining nexus of scientific, social and political factors that connect with the scientific debate. The tremendous growth of global capitalism in the later half of the twentieth century has afforded it the power to frame the discussion regarding cancer causality within a perspective that casts responsibility for the disease on the individual – *blaming the victim* – while allowing industry to function with minimal regulations and controls (Epstein 1998, pp. 330-331). Our understanding of the pathogenesis of cancer, which is a multifactoral disease, does not allow us to confidently assign a specific weight to single causes. Cancer agencies, however, tend to argue that the predominant causes of cancer are personal lifestyle choices rather than socially determined factors (Tomatis and Huff, 2001). Occupational risks are still assigned a minor role in spite of their recognised impact particularly on industrialised workers (Infante, 1995). New scientific insights into the role played by xenoestrogens and endocrine disrupters offer fresh insights into breast cancer aetiology. This new knowledge coupled with the activism of the populations at risk may provide a synthesis to challenge the dominant scientific views of cancer causality.

Chapter 4 critically examines the known or suspected aetiological risk factors that influence breast cancer research. The process of carcinogenesis is explored as it informs the case studies and explains the potential harm posed by exogenous exposures. The majority of breast cancer cases cannot be explained by known risk factors (Health Canada, 2001, p.4). There has been very limited research carried out on potential environmental and occupational links to breast cancer. Experimental studies suggest links to exposures that disrupt the endocrine system. Chemicals that "mimic" estrogens (xenoestrogens), such as some pesticides, polycyclic aromatic hydrocarbons, organic solvents and components of plastics, may very well contribute to cellular proliferation and the cancer process.

Animal studies have identified over 200 chemical substances that trigger breast cancer. Some of the scientific literature suggests the increasing trend in breast cancer incidence is not linked to any one specific factor, but to a variety or combination of factors: environmental, occupational, genetic, lifestyle, and socioeconomic. The timing of these exposures during the life cycle, particularly during prenatal and childhood periods, can be as important as the dose. It is possible and plausible that female breast tissue is more susceptible to tumour initiation and progression during periods of great morphological and biochemical change, that is, beginning at puberty and continuing throughout the reproductive years.

The Canadian cancer agencies have generally been unreceptive to the demands of trade unions, environmentalists and women's health advocates who are insisting on an aggressive cancer prevention programme based on the Precautionary Principle[1]. These movements are challenging the old paradigms regarding cancer causality. Such groups are demanding inclusion into decision-making processes, while

[1] "When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically." (Kriebel et al., 2001)

challenging the rights of industry to expose workers to carcinogens and to release carcinogens into the environment. They are also challenging irresponsibility of government regulators who ignore information about the potential harm posed by environmental contamination to human health (Toronto Cancer Prevention Coalition, 2001).

Chapter 5 examines the limited epidemiological research on Canadian occupational cancer; much of it accomplished through the use of national and provincial data sources. Breast cancer is examined in only one such study. Differing perspectives emerge from the examination of provincial compensation board data. A critical review of the key breast cancer occupational epidemiological literature is presented. Special reference is made of the British Columbian cancer registry study because of its parallels to the Windsor case studies. Farming, nursing and health care breast cancer epidemiology is explored in more detail as it informs the Windsor research. Chapter 5 frames the significance of the collaborative initiative to collect the occupational histories of cancer patients in Windsor.

Chapter 6 contextualises the case studies contained within this dissertation by examining studies on the health of the population of Windsor – Essex County, Ontario, Canada. Public health issues are of serious concern to much of the population in this industrial community due to exposures to occupational and environmental contaminants. It is a "population-at-risk", documented in numerous environmental and human health studies, which have identified carcinogens and endocrine disrupters in the occupational setting, as well as in the ambient environment. Of particular importance is a study that examines the health of 17 communities in the Great Lakes Basin and which found the health of the Windsor population to have the most serious adverse health outcomes, including cancer (Gilbertson and Brophy, 2001). In reaction to these public health concerns, trade union health and safety activists have engaged in an active health and safety movement that views the prevention of occupational cancer morbidity and mortality as a major objective.

Chapter 7 sets the stage for the two Windsor case studies. Previously chapters have provided the necessary context to understand the scientific debates about occupational cancer and the barriers to collecting the occupational histories of cancer patients. The local background and genesis to the action research is presented. The ethical approval for each case study is outlined.

Chapter 8 presents the first of two case studies. In 1994, a community-based occupational cancer research project emerged through the collaboration of the Windsor Regional Cancer Centre (WRCC), the Occupational Health Clinics for Ontario Workers (OHCOW), the Windsor Occupational Health Information Service (WOHIS) and the Ontario Occupational Disease Panel (ODP). A computerised data collection project, titled *Computerised Recording of Occupations Made Easy* (CROME) captured detailed chronological work histories in Windsor - Essex County cancer patients. This initiative represented the first time that an Ontario regional cancer treatment centre had attempted to address the lack of data regarding the work histories of their patients. Without any a priori hypotheses regarding specific associations, occupational data collection began in 1995. CROME employed a user-friendly touch screen to gather the patients' chronological occupational data for 16 major industries and over 300 occupational categories providing such information as the type of job, duration and latency. Peer reviewed papers and presentations have arisen from this research (Brophy et al., 2002).

Chapter 9 examines the second case study in of this dissertation. The Lifetime Occupational History Record (LOHR) arose from the initial findings of the CROME study in which women with breast cancer who were 55 years of age or younger and had ever engaged in farming bore an elevated breast cancer risk. In the course of a two-year case control study (LOHR) over 1100 women were interviewed. The research team developed a questionnaire that captured such covariates as age, socioeconomic status, parity, age at menarche, family history, body mass index (BMI), age of menarche and menopause, use of oral contraceptives, age at first pregnancy, number of children, lactation, menopausal status, use of hormone-replacement therapy and marital status. Questions were asked about occupational exposures, including pesticides. Community controls were randomly selected from the population rather than using hospital-based controls.

Chapter 9 examines the new three-year case-control study, *Lifetime Occupational and Environmental History Record (LOEHR),* which is currently in progress. *LOEHR* has developed as a result of the previous two research studies. The new questionnaire further refines the previous *LOHR* tool. *LOEHR* attempts to capture information about such risk factors as parental and residential exposures. In addition, a more sophisticated exposure profile is developed that includes open-ended questions about working conditions accompanied by an evaluation of each job by a expert panel in order to more accurately access specific exposures.

Chapter 10 evaluates the occupational history gathering processes in Windsor, with reference to the dissertation research questions as stated in the beginning of this chapter. The three research studies, *CROME, LOHR and LOEHR*, are examined for their respective impacts on the scientific understanding of breast cancer aetiology and on public policy. Their respective strengths and limitations are explored. A new paradigm which links the populations at risk with occupational history gathering is examined for its applicability to other communities. The paradigm's possibilities and obstacles are discussed. Institutional barriers that continue to thwart occupational cancer prevention activities are analysed and ideas for advancing social policy are presented.

Chapter 11 concludes the dissertation with a summary of the major arguments regarding the need to pursue valid, accurate occupational history collection among cancer patients. The implications for this research in the future are also examined.

# CHAPTER 2: OVERVIEW OF CANCER MORBIDITY AND MORTALITY, WITH PARTICULAR ATTENTION TO BREAST CANCER

## 2.1 Introduction

The chapter will firstly provide an important and necessary overview by critically examining the body of literature regarding cancer morbidity and mortality globally, in the United States and Canada, as well as, more specifically in the province of Ontario, Canada and within the community of Windsor in the County of Essex. This information provides the context in which to evaluate the approaches to understanding cancer aetiology. Secondly breast cancer morbidity and mortality will be highlighted, as it is the focus of the case studies to follow in later chapters of the dissertation. Thirdly cancer trends and their relevance to this thesis will be re-assessed. In this context, the concept of age-standardised rates is explained in order to evaluate whether the ageing population in industrialised countries – the 'age as a carcinogen itself argument' - is the cause of the increasing incidence of cancer. Fourthly and finally, some assessment is offered of the effectiveness of the dominant strategies to reduce cancer morbidity and mortality.

Cancer represents a major cause of human morbidity and mortality. It is, after cardiovascular disease, the second most common cause of mortality among the sixty million deaths that occur each year throughout the world (Montesano, 2001). In some industrial countries, such as Canada and the United Kingdom, cancer is now becoming the leading cause of death (Statistics Canada, 2003; Encarta, 2003). In Canada, current projections estimate that, in the course of their lifetimes, 38 per cent of women and 41 per cent of men will develop cancer (Canadian Cancer Society, 2003).

The recorded increase in the incidence and resulting mortality from cancer is having a profound effect in terms of human suffering and financial cost. It is important to understand that this disease, which has been generally agreed to be largely preventable, continues to rise with minimal attention paid to primary prevention (Epstein, 1998a). The purpose of the dissertation is to contribute to a better understanding of the preventable causes of cancer generally and of breast cancer specifically.

## 2.2 All cancer burden

*Table 2.1* comprises data on the overall cancer incidence and mortality collected by mainstream cancer research agencies for: the global population; the United States; Canada; and Ontario in the year 2000. These data are discussed in more detail in the following sections.

**Table 2.1: Overall Cancer Burden**

| | Incidence | Mortality |
|---|---|---|
| **Global** | 10,000,000 | 6,200,000 |
| **United States** | 1,334,100 | 556,500 |
| **Canada** | 139,900 | 67,400 |
| **Ontario** | 52,700 | 24,600 |

Source: Globocan 2000, 2001; Canadian Cancer Society, 2001.

### 2.2.1 Global cancer burden

According to the International Agency for the Research on Cancer (IARC), there were over 10 million new cases of cancer, not including skin cancer, throughout the globe in the year 2000 and over 6 million were projected to die from the disease

(GLOBOCAN 2000, 2001; Parkin et al., 2001) (See *Table 2.1*). The World Health Organization (WHO) estimates that by 2020 the number of diagnosed cases will double; there will be some 20 million new incident cases of cancer, and a prelevance of 22.4 million people living with cancer. Lung cancer is the most commonly recorded cancer in the world with over 1.2 million new cases, followed by breast cancer with over 1 million new cases (Parkin et al., 2001). The WHO estimates that, in the future more than 70 percent of all cancer cases will be found in developing and newly industrialised countries (WHO, 2003; WHO, 1998). Globally, almost 13 percent of all deaths are said to be related to cancer, which is greater than the percentage of deaths due to malaria, tuberculosis and HIV/AIDS combined (WHO, 2003). It is argued that early childhood mortality and infectious diseases in developing countries reduce life expectancy. As a result, deaths occur from causes other than cancer, which generally occurs later in life. While improved life expectancy may account for some of the increased number of diagnosed cancers expected in the future in developing countries, it is interesting to note that this trend also coincides with the transfer of hazardous industries to these countries, where the exposures to carcinogens are often much greater than currently tolerated in industrialised nations (Tomatis and Huff, 2001). It would be expected that, due to the latency characteristic of carcinogenesis, cancers related to these exposures will appear over the course of the next few decades.

### 2.2.2 United States all cancer burden

Cancer is the second leading cause of death in the United States exceeded only by heart disease. One in 4 Americans will die from cancer (American Cancer Society, 2003). The American Cancer Society and the National Cancer Institute estimate that by 2050 the number of cancer diagnoses will double based on a review of American cancer incidence rates from 1973 to 1999. Controlling for the ageing population, there was still an overall increase of 24 percent (Edwards et al., 2002). Cancer mortality rates, however, are beginning to decline due to improved treatment modalities, early detection, and particularly, decreasing use of tobacco (American Cancer Society, 2003).

Cancer costs the United States economy $171.6 billion dollars in 2002 according to the National Institutes of Health. Direct health care costs were estimated at $60.9 billion dollars; indirect mortality costs were $95.2 billion dollars and indirect morbidity costs were $15.5 billion dollars (American Cancer Society, 2003).

Industrialised countries, such as the United States and Canada, continue to experience overall increases in diagnosed cancer in spite of billions of dollars allocated to reduce cancer morbidity and mortality (Beardsley, 1994). This discrepancy, between the goal of reducing the overall morbidity and mortality of cancer and the continuing increase in the recorded incidence of the disease, is a major theme of the dissertation and is at the heart of a decades long debate regarding cancer causality (Sellers, 1997).

### 2.2.3 Canadian all cancer burden

In 2000, the National Cancer Institute of Canada (NCIC) calculated a lifetime risk for developing cancer as 40% among men and 35% among women, not including skin cancer (Clapp, 2000). In 2003 the Canadian Cancer Society further upwardly revised the estimated lifetime risk; 41% among men and 38% among women. While controlling for ageing, incidence of diagnosed cancers increased between 1970 and 1998 increased by 35 percent for men and 27 percent for women (Chernomas and Donner, 2004). Cancer is now the "leading cause of premature death" (Canadian Cancer Society, 2003, np) and while cancer mortality is declining, incidence rates continue to climb.

It was estimated in 1993 that cancer cost the Canadian economy $13.1 billion per annum (Health Canada, 1997). The direct annual costs in terms of productivity losses due to premature death are estimated to be $10.6 billion Canadian dollars with another $1.8 billion in health care costs. These estimates were made in 1998, which was the last year such data were available (National Cancer Leadership Forum, 2003).

### 2.2.4 Ontario all cancer burden

Cancer is the leading health problem in Ontario in terms of lost years of life (Cancer Care Ontario, 2003). Among men, the most prevalent cancer site is the prostate gland (N =7,200). Among women, the most prevalent cancer site is the breast (N = 8,000). Lung cancer is the leading cause of death for both men and women in Ontario (Canadian Cancer Society, 2003).

It is estimated that, within a few decades, cancer will be the leading cause of death in Ontario (Kreiger et al., 2003). Based on existing patterns of diagnosed cancers, by the year 2020 the new incident cases of cancer will have increased by almost two-thirds from the current numbers to 91,000 per year. It is further forecast that the number of cases will double by 2028 (Cancer Care Ontario, 2003).

### 2.2.5 Windsor all cancer burden

The community of Windsor, located within the County of Essex, is the setting for the case studies contained herein. (Chapter 6 will explore in greater detail the health issues facing this community.) Cancer has been identified as being significantly elevated in males in Essex County compared to the rest of the province (Gilbertson and Brophy, 2001). The Windsor Essex County Health Profile (2000), produced by the Essex County Health Unit, cited Standard Morbidity Ratios (SMRs) based on hospital separations. Among Essex County women for all neoplasms in 1998, there was a frequency of 1,638 per 100,000 representing an elevation of 11 percent compared to the "same age-specific hospital separation rates as all of Ontario" (p. 117); this was statistically significant with a p value <.01[1]. Among men for all neoplasms, there was a frequency of 1,403 per 100,000 that was 23 percent higher frequency than the rest of the Ontario population.

## 2.3 Breast cancer burden

Cancer of the breast refers to a group of diseases with differing genetic, cellular and molecular composition (Dickson and Lippman, 2001, pp. 1633 - 1651). There are several reasons that the dissertation focuses on the occurrence of breast cancer. Breast cancer has become the most prevalent cancer among women and, overall, the second most common cancer with half the cases found in industrialised countries

[1] P value refers to the probability value. P<.01 means that there is less than a 1 percent probability that the observed finding would have occurred by chance (Friedman, 1987).

(Parkin et al., 2001). It has been suggested that it is increasing at the rate of about 1% per year. The attributable risk factors only account for a small fraction of the cases and little research has been undertaken to address the discrepancy between what is known and the continuing prevalence of the disease (Davis et al., 1998).

It has been argued that about half of the breast cancer incidence cases occurs in Europe and North America (Parkin et al., 2001), but these figures are affected by the differential ability to diagnose the disease. In developing countries, breast cancer incidence continues to rise (p. S19), and is increasingly seen in younger women (p. S22). Breast cancer is projected to remain the most common cancer among women for the next fifty years.

Breast cancer incidence and deaths are reported in *Table 2.2* for the global population, the United States, Canada and Ontario. These figures, needless to say, reflect the differential ability of different regions to diagnose the disease.

**Table 2.2: Breast cancer incidence and mortality in 2003**

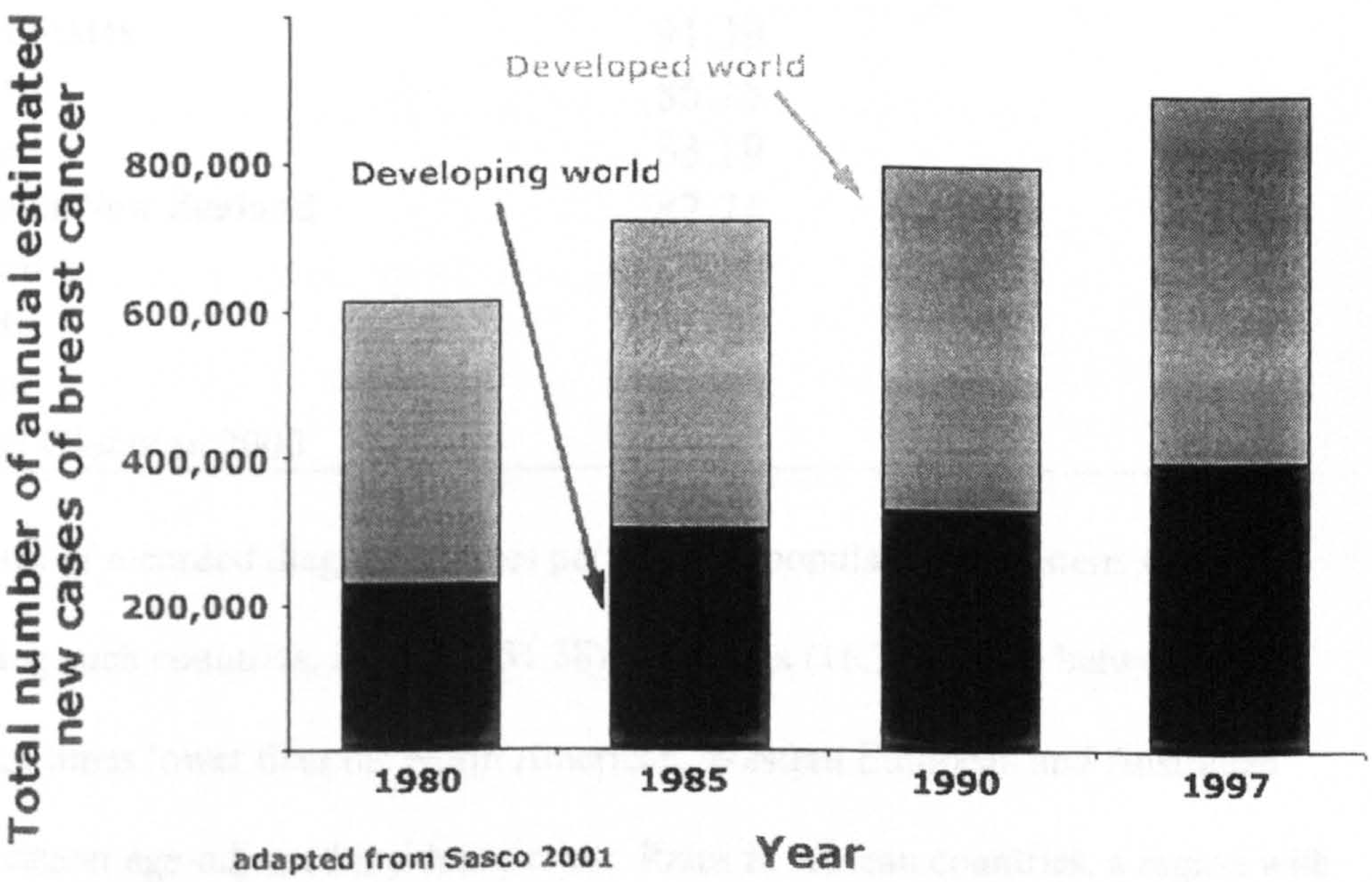
| | **Breast Cancer (female) cases** | |
|---|---|---|
| | **Incidence** | **Mortality** |
| **Global** | 1,050,000 | 373,000 |
| **United States** | 211,300 | 39,800 |
| **Canada** | 20,500 | 5,400 |
| **Ontario** | 8,000 | 2,000 |

Source: Parkin et al, 2001; American and Canadian Cancer Society, 2003

### 2.3.1 Global breast cancer burden

By 2050 IARC estimates that globally there will be nearly 2 million new cases of breast cancer each year (p. S55). Over half recorded breast cancer cases occur in the developed countries, with over 530,000 new cases diagnosed in Europe and North America regions alone. The highest incidence of recorded breast cancer occurs in North America, Northern Europe, and Australia with age-adjusted rates ranging from 75 to 92 per 100,000 women (standardized to year 2000 world population). Africa and Asia have the lowest rates, where the incidence rates are less than 22 per 100,000 (p. S17-S22) (See Figure 2.1). The uneven global distribution of breast cancer reflects differential diagnostic capabilities as well as the potential of environmental factors (Davis et al., 1998).

**Figure 2.1:** *Breast cancer comparison between developed and developing countries*




The recorded breast cancer incidence and mortality vary between developed and developing countries, and between different ethnic groups within countries. The International Agency for Research on Cancer (IARC) estimates that roughly 25% of the cases will be among premenopausal women whose premature mortality results in hundreds of thousands of years of lost life annually worldwide (Parkin et al., 1997).

Ignoring differences in recording and diagnostic capabilities, the Netherlands has the highest Age Standardised Rate of breast cancer (ASR) (91.64) followed closely by the United States (91.39). Canada has the seventh highest rate (81.78) among industrialised countries (see Table 2.3).

**Table 2.3: Breast cancer rates per 100,000 population in developed countries**

| Population | Age Standardized Ratios (ASR) |
|---|---|
| Netherlands | 91.64 |
| United States | 91.39 |
| Demark | 86.15 |
| France | 83.19 |
| Australia/New Zealand | 82.71 |
| Belgium | 82.20 |
| Canada | 81.78 |
| Sweden | 81.03 |

Source: Globocan 2000

The rates of recorded diagnosed cases per 100,000 population in eastern Asia including such countries, as Japan (31.38) and China (16.39), range between three and four times lower than the North American, Western European and Australian breast cancer age-adjusted incidence rates. Rates in African countries, a region with lower breast cancer rates, range from 10.20 in Rwanda to 33.52 in South Africa (Globocan, 2000).

Apart from reflecting differences in diagnoses and recording, the differences in breast cancer incidence between more industrialised and less industrialised countries and the unequal distribution within industrialised countries raise the possibility of exogenous exposures as causative factors. It has been hypothesised that environmental exposure to carcinogens and hormonal disrupters in industrialised countries, particularly North America, Western Europe, Australia and New Zealand, may be strong contributing factors in the elevated breast cancer incidence rate (Kelsey and Bernstein, 1996). It has also been suggested that the variation of breast cancer incidence geographically, coupled with the inability to establish individual causes, emphasises the need to explore such modifiable risk factors as exogenous exposures. Subsequent chapters of the dissertation will explore these ideas, particularly from the perspective of the risks posed by endocrine disrupting compounds, synthetic chemicals and other potential occupational risks encountered by women in the work environment.

### 2.3.2 United States breast cancer burden

As far as recorded and diagnosed cancers are concerned, breast cancer is the most prevalent female cancer representing 32% of all cancers among women in the United States. Approximately 40 percent of the new cases are diagnosed among women less than 60 years old (Brody and Rudel, 2003). Among women aged 35 to 54 breast cancer is the leading cause of death (p. 1007).

### 2.3.3 Canadian breast cancer burden

Breast cancer is also the most common form of cancer diagnosed among Canadian women (Health Canada, 1999). Breast cancer will represent almost one third of all new cancer cases in Canadian women this year. In 2004, an estimated 21,200 Canadian women will be diagnosed with breast cancer and 5,200 of them were projected to die from this disease (Canadian Cancer Society, 2004a). Since 1981 there has been an almost 1.5 % annual increase in diagnosed of breast cancers in Canada. The mortality rates in Canada have declined, as is the case in most industrialised countries, due to earlier intervention resulting in a more favourable prognosis (Canadian Cancer Society, 2002, pp. 32-33). While lung cancer has a slightly greater impact of lost years of life for Canadian women, breast cancer accounts for more than twice as many new cancer cases as lung cancer. Women under 50 with newly diagnosed breast cancer represented 23 percent of the cases; the largest number (46%) occurred among women between the ages of 50 to 69, while women 70 and over represented 32% (National Cancer Institute of Canada, 2001).

Table 2.4 shows the demographic distribution of diagnosed breast cancer in women by Canadian province. In 2002, Ontario had the same age-adjusted standardised rate (ASR) as Canada as a whole. These rates, needless to say, also reflect differences in diagnostic capabilities and are subject to recording effects.

**Table 2.4: Estimated age-standardised incidence and mortality for Canadian women with breast cancer, 2002 (rate per 100,000)**

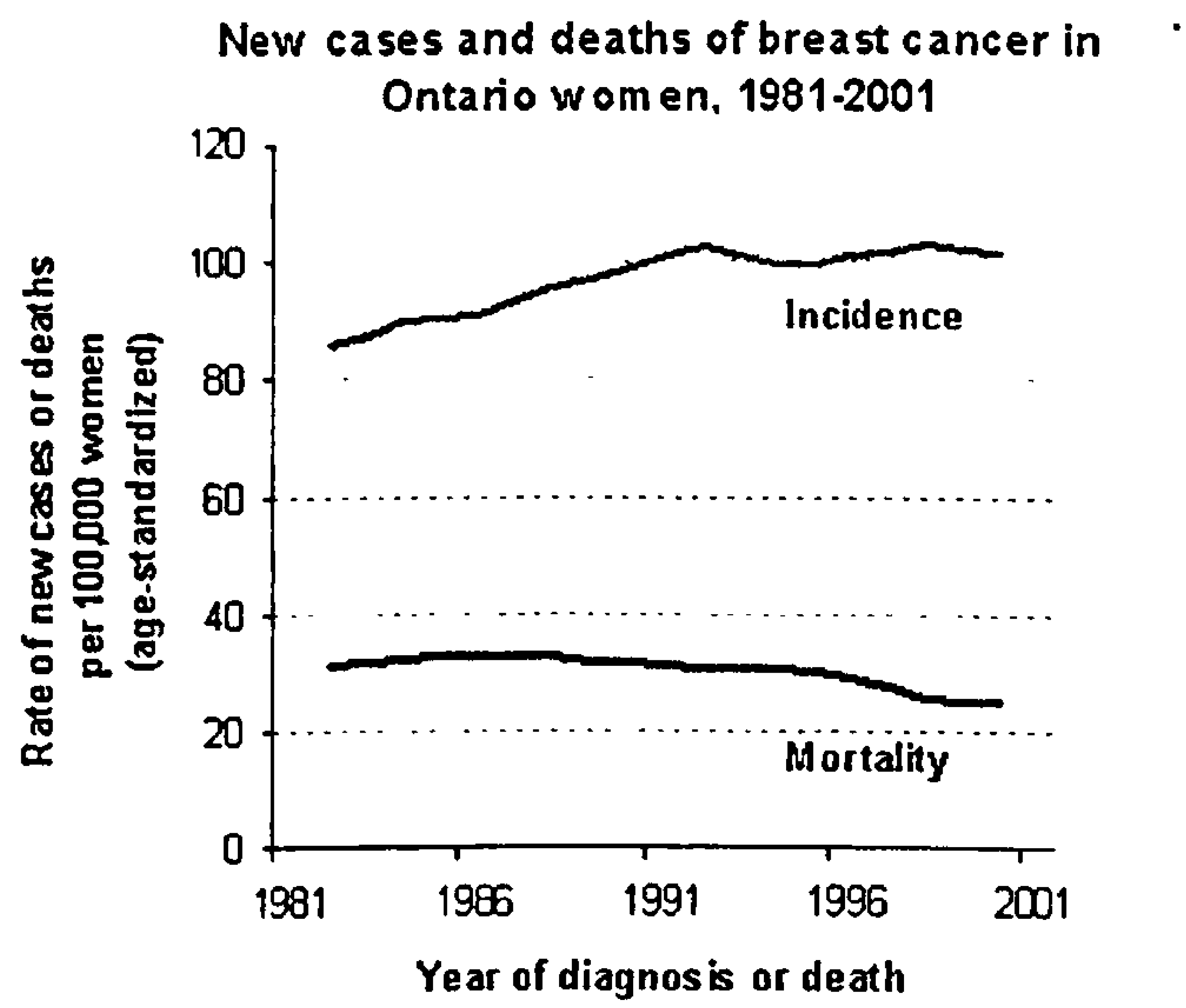
| | Incidence | Mortality |
|---|---|---|
| **Canada** | 106 | 26 |
| **Newfoundland** | 94 | 29 |
| **Prince Edward Island** | 107 | 23 |
| **Nova Scotia** | 112 | 29 |
| **New Brunswick** | 110 | 28 |
| **Quebec** | 107 | 28 |
| **Ontario** | 106 | 25 |
| **Manitoba** | 114 | 28 |
| **Saskatchewan** | 98 | 22 |
| **Alberta** | 108 | 25 |
| **British Columbia** | 102 | 23 |

Source: Canadian Cancer Society, 2002

### 2.3.4 Ontario breast cancer burden

The recorded Ontario breast cancer incidence rate is "among the highest in the world (Chiarelli et al., 2000, p. 23). In 2002, 7,800 women were diagnosed with breast cancer and 2,700 were projected to die from it (Canadian Cancer Society, 2002). In Ontario a woman has a 1 in 9 chance of developing breast cancer in the course of her lifetime (Canadian Cancer Society, 2002). Figure 2.2 shows that the incidence of diagnosed breast cancers rose during the 1980s and early 1990s but has remained stable for the remainder of the decade, while breast cancer mortality declined.

**Figure 2.2: Breast cancer incidence and deaths in Ontario.**
**(Source, Canadian Cancer Society, 2002)**




### 2.3.5 Windsor Breast Cancer Burden

As will be highlighted in Chapter 6 on the health issues in Windsor, the officially recorded incidence of breast cancer in Essex County is comparable to the province of the Ontario where the rate is high in relation to the rest of the world. The Windsor – Essex County District Health Council (1995) found that the recorded breast cancer mortality was slightly below the Ontario rate (Standard Mortality Rate (SMR) = 0.962, 95% CI (0.861 – 1.063) (p. F-18). On the other hand, the officially recorded breast cancer incidence was somewhat higher than the Ontario population for the period 1989 to 1992. Based on an age-standardised rate per 100,000 population the recorded Windsor-Essex County breast cancer incidence was 85.1, while the Ontario rate per 100,000 was 80.3 (p. F-39).

The identification of possible causes of breast cancer among Windsor women, particularly from occupational and environmental exposures could have important implications for breast cancer prevention. Windsor is an important Canadian industrial and agriculture centre because women are integrated into the workforce, including the manufacturing sector, where they may be exposed to carcinogens. It is also an area identified as having elevated diseases possibly related to environmental factors (Gilbertson and Brophy, 2001). Because of the stable population with little migration; it is ideal for the investigation of aetiological factors.

## 2.4 Trends

### 2.4.1 Age standardised rates

In spite of the billions of dollars spent over the last three decades, the incidence rates for many types of cancer continued to rise (Epstein, 2002). This potentially reflects increased diagnostic capabilities, but it may also be due to other factors.

Between the years 1973 to 1999, there was an overall increase of 24% in American in officially recorded cancer incidence rates after controlling for the ageing population[2]. In the same period, the recorded lung cancer incidence, which is one of the leading causes of mortality, increased by 30% (reduced by 6% among men and increased by 143% among women) (Epstein, 2002, p. 6). While this increase among women is generally attributed to the increased prevalence of tobacco use among women (and potentially to improved diagnosis), it is important to note that this same time period also coincides with a major shift in female employment with women entering the once exclusive male job market. These newly available occupations could involve exposures to hazardous substances that may contribute to an increased cancer risk (Zahm and Blair, 2003). Of cancers that are not smoking-associated, there have been a number of recorded increases: malignant melanoma (156%); liver cancer (104%); non-Hodgkin's lymphoma (87%); thyroid cancer (71%); testicular cancer (67%); post-menopausal breast cancer (54%); brain cancer (28%) and acute myeloid leukaemia (16%). Childhood cancers have increased almost 1% per year during this 26-year period (Epstein, 2002 p.6; Ries et al., 2002).

From 1970 to 1998, the recorded age standardised incidence data for Canada reflects an overall increase in cancer morbidity (Canadian Cancer Society, 2003). The recorded cancer incidence in this period increased 35 percent for men and 27 percent for women. One in every 2.4 Canadian men (41.2%) will develop cancer

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[2] Age standardised incidence is a term that refers to a method of examining cancer incidence where age of the population is factored into the comparison so that a population with more elderly persons, for example, is not matched with a population of younger people (Last, 2001; p. 3). This statistical technique can account for changes in the age distribution of the population over time. When cancer incidence or mortality rates are adjusted for age, 65 year old men and women in 1970 are compared to 65 year old men and women in 1995, so that living longer can not skew the relationship.

and one in every 3.6 (27.4%) will die from it. One in every 2.7 Canadian women (37.6%) will develop cancer and one in 4.3 (23.1%) will die from it (p.56).

Age is a major risk factor for cancer. Though not a carcinogen itself, age can be a surrogate for other factors. It is argued that as the population ages there will be a greater prevalence of the disease because as the body wears out its defensive capacities diminish. This assertion is difficult to prove but the age-adjusted comparisons show that the continuing increase in cancer incidence cannot be explained by the increased life expectancy of the population alone. Just as the uneven geographic distribution of cancer incidence lends credence to the argument that exogenous risk factors are important contributors in cancer causality, so too does the continuing increase of the disease after adjusting for ageing. Further, the recorded increased incidence of cancer among children cannot be explained by the concept of an ageing population (Goldsmith, 1998). These arguments are important for the dissertation because, as will be further elaborated in the next chapter, the personal, individual focus on cancer prevention through lifestyle modifications has failed to substantially reduce the incidence of cancer, yet it remains almost the complete focus of the agencies responsible for cancer treatment and prevention (Hall, 1998).

## 2.5 Risk Factors

Cancer is defined as the uncontrolled growth of damaged cells (Watterson, 1998b). Cancer is a multifactoral disease linked to a variety or combination of the following factors: age, environmental, occupational, genetic, lifestyle, and socioeconomic

(Davis and Muir, 1995). There is intense scientific debate regarding the attributable risks of cancer and what part each of these potential aetiologic agents plays in the process of carcinogenesis. There is generally a hierarchy of risk factors with tobacco use and diet designated as the strongest contributors to cancer risk. This perspective is referred to as the "lifestyle" paradigm (Walker, 1998, p. 83). The other perspective, referred to as the " dissident" paradigm, attributes the increasing rise in cancer incidences to exposure to synthetic chemicals in our food, air, consumer products and workplaces (pp. 83-84). In the following chapter (Chapter 3) this conflict will be presented in greater detail. It will also appear, for different reasons and providing new perspectives, in the examination of known or suspected risk factors of breast cancer (Chapter 4) and in the chapter that reviews the Canadian occupational cancer literature and more specifically, breast cancer epidemiology (Chapter 5). This debate holds profound implications for the potential strategies that might be utilised to reduce it.

Occupationally related cancer with a particular focus on breast cancer is a central theme of the dissertation. It will explore in the following chapter the notion that cancer is part of the "accepted" epidemic of occupationally related diseases in industrialised societies (Watterson, 1999, pp. 109-11). Epidemic refers to "the occurrence in a community of a group of illnesses of similar nature, clearly in excess of normal expectation" (MacMahon et al., 1960, p.4). By such a definition, it will be argued that cancer, occupational cancer and breast cancer can all be classified as 'silent' epidemics; that is, they are not generally accepted by mainstream science and medicine as being epidemics and yet, their incidence continues to occur and even increase (Brophy, 2004).

## 2.6 Is the war against cancer being won?

In 1996 the U.S. Secretary of Health and Human Services, Ms. Donna Shalala, announced that the "war on cancer" was showing results (Hoeksema and Law, 1996). Her remarks were based on United States cancer statistics that appeared to show a decline in the cancer mortality rate of 2.6% from 1991-1995. This was the first such reduction since the U.S. government began to record cancer statistics in the 1930s. However, over 1,228,000 Americans developed cancer in 1998 and 564,800 died from it. "Clearly, we have a very long way to go before we can claim that the war on cancer has been won" (Montague, 1999, np).

The Shalala pronouncement was challenged by the American Medical Association on the basis that cancer morbidity and mortality statistics may not reflect accurately the true recent occurrence of the disease (Clegg et al., 2002). The researchers examined the time involved in reporting on cancer morbidity and mortality to the United States National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER), which functions as a national cancer registry. Their findings demonstrate that there was a 4 to 17 year delay in recording 99 percent of the cancer cases and corresponding adjustments are needed for estimating the incidence (See *Table 2.5*).

These gaps in reporting introduced bias into the projections of cancer incidence trends. The new analysis shows that recorded breast-cancer rates actually have been rising 0.6% a year since 1987. Specifically, the National Cancer Institute researchers are calling for research "to explain the cause for the recent rise in breast cancer incidence" (Begley, 2002, np). Breast cancer was being underreported and

Dr. Clegg and colleagues (2002) estimated that it was actually 4 percent higher than initially reported.

**Table 2.5: Adjustment Needed for Estimation of Incidence data (US)**

| Cancer | 1998 Adjustment |
|---|---|
| Female breast cancer | +4% |
| Prostate cancer (white males) | +12% |
| Prostate cancer (black males) | +14% |
| colorectal cancer | +3% |
| melanoma (whites) | +14% |

Source: Clegg et al., 2002.

These results suggest that ignoring delays and errors in reporting may result in the false impression of a recent decline in cancer incidence: the apparent decline is, in fact, caused by delayed reporting of the most recently diagnosed cases (Clegg et al, 2002).

The National Cancer Institute in the United States has focused its attention on the lifestyle risk factors of cancer (Clapp, 1998). There is considerable public pressure for reduced cancer morbidity and mortality, so these institutions attempt to justify their respective strategies through the use of statistical trends and lifestyle risk factors. It is interesting to note cardiovascular disease mortality declined by almost 50 percent in the last 25 years, apparently due to reduced tobacco use, changed diets and increased physical activities, while cancer mortality trend has shown almost no change (p.749). If lifestyle factors are the predominant cause, why has cancer not shown the same type of trend?

While many scientific and social policy representatives have critically deemed the efforts to discover a cure for cancer a failure (Beardsley, 1994), the life expectancy of many cancer patients in both Canada and the United States has increased, as it has in other industrialised countries. This improved prognosis is due to such factors as early detection, more accessible medical care, smoking reduction, improved diet and new treatment modalities (Canadian Cancer Society, 2003).

The enormous sums of money allocated to cancer research, although still not being able to provide a cure, has generated new knowledge about certain aspects of carcinogenesis, such as the genetic mechanisms and the initiation, promotion and progression stages in the pathogenesis of cancer (Brody and Rudel, 2003). While agreeing with the importance of understanding the biological aspects of DNA alteration and damage, others contend that this focus on treatment and genetics is being used to distract the public from the fact that the *winnable war against cancer* is being lost due to the failure to adequately address the impact of synthetic chemicals exposures and to develop corresponding preventive strategies (Epstein, 2002). The next chapter will examine the different facets of this debate and its implications for industrial workers, in general and women, in particular,.

Challenging the current accepted understanding of cancer causality, particularly for occupationally related cancer in general and for breast cancer in particular, is the focus of the research described herein. The next chapter will explore how the scientific conflict regarding cancer aetiology has failed to be resolved with the consequence that cancer remains a threat to increasing portions of the human population.

## 2.7 Summary

While affected by changes in diagnostic capabilities and recording conventions, cancer incidence and mortality rates represent an enormous public health challenge that directly affects millions of people throughout the world. Incidence rates for many cancers are increasing while mortality, particularly in industrialised countries, is modestly declining. Breast cancer is the most prevalent cancer among women. Industrialised countries, including Canada, have the highest rates of breast cancer compared to less industrialised countries. In addition to the human suffering and loss, there are increasingly higher burdens being borne in terms of economic costs to the national health care systems and lost productivity.

# CHAPTER 3: A CRITICAL REVIEW OF THE SCIENTIFIC DEBATES AND BARRIERS TO CHANGE IN RELATION TO OCCUPATIONALLY - RELATED CANCER AND BREAST CANCER AETIOLOGY

## 3.1 Introduction

The search for the explanation for the cancer trends outlined in Chapter 2 is at the centre of this thesis. This chapter explores the major debates past and present that have attempted to explain those trends. Firstly the chapter will provide a short background to the differing perspectives on cancer causality and situate the role of the populations at risk in helping to resolve aspects of the scientific quandary. Secondly it will critically examine the historical debate within the scientific community regarding the aetiology of cancer beginning with the hypotheses presented by Hueper and Carson. Thirdly the chapter will examine the differing perspectives regarding the attributable risks of cancer as argued by epidemiologists Doll and Peto. Fourthly it will explore the analysis provided by physician and toxicologist Epstein. Fifthly it will draw on new insights into the role of hormonally mediated substances and their potential deleterious role with regards to breast cancer. Finally the chapter points to some of the systematic barriers within the 'cancer establishment' that prevent the resolution of this conflict.

### 3.1.1 Background

There is not an established consensus within the scientific community regarding cancer risk posed by such aetiologic factors as lifestyle, genetic susceptibility, viruses, reproductive factors, and environmental and occupational exposures. There are two principal perspectives that have dominated the scientific controversy surrounding the risk factors that contribute to cancer causality. The two paradigms can broadly be described as personal *lifestyle* risk factors versus the more socially determined *environmental* risks factors, which include exposures to synthetic chemicals (Walker, 1998; Colborn et al. 1997, p. 183; Steingraber, 1997). There is also a variety of opinions that exist along a continuum between these two perspectives (Walker, 1998; Clapp, 1998; Landrigan and Markowitz, 1989; Davis and Muir, 1995; Infante, 1995; Rose, 1992). A further synthesis of these diverse perspectives should include another proposition. Our current state of knowledge does not allow us to confidently link cancer incidence to any one specific factor. More likely, given the current evidence, the incidence of cancer is related to a variety or combination of factors, including environmental, occupational, genetic, lifestyle and socioeconomic that should all be included in future epidemiologic studies (Brophy, 2004).

The scientific tools of epidemiology and toxicology, after being mired in over a quarter century of conflict regarding the specific causes of cancer, are limited in terms of their ability to adequately analyse and account for the prevalence of this disease (Myers, 2002a; Susser and Susser, 1996a; 1996b; Pearce, 1996). The scientific and political conflicts over the causes of cancer have created an impasse that has thwarted efforts to reduce cancer incidence.

The scientific community appears unable, through its own efforts, to resolve this conflict alone. To develop a winnable war against the cancer epidemic the populations-at-risk must become directly involved in this process of research and primary prevention if society is to ever effectively reduce the threat of cancer which claims more and more of its citizens (Rosenstock and Lee, 2002; Epstein, 1990;

Brown and Mikkelsen, 1990). Primary prevention of cancer can be achieved, in part, through identifying and avoiding the introduction of carcinogens into the environment and eliminating or "dramatically reducing" the exposure of cancer causing agents currently in use (Tomatis et al., 1997, p. 97). Public involvement and participation in cancer prevention are crucial aspects of the cancer debate that are generally overlooked. The dissertation argues that these are key components for resolving the *lifestyle versus environmental* impasse. Further, the precautionary principle must be adopted as the basis for regulatory interventions with regards to the control of carcinogens for reasons outlined below (Toronto Prevention Coalition, 2001, p.140; European Environment Agency, 2001; pp: 11-16).

> We must act on facts, and on the most accurate interpretation of them, using the best scientific information. That does not mean we must sit back until we have 100% evidence about everything. Where the state of the health of the people is at stake, the risks can be so high and the costs of corrective action so great, that prevention is better than cure. We must analyse the possible benefits and costs of action and inaction. Where there are significant risks of damage to the public health, we should be prepared to take action to diminish those risks even when the scientific knowledge is not conclusive, if the balance of likely costs and benefits justifies it (Horton, 1998).

The scientific impasse regarding the avoidable causes of cancer exists within a social, political and economic context that promotes the notion of individual behaviour as the primary aetiologic factor. The debate masks the fact that diseases, including cancer, exist as a specific interplay of factors produced by social arrangements and the distribution of social power. Different sections of the population bear different risks with the highest risks being borne by the least powerful classes and groups in capitalist societies (Levins, 2003; Woodward and Boffetta P, 1997). Science alone cannot resolve this problem. Science is not a neutral, value-free activity but rather is political and serves to reinforce current social relations and corporate power (Rose and Rose, 1980; Noble, 1980). The redistribution of power and social change are essential components of resolving the cancer epidemic.

## 3.2 Scientific conflict regarding cancer aetiology

The focus of the dissertation is on the occupational associations with cancer in general and breast cancer in particular. Identification of the relative importance of attributable risk factors is important because it can form the basis of occupational and public health interventions. In designing a questionnaire for researching the incidence and causes of cancer within a community it is necessary to identify all of the plausible putative risk factors. During the past thirty years there has been a debate among scientists about the relative importance of various aetiological factors. A brief history will contextualise this discussion because it sheds light on the salient points that have been taken into account in designing the questionnaires used in the case studies reported later in the dissertation.

### 3.2.1 Hueper and Carson: early warnings

Occupational cancer research was historically a primary method of determining the carcinogenicity of substances (Doll and Peto, 1981b, p.1238). The majority of substances, for example, identified to cause lung cancer by the International Agency for the Research of Cancer (IARC) were based on the excessive risk borne by exposed workers (Infante, 1995).

One of the pioneers in occupational cancer research in the twentieth century was Dr. Wilhelm Hueper, the author of the first textbook on occupational cancer and the first Director of the United States National Cancer Institute (NCI) Environmental Cancer department (Sellers, 1997). He began his career in the 1930s investigating a bladder cancer cluster among American Dupont workers (Hueper et al., 1938). After a stormy relationship with Dupont, often triggered by his concern about carcinogenic exposures among its workers, his position was terminated (Proctor, p. 40). In 1952 Hueper was ordered by the U.S. Surgeon General to cease all his epidemiological work at the National Cancer Institute on occupational cancer. This curtailment of his life's work was triggered by a number of factors. He was supplying study results to an Ohio Federation of Labour official, Jacob Clayman, who was pressuring for more legislative protection for workers (Ringen, 1989). Hueper was also reporting on elevated lung cancer risk among American uranium miners at a time when the United States nuclear arsenal was being expanded. These activities ended his scientific research. He was forbidden from any further work related to "the causation of cancer in man related to environmental exposure to carcinogenic chemical, physical, and parasitic agents" (Proctor, 1995, p 44). In 1976 he forecast a steady increase in cancer arising from exogenous exposures to "biological death bombs...that may prove to be, in the long run, as dangerous to the existence of mankind as the arsenal of atom bombs prepared for future action" (p.46).

The experience of Hueper is revealing and has importance to the dissertation for a number of reasons. Hueper believed that synthetic chemicals were of primary importance in cancer aetiology and warned of their potential harm if left unchecked (Sellers, 1997). Secondly, his career demonstrates the barriers that exist for scientists and public health advocates who seek to address the cancer risks of industrial workers. The reaction of manufacturers that produce or employ products that might be deemed carcinogenic has at times been to suppress the damning research rather than to take steps to prevent harm to the exposed populations (Kitman, 2000). The history of the asbestos industry and the petrochemical industry are but two examples of the tendency of corporations to suppress or divert research away from findings that might cause them to incur liabilities or have their products regulated (Gee and Greenberg, 2001; Infante, 2001; Hayes et al., 1997; Lilienfeld, 1991).

Hueper's concerns were to be echoed with the publication of Dr. Rachel Carson's seminal book, *Silent Spring* (1962). While the words, *Silent Spring*, held a multifaceted meaning, it expressed more than a lament for the lost bird species and their melodies. It also referred to a deeply held concern of Carson that the scientific community was complicit by remaining "silent" about the danger posed by toxic substances as wildlife became poisoned and the ecosystem damaged. The title was metaphorically drawing attention to the tendency of the scientific community to become reticent about challenging industries prerogatives (Steingraber, 1997, pp: 16-18). Rachel Carson's own voice was sadly prematurely "silenced" in 1964 when she died of breast cancer at the age of fifty-six.

As the decade progressed following Carson's revelations, public concern began to mount over reports about the asbestos and the petrochemical industries' role in suppressing scientific information regarding the harm being caused to thousands of workers exposed to their products (Markowitz and Rosner, 2002, pp.195-233).

In 1970, President Richard Nixon, in establishing two important public health agencies: the Occupational Safety and Health Administration (OSHA) and the Environmental Protection Administration (EPA), declared a "war on cancer" and promised to eradicate cancer before the end of the century (Proctor, 1995, p.54). In 1978, the Secretary of Health, Education and Welfare, Joseph Califano, released a draft report from the National Cancer Institute, The National Institute for Environmental Health Sciences and the National Institute of Occupational Safety and Health that indicated that between twenty and forty percent of cancers could be attributed to exposures to asbestos, benzene, chromium, arsenic, petroleum fractions and nickel oxides (Bridbord, 1978). These scientists stressed, however, that their estimates of occupational cancer causality had serious limitations because of the multifactoral nature of the disease, the lack of data on occupational histories of cancer patients, the scarcity of information regarding the actual carcinogenic exposures of workers in the work environment, and the complexity of establishing disease causality due to both latency and synergism (Proctor, 1995, p.65). The United States chemical industry, in an effort to discredit the report, commissioned its own report to project the cancer risk posed by occupational exposures. To the corporations' dismay, their own researchers generally agreed with the government analysis and concluded that the estimates indicate "a public health catastrophe" (p. 67).

### 3.2.2 Doll and Peto: causes of cancer

In 1980, Ronald Reagan assumed his presidency, which was marked by a sharp decline in environmental protection and government regulations. The United States government commissioned a new review of the causes of cancer from two renowned international cancer epidemiologists, Dr. Richard Doll and Dr. Richard Peto. These two researchers examined United States cancer mortality data from 1933 to 1977. Changing diagnostic abilities and recording conventions, needless to say, had affected these data. Their publication, *the Causes of Cancer* (1981a) argued that: tobacco smoke and poor diet were primarily responsible for the majority of cancers; the cancer mortality rates were diminishing and could be eradicated within a few decades; and that scientific attention should be on smoking cessation and on finding the biological basis of cancer and ultimately, the cure. The Doll and Peto estimates were based on several assumptions that were later questioned including the following: exclusion of people over age 65 years old on the basis that older medical records were often unreliable; and African-Americans were not analysed separately. Since the elderly and African Americans represent more than half of the American cancer deaths, their data are essential in any estimates regarding possible causes of cancer.

The mixing of Caucasians and African-Americans into one large group would dilute the overall risk due to occupational and social class factors. This is due to the fact that historically, minority workers have held some of the most dangerous jobs in American society (Page and O'Brien, 1973, pp: 25-27, 60-61, 103). African-American workers likely bear an elevated occupational cancer risk related to increased exposure to carcinogens at work (Briggs et al., 2003). Also, given the recognised cancer risk factors associated with socioeconomic status, one would expect greater cancer morbidity and mortality among African-Americans due to the influences of poverty. Their lack of access to medical care, lower socio-economic status and disproportionately higher-risk occupations compared to white workers contribute to their elevated cancer burden (Montague, 1991, p 18).

An additional limitation to the Doll and Peto hypothesis was that the estimates were based on cancer mortality data rather than incidence. Cancer incidence data, if they can be obtained and are accurate, are better indicators of cancer burden for many cancers rather than mortality data. Further, the estimates excluded consideration of the available toxicology and animal bioassays. This evidence is extremely important for cancer prevention because such data are more readily available than human health data. In the case of endocrine disruption, animal bioassays are providing important insights to related microbiological activity.

Doll and Peto constructed a hierarchy of risk factors based on their analysis that they believed were the principal causes of cancer. This model of attributable risk factors has acted as the foundation for developing cancer prevention strategies and setting research agendas throughout the industrialised world (Boffetta and Kogevinas, 1991). Their estimates ranked as follows: dietary factors likely contribute 35 percent of all cancers; tobacco smoke to 30 percent; reproductive and sexual behaviours to 7 percent; occupational exposures to 4 percent; alcohol use to 3 percent; geophysical factors to 3 percent; air pollution to 2 percent; medical procedures and pharmaceutical products to 1 percent. Doll and Peto totalled the avoidable causes of cancer to equal 100 percent. They recognized, however, that due to the synergistic effect of many cancers that the actual contribution could easily exceed 100 percent (Doll and Peto, 1981b, pp. 1219-1220).

The issue of the importance of cancer risk posed by occupational carcinogens is central to the dissertation. Doll and Peto's analysis was directed, at least in part, in response to the earlier report on occupational related cancer issued by Califano. They accused the authors of the Califano estimates of having prepared their report for "political rather than for scientific purposes" (p 1241). Doll and Peto argued that 20 to 40 percent estimates of cancer related to occupational exposures "should not be taken seriously" because, neither intensity of the dose nor duration of exposure, had been adequately factored into the potential cancer risks (p.1240). While dismissing the Califano estimates, Doll and Peto did acknowledge that it was "impossible to make any precise estimate of the proportion of the cancers of today that are attributable to hazards at work" (p. 1239). It was only possible to make informed guesses because of the lack of data about the occupational histories of cancer patients, their likely intensity and duration of exposure, and the almost total lack of information regarding the carcinogenicity of thousands of substances used in the workplace (pp: 1237-38).

**Table 3.1: Doll – Peto lists of cancer sites in Relation to Occupational Exposures**

| Cancers not known to be produced | Cancer possibly produced | Cancers likely produced |
|---|---|---|
| Lip | Mouth | Mesentery and peritoneum |
| Tongue | Oesophagus | Liver and intrahepatic bile ducts |
| Pharynx | Stomach | Larynx |
| Small Intestine | Colon and rectum | Lung |
| Gallbladder and bile ducts | Pancreas | Pleura, nasal sinuses and remaining respiratory sites |
| Melanoma | Connective tissue | Bone |
| Breast | Kidney | Skin |
| Cervix uteri | Brain | Prostate |
| Other uterine cancers | Hodgkin's disease | Bladder |
| Ovary | Non-Hodgkin's lymphoma | Leukaemia |
| Other female genital organs | | Other and unspecified cancers |
| Male genital organs other prostate | | |
| Eye | | |
| Thyroid | | |
| Myeloma | | |

Source: Doll and Peto (1981b): pp: 1242-44.

In *Table 3.1* cancers are categorised by Doll and Peto by their likelihood of association to occupational factors. Certain cancer sites were excluded as having any potential occupational aetiology (Doll and Peto, 1981b, p. 1243). The most prevalent cancer among women, breast cancer, is excluded from any contribution arising from occupational exposures (p. 1243). Prostate cancer, the most prevalent cancer among men, was cited as an occupational risk among only cadmium-exposed workers (p.1244). Such cancers as non-Hodgkin's lymphoma, melanoma, brain cancer and testicular cancer, which have increased dramatically from 1973-1999 and some of which have since been found to be elevated among different groups of exposed workers (Steenland et al., 2003; Epstein, 2002, Steingraber, 1997), are either classified as cancers without occupational aetiology or as having only a slight risk association and likely impacting on only relatively few workers. The overall impact of excluding the above-mentioned cancers was to *lower* the overall risk estimates attributable to occupational factors, since Doll-Peto assumed that these cancers had no aetiologic relation to exogenous environmental exposures. New understanding about the potential elevated risks associated with different occupations or carcinogenic exposures, established since Doll – Peto's 1980 estimates, has had very limited impact on current scientific thinking about attributable risks associated with the avoidable causes of cancer (Tomatis et al., 1997).

Doll – Peto based their estimates on United States cancer mortality that occurred during the period of 1933-1977. With the 20 to 30 year lag time given the long latency in the pathogenesis of cancer; this would represent, from an occupational cancer perspective, exposures that occurred roughly between 1900 and 1950. Women generally did not enter into the industrial workplace, except for a brief period during World Ward II, until the 1970s. Estimates of their cancer risk would be artificially low based on the Doll and Peto analysis (Zahm and Blair, 2003). Cancer associated with the enormous increase in the production of synthetic chemicals would not be properly captured until much later (Landrigan, 1992).

Doll and Peto's publication was fully endorsed by the United States Office of Technology Assessment, the National Cancer Institute and newspapers like the New York Times, which referred to their work as initiating "a less alarming view of the danger from carcinogenic pollutants" within the agencies responsible for cancer prevention (Proctor, 1995, p. 69). Their report also coincided with the anti-regulatory agenda of newly elected Ronald Reagan in 1980. Michael Gough, the Director of the Office of Technology Assessment, which hired Doll and Peto to prepare their *Causes of Cancer*, felt that it "fit into the anti-regulatory bent of the new administration" (p.69).

**3.2.3 Epstein: politics of cancer**

The most serious scientific challenge to the perspective on cancer causality as propagated by Doll and Peto came from Dr. Samuel Epstein. He presented an argument for an essentially different paradigm to understanding cancer aetiology in the first and second editions of his seminal book, the *Politics of Cancer* (1998, 1979), Epstein suggested that cancer causation could be largely attributable to environmental exposures to synthetic chemicals as the increasing incidence of cancer in industrialised countries essentially matches the sharp increase in the production of synthetic chemicals. Cancer is a multifactoral disease that is influenced by an array of factors, both endogenous and exogenesis: that exposure was both voluntary and involuntary; and it is not possible to designate a safe threshold of exposure to carcinogens for either individuals or for wider populations (Epstein, 1998b, pp: 1-2).

Epstein's analysis provides a more holistic approach that utilises the scientific insights of toxicology and microbiology. His perspectives are useful as well to the dissertation because they help to account for the potential harmful effects of synthetic chemicals that are now found in our air, water and food, as well as, used in our workplaces. The massive introduction of these substances coincides with women's entry into the workforce into occupations that were previously held only by men, as well as with social environmental factors such as changes in time of menstruation, menopause, age of birth of first child, reduction in number of women having children, and so on. It provides another rationale for the increasing incidence of breast cancer that, in the majority of cases, is unexplained by such modifiable risk factors as diet and physical activity.

Epidemiology is still unable to provide even minimal evidence of human toxicity or safety on the over 85,000 chemicals now is use (Evans, 2001). By utilising toxicological and animal bioassay data, Epstein is better able to evaluate the potential harm posed by synthetic chemicals. His use of toxicology findings represents a divergent point in his running debate with Doll and Peto.

Unlike Doll and Peto's analysis, Epstein believes that there is a cancer epidemic. Increased life expectancy cannot explain the increasing incidence of cancer. Cancer now strikes "nearly one in two men (44%) and more than one in three women (38%) in their lifetime" (Epstein, 2002, p.6). These increases represent a 56% greater incidence among men and a 22% greater incidence among women in the United States in the course of just one generation (p. 6).

A revised public health strategy, based on the Epstein analysis, would emphasise governmental regulations and accountability to curtail worker and community exposures to carcinogens rather than relying on individual behaviour modification or allocating the bulk of research dollars to discovering a cure for cancer. His analysis would include strong grassroots, community participation as an essential factor in reducing the threat of cancer because he believes that cancer prevention is essentially a political issue, and not a primarily scientific one (Epstein, 1990).

Though there is agreement between Doll, Peto and Epstein on the primary role of tobacco smoke in causing lung cancer, further work has shown the interactive synergy of tobacco smoke with exposures to other carcinogens such as asbestos and radiation. Epstein is critical of the major studies examining lung cancer and tobacco exposure for failing to control for occupational factors (Epstein, 1998a). This failure to account for the possible confounding of occupational exposures in the lung cancer studies will likely overestimate the overall lung cancer risk associated with tobacco smoke alone. Further, the campaigns on tobacco cessation are still constrained by unwillingness to cross the threshold of private property rights. The multinational tobacco industry is not called upon to fully pay for the harm they are causing to individuals addicted to their product or to the corresponding drain on the public health care system. Criminal action has not been taken towards industry executives for deliberately suppressing what was known about the harmful effects of their product. Similarly, there is agreement on the importance of diet in relation to cancer, but disagreement on whether fats, specifically, are a risk factor per se or whether it is because they are the storage sites for such carcinogenic compounds as organochlorine pesticides. The interactive effects of other factors such as shift work that disrupts circadian rhythms, the use of oral contraceptives, alcohol consumption and physical activity need to be considered.

Peter Infante (1995) has identified social class as a possible risk factor because of the disproportionate death from cancer among blue-collar workers and has recommended collection of data on social class as well as sex and race. The risk factors reviewed so far have been traditionally included in epidemiology. While they have shown associations with some cancers there are several cancers that remained unexplained by these traditional risk factors. There has been a pressing need for a new hypothesis.

## 3.3 Hormonal disruptors: possible new paradigm

In the past decade there has been a new hypothesis proposed to account for observed increases not only in cancer but also in certain congenital deformities. There is a new paradigm that is of particular relevance to providing a new scientific approach to understanding the causes of cancer. This new hypothesis asserts that hormonally mediated carcinogenesis, such as breast cancer, is triggered by exposure to synthetic substances that may disrupt the hormonal system. They are referred to as endocrine disruptors (Colborn et al, 1997; Davis et al., 1997; Davis et al., 1993). To date this new hypothesis has not been incorporated into the mainstream medical literature, training and practice nor into epidemiology. Since there is considerable scientific interest in the role played by endogenous oestrogens in breast cancer risk, exogenous oestrogen-like compounds are now being hypothesised as important agents to be investigated (Davis et al., 1997). Devra Lee Davis emerged as a leading scientific advocate in the 1990s with regards to the possible contribution of environmental exposures and breast cancer in women (Davis et al., 1997; Davis et al., 1998; Davis, 2001; Davis, 2002). She is particularly concerned about the environmental exposure to synthetic chemicals that mimic oestrogen, in other words, xenoestrogens, and for the need to employ the precautionary principle to prevent cancer.

As demonstrated in *Table 3.2*, these new insights challenge long held notions previously accepted in toxicology and epidemiology (Myers, 2002). Even if not carcinogenic themselves, the substances that mimic hormones accompanied by the time of exposure might play a role in carcinogenesis, which is as biologically significant as the previous accepted concept regarding the role of carcinogens in altering the DNA (Myers, 2002).

These are important and valid insights. They can help explain how even low level exposures can pose a risk to susceptible populations, such as younger women. It has particular relevance to the Windsor breast cancer research where women at a relatively young age had an elevated breast cancer risk possibly associated with exposure to agricultural chemicals.

Possibly the most radical new hypothesis that has been proposed in relation to cancer, as well as other biological processes, concerns prenatal exposures to substances that act on the endocrine system and affect developmental processes at minute concentrations far below the "safe levels" determined by traditional toxicology. These endocrine disruptors are extremely difficult to research in the human population because by the time cancer has developed after a long latency period, the concentrations measurable in the patient may be quite different from those at the time of the exposure. Endocrine disruptors that have oestrogenic action (xenoestrogens) may be important in relation to predisposing the developing foetus to subsequent development of breast cancer following puberty (Birnbaum and Fenton, 2003).

There will be a more detailed presentation of the endocrine disruptor theory in the next chapter of the dissertation. The new hypothesis should be recognised as potentially providing new knowledge that will help our understanding of breast cancer aetiology and a new scientific perspective that could help move beyond the current scientific conflict exemplified by the Doll, Peto – Epstein debate. In particular, this new hypothesis might shed light on the unsolved mystery of why breast cancer incidence, a central focus of the dissertation, continues to rise, throughout the industrialised world especially, with the majority of cases unexplained by the known risk factors (Health Canada, 2001; Madigan et al., 1995). It is also an important component for understanding how the occupational history questionnaire was developed in the research initiated in Windsor, Ontario, which is examined later in the dissertation.

| Table 3.2: Conceptual Shifts | |
|---|---|
| **Old** | **New** |
| High level contamination overwhelms detoxification and other defence mechanisms | Low level contamination hijacks control of development |
| "The dose makes the poison" | "Non-monotonic" dose response curves are common, in which low level exposures cause effects that disappear at higher levels |
| Only high levels of exposure matter | Impacts caused at what had been assumed to be "background" levels |
| Focus on adults | Periods of rapid growth and development (prenatal through puberty) are most sensitive to exposure |
| A small number of "bad actors" | Many chemicals thought safe are biological active and capable of interfering with signalling systems |
| Immediate cause and effect | Long latencies are common; fetal programming can lead to disease and disabilities decades later |
| Examine chemicals one compound at a time | In real life, mixtures are the rule. They can lead to effects at much lower levels than indicated by simple experiments with single chemicals. |
| Focus on traditional toxicological endpoints like mutagenesis carcinogenesis, cell death | Wide range of health endpoints, including immune system dysfunction (both hyper and hypo-active); neurological, cognitive and behavioural effects; reproductive dysfunctions; chronic diseases |
| One-to-one mapping of contaminant to disease or disability | Same contaminant can cause many different effects, depending upon when exposure occurs during development and what signals it disrupts. Multiple contaminants can cause same endpoint, if they disrupt the same developmental process. |
| Source: Myers, 2003. | |

In light of the emerging endocrine disruptor hypothesis it would be prudent to employ the Precautionary Principle in order to prevent harm now while our ability to measure, codify and understand the microbiological processes progress. A parallel example would be the harm associated with tobacco smoke exposure. It was deemed necessary to implement protective measures before the exact causal association between the genetic damage and tobacco smoke was understood because of the grave public health crisis posed by tobacco (DeMarini et al, 2001; Yano et al, 2000; Hashimoto et al, 2000; Wiencke et al, 1999; Vineis and Caporaso, 1995). It will likely be decades before a similar understanding will be biologically established within the human population thereby confirming the intricate biological pathogenesis of hormonal modulation and breast cancer. It is imperative that we push ahead with research that controls for this factor while we develop societal controls over the production and use of endocrine disrupting compounds. It is also essential that the populations at risk be fully integrated into scientific and policy-making decisions to ensure the greatest level of protection and compliance. These themes will be revisited in the concluding chapter of the dissertation when the implications of the Windsor cancer research are illuminated.

## 3.4 Barriers to resolving conflict

With the incidence of cancer continuing to climb, and adversely affecting increasing numbers of children and adults, one might expect that the conflict regarding cancer causality would be resolved and new approaches be adopted in the war against cancer. What factors have acted as barriers to resolving this public issue crisis? The unresolved scientific disputes mask broader societal tensions and interests that impede the emergence of an effective cancer prevention strategy (Proctor, 1995). The current economic and social order acts as a barrier to developing effective strategies to reduce the incidence of cancer.

It is beyond the scope of the dissertation to explore the convergence of ideology that rationalises the global economy with public health. It is important, though, to note that the ascendancy of the anti-regulatory practices of industrialised countries, beginning in the 1980s, coincided, as previously mentioned, with the promotion of the scientific explanation of lifestyle risk factors as the dominant cause of cancer. This perspective prescribes the most prevalent mode of cancer prevention as each individuals taking personal responsibility for themselves. In other words, this orientation towards individual solutions coincides with the current, dominant political ideology about the primacy of the market and the minimising of the role of the state as an arbitrator of social equity and justice (Brophy, 1992).

In industrial societies like Canada, power and property relations shape the public health agenda (Krieger, 2003). From a social medicine perspective, these institutions are formed within the contextual dynamics of the capitalist mode of production and play an important social role in defining public perception of issues such as health while maintaining the complex social relations that will ensure the reproduction of the rights and privileges of society's elites (Victoria, 2003). There is a strong connection between politics and science with the onus being placed on workers and the community to prove associations rather than on the scientific community (Watterson, 1999, p. 118). Given the imbalance of power and access to other resources, workers face many obstacles to having their conditions recognised (p.111), not the least of which is that their demands often challenge the "knowledge" of the professionals, and expose the truth about the hazards created by the corporate system (Brown and Mikkelsen, 1990, p. 151). Neo-conservative, corporatist thinking, which now dominates capitalist societies in North America, discourages citizen participation. Experts and the technocrats preclude popular involvement and criticism and critical thinking are curtailed (Saul, 1995).

The dissertation holds to the premise that the inequities of power inherent in capitalist society contribute to the inability to resolve the scientific issues regarding cancer prevention thus placing a disproportionate cancer burden on working class individuals, women, and minorities (Epstein, 2002). In this sense, the prevention of cancer is thoroughly political. "While much is known about the science of cancer, its prevention depends largely, if not exclusively, on political action" (Proctor, 1995, p. 60).

The political dimension to cancer-related activities elucidates the debate over cancer causality and the perspective proposed within the dissertation: if occupational and environmental factors were acknowledged as playing a greater role in cancer causality than is currently accepted by dominant cancer institutions, it would follow that there would be greater attention paid to minimising exogenous carcinogenic exposures. Employers would have to bear greater financial and legal responsibility for the harm their products and processes cause. The economy might need to be altered to reduce dependency on synthetic chemicals and democratic decision-making over economic policy expanded to include all of society.

Governments would be obliged to take more action to insure safety from exogenous exposures in the air, food and work environment. Since people cannot really choose their socioeconomic status or genetic makeup or even the hazards they might face in the workplace, governments would have to take greater responsibility for social conditions (Tomatis and Huff, 2001). By deflecting concern away from such exposures while emphasising lifestyle causes, the individual's attention is diverted away from demanding societal change that would protect them from exposure to carcinogens, in favour of personal behaviour modification.

### 3.4.1 Cancer establishments: a barrier

The social functions of cancer treatment, research and prevention are managed by a well developed and powerful "cancer establishment" that dictates the direction of cancer activities (Epstein, 2002, pp 9-26; Hall, 1998, pp 62-68.). It is beyond the scope of the dissertation to fully explore the concept and criteria for a cancer establishment. In general, however, the "cancer establishment" refers to those governmental, quasi-governmental and private organisations that help direct cancer treatment, research, prevention and care.

The Canadian cancer establishment, which includes such organisations as the National Cancer Institute of Canada (NCIC), the Canadian Cancer Society nationally, and Cancer Care Ontario provincially, is interwoven with a network of pharmaceutical and related industries and universities.

Cancer Care Ontario (CCO) is the provincial governmental body created to oversee the administration and management of cancer treatment and prevention in Ontario. It has responsibilities for "surveillance, prevention, screening, research, treatment and supportive care". It supervises nine cancer treatment centres including the Windsor Regional Cancer Centre, the location of the dissertation case studies (Cancer Care Ontario, 2003). CCO's resources and activities focus, however, almost exclusively on "genetics" and "lifestyle behaviours" such as smoking and diet while minimising avoidable causes of cancer that arise from environmental and occupational exposures (Cancer Care Ontario, 2000, p. 4).

Cancer Care Ontario has justified its orientation based on reports such as the Harvard Centre for Cancer Prevention findings for the avoidable causes of cancer (Cancer 2020 Summary, 2003, p. 5). The Harvard Centre has mirrored the Doll-Peto estimates of attributable risk, which emphasise lifestyle choices such as the use of tobacco and the consumption of fatty foods and other dietary factors, as the major causes of cancer within the population (Cancer Care Ontario, 2003; Clapp, 1998). Its strategy for reducing cancer incidence would include prioritising individual behaviour modifications and developing better treatment modalities including the quest for a cure for the disease. Unfortunately, one weakness of this strategy is that individual choices are considered "free choices" without regard for the social circumstances, such as class position, socioeconomic status or personal demands, that influence individual behaviours (Tomatis and Huff, 2001, p.5).

The Harvard Centre for Cancer Prevention has more recently revised the cancer risk attributable to diet from 35 percent to 30 percent, while leaving occupation essentially unchanged at 5 percent (Clapp, 2000). Other lifestyle-oriented researchers have cited the Harvard report and given similar estimates (Schabas, 2003; Adami et al., 2001; Harvard Report on Cancer Prevention, Summary 1996). Neither Doll and Peto, since the release of the *Cause of Cancer*, nor the other above mentioned researchers factored into their analysis what is now known about possible occupational associations to breast, prostate, melanoma, non-Hodgkin's lymphoma or testicular cancer, despite the fact that these cancers represent some of the most prevalent cancers among men or women and have been increasing substantially over the last few decades (Steenland et al., 2003; Epstein, 2002, Steingraber, 1997). As mentioned earlier, excluding these cancers as if they have no occupational association will *underestimate* the overall impact of occupation as a potential risk factor. These researchers have also ignored the toxicological bioassays with their new discoveries and biological theories, including the endocrine disrupting hypotheses.

The Harvard Report on Cancer Prevention was issued to guide the field of cancer research, education and policy (Clapp, 2000). The report was written to counter the public's concern "about minimal risks while losing sight of the major cancer risk factors that can be controlled or modified, in particular, tobacco use, diet, exercise, and sun exposure" (p.748). Industry groups have promoted this perspective,

> ...seeking to reduce federal and state regulation of carcinogens in the workplace and the general environment. To the extent that occupational, environmental, and consumer products have been responsible for any cancer, this has been minimised by industry spokespeople and attributed to historical conditions that responsible companies have corrected (p. 748).

It is important to note that the funding for the Harvard Centre that prepared this report came from donations from some of the largest American chemical and pesticide producers, and their respective trade groups, including the "Chemical Manufacturers' Association, Dow Chemical, the American Crop Protection

Association, Chevron, Union Carbide, Monsanto, and Procter & Gamble" (Ontario Federation of Labour, 2000c, p. 5).

Trade union organisations and women's groups have challenged these perspectives (pp. 5-9). Their demands for primary prevention with the use of the Precautionary Principle and a research agenda directed towards the collection of lifetime occupational histories of cancer patients are generally ignored (Ontario Federation of Labour, 1999). In a letter to the president of the Ontario Federation of Labour, the executive director of the Canadian Cancer Society claims that the organisation is not ignoring occupational and environmental carcinogens but "urge[s] workers to protect themselves by following the Canadian government's guidelines for handling cancer-causing substances" (Thomson, 2001).

Such a statement is reflective of the social perspective espoused by the Canadian cancer establishment. Their prevention strategy for occupationally related cancer primarily puts the onus on the ability of individual workers to secure the necessary protection against egregious working conditions irrespective of their actual power to do so. The real, historical experience of the Canadian working class, however, has demonstrated that this strategy often leads to workplace cancer epidemics (Keith and Brophy, 2004; Firth et al., 1997; Tataryn, 1979). The cancer establishment strategy also avoids any conflict with multinational corporations and governmental regulatory bodies, thereby securing a consensual relationship and stable funding (Epstein, 2002). By focusing on the individual, cancer prevention is depoliticised and reduced to behaviour modification, rather than confronting the social power relations which contextualise the risk of cancer.

It is important to appreciate, in the context of the dissertation, the serious public health threat posed by cancer in Canada. It is also important to understand how the Canadian cancer establishment defines this problem, relying on the underlying assumptions of the Doll-Peto analysis, and what strategies they employed to reduce cancer's impact on individual health and public spending. The purpose of this critique is not to trivialise such avoidable causes of cancer as tobacco smoke or a poor diet, but rather to develop a broad social strategy that advances primary prevention of cancer across a wide stratum of the population and, where possible, does not rely primarily on individual behavioural changes (Tomatis et al., 1997).

### 3.5 New initiatives: lifetime histories of cancer patients in Windsor, Ontario

The outlook of the Canadian cancer organisations towards the avoidable causes of cancer has particular relevance for a community such as Windsor, Ontario, Canada, which is home to the case studies that are presented later in the dissertation. Windsor is a motor vehicle assembly and motor vehicle parts industry centre with recognised high levels of air pollution containing carcinogens (Gilbertson and Brophy, 2001), and widespread use of carcinogens found in the automotive industry (Delzell et al., 2003; Mirer, 2003; Brophy, 1999a; Firth et al., 1997, p. 42-48; Brophy, 1995; Eisen et al., 1992). It is in the interest of society that the exposures to occupational and environmental carcinogens are taken seriously and a concerted effort be made to prevent potential exposures because such reductions could have a substantial public health impact, even if actual risk for individuals was relatively small (Brody and Rudel, 2003). This strategy seems intuitively correct and appropriate, yet it has not been initiated in spite of the advocacy of many groups (Ontario Federation of Labour, 1999).

The process of collecting the occupational histories of cancer patients was first undertaken in Windsor in 1995 through the collaboration of the Windsor Regional Cancer Centre, local occupational health groups, and trade union health and safety activists (Firth et al., 1997, p. 89). It was the first such initiative of its kind in Canada and will be described in greater detail in later chapters. The questionnaires used to capture these histories have evolved over time but each one attempted to control for the known or suspected risk factors. It was a method to address some of the issues contained within the scientific controversy surrounding cancer causation.

The questionnaires were also developed with the direct participation of Canadian Auto Worker health and safety representatives and other community activists (Brophy et al., 2002; Firth et al., 1997). The direct participation of the populations at risk was meant to help address the other dilemma confronting cancer prevention: the essential component of societal change as a necessary prerequisite to prevent cancer. By directly involving those whose health could be damaged and who had intimate knowledge of the work environment, the outcome of the study would have direct relevance and meaning to their collective well being. The results would be known and have direct applicability.

The purpose of the questionnaire was to elucidate the potential risk factors associated with cancer. However, while addressing some, it would not be able to resolve the scientific conflict regarding cancer causality. Without community participation and a strategy for social change and empowerment, one could speculate that the scientific debate would continue ad infinitum with each new finding calling for improved scientific methods and more research funding while the exposures are continued to be tolerated. This conundrum that will be further analysed in the concluding chapter of the dissertation.

## 3.6 Summary

The history of cancer prevention in industrialised countries over the last twenty to thirty years is revealing. The scientific community has engaged in a debate regarding the avoidable causes of cancer that continues to be unresolved. Billions of dollars have been spent searching for the "cure". Public education and governmental regulations have targeted known carcinogens such as tobacco smoke. While the rates of smoking –related lung cancers have either stabilised or decreased, the overall cancer trend has continued to rise.

The rise in cancer incidence has occurred in the context of the tremendous post World War Two growth of the use of synthetic chemicals with a corresponding increase in the political power of the chemical industry (and Capital as a whole). There has also been a corresponding growth of the cancer establishment and its ability to frame the debate about the avoidable causes of cancer (Epstein, 2002). In general these institutions have focussed the issue of cancer causality on lifestyle factors while, when necessary, using political pressure to downplay the potential role of exogenous occupational and environmental risk factors (Clapp, 2000; Brown and Mikkelsen, 1990). Cancer research pioneers like Dr. Hueper are isolated. The Doll-Peto analysis is promoted, while other researchers like Epstein, Infante and

Davis that challenge the prevailing wisdom are marginalised. This strategy has successfully maintained the vested interest of the corporations, but has failed to win the war against cancer.

Industrial workers still bear a disproportionate and preventable cancer burden but with little public interest [Infante, 1995]. Prevention of occupationally related cancer would have a dramatic impact, particularly among the exposed population, but there is minimal scientific interest to pursue such a goal (Nicholson, 1984).

The major cancer agencies have focused their resources on treatment, microbiology and early detection. Occupational exposures have been generally reduced, primarily through trade union organising (O'Neill, 1997) but often only to levels that prevent acute illness, rather than cancer (Ward et al., 2003). Environmental risks have received minimal attention, even though the evidence is mounting with regards to the association between air pollution and lung cancer (Pope et al., 2002) and between endocrine disruptors and breast cancer (Davis et al, 1997, Colborn et al., 1999).

In Ontario there is little activity on the part of Cancer Care Ontario to address the avoidable occupational risks of cancer. It focuses cancer prevention activity on essentially lifestyle factors, while attributing less than 5 percent of cancer incidence to occupational factors (Cancer Care Ontario, 2003). This strategy, rooted in the analysis of Doll and Peto, continues while the cancer rates continue to rise with the projection of new incident cases doubling over the course of the next twenty-five years (Cancer Care Ontario, 2003).

The Ontario Task Force on the Primary Prevention of Cancer (Miller, 1995), Canadian Labour Congress (2002), and the Toronto Cancer Prevention Coalition (2001) have argued for a new strategy that recognises the precautionary principle and the important role that occupational and environmental exposures play in the genesis of cancer. Their perspectives echo the analysis of Drs. Epstein, Infante, Davis, and Colborn that challenges the current dominant cancer prevention strategy.

Through a collaborative process between oncologists at the Windsor Regional Cancer Centre and local occupational health organisations, research into the potential causes of cancer, controlling for a wide array of factors, was started in part as a result of the conflict surrounding cancer causation.

It is important to establish the possible occupational and environmental associations for breast cancer. It is now the most prevalent cancer among women. The majority of the cases cannot be explained by the currently known or suspected causes (Health Canada, 2001). The theory that hormonally mediating compounds may be an important factor in breast cancer aetiology (Evans, 2002) will be a focus of the next chapter.

# CHAPTER 4: CRITICAL REVIEW OF CURRENT STATE OF KNOWLEDGE RELATING TO BREAST CANCER CAUSALITY

## 4.1 Introduction

The brief outlines of cancer trends in Chapter 2 and of endocrine disruptors in Chapter 3 have set the scene for Chapter 4. The chapter provides a necessary and thorough examination of breast cancer causality. Firstly the processes of carcinogenesis that is relevant to breast cancer are examined in the context both of empirical evidence and theoretical research. Secondly following on from that pertinent examination comes an analysis of the breast cancer literature that draws on global assessments of cancer aetiology which links with the third section which looks specifically and closely at known and suspected factors associated with breast cancer causation. Fourthly, new hypotheses for breast cancer causation are described and analysed as these have relevance to the case studies. Fifthly, and for the same reasons as section four, the scientific limitations of current approaches are probed, including epidemiology. This leads to the final section where alternative approaches relevant to the empirical work of the thesis are rooted. These approaches included the involvement of trade unions, and women's and community groups in framing, conducting, and analysing future work.

The inclusion of the populations at risk in the process of cancer research and in the setting of prevention strategies are cornerstones of the research case studies contained in the dissertation.

Of particular importance to the dissertation is the cancer risk due to occupational exposures that remains largely unrecognised. There is, as well, sparse research regarding breast cancer and the role of occupational exposures, some of which mimic oestrogen, a known risk factor for breast cancer. Understanding breast cancer aetiology provides an important occasion to reexamine a number of previously held epidemiological and toxicological assumptions regarding the avoidable causes of cancer.

The chapter examines current aetiological factors associated with breast cancer to shed light on the attitudes, and influences of the professional, scientific and lay community on breast cancer research within Canada generally and Windsor specifically. These influences, and the analysis associated with them, informed the direction of the research project, as presented in the following chapters of the dissertation.

## 4.2 Process of carcinogenesis linked to breast cancer studies

Some literature suggests the increasing trend in breast cancer incidence is not linked to any one specific factor, but to a variety or combination of factors: environmental, occupational, genetic, lifestyle, and socioeconomic factors (Krieger 1989; Kuller, 1995; Kelsey, 1993; Kelsey and Horn, 1993). Toxic insults, single or in combination, may be significant in the initiation, promotion and progression of carcinogenesis (Brody and Rudel, 2003).

However, there are critical moments in breast development when the emerging cells may exhibit particular vulnerability (Davis et al., 1998). Timing of exposure may have greater impact than the dose (Myers, 2002). It is possible and plausible that female breast tissue may be more susceptible to tumour initiation and progression during periods of great morphological and biochemical change, that is, beginning during gestation and continuing through puberty to time of first pregnancy and possibly continuing throughout the reproductive years (Brody and Rudel, 2003). Lifetime exposures to hormonally active substances and to carcinogens may also be critical (Brody and Rudel 2003, p. 527). Genotoxic agents, that is substances that damage DNA, in conjunction with oestrogen can "impede(s) critical cell repair systems, hinder(s) recognition of aberrant cells, and allow(s) the accumulation of harmful mutations" (Davis et al., 1998, p. 525).

Mandeville's *"Review of the Mechanism of Action of Some Etiologic Risk Factors for Breast Cancer"* (2001) acknowledges the complex, multifactoral nature of the disease that is caused, in part, "by endogenous metabolic or other imbalances associated with age or genetic makeup and, in part, by a wide variety of exogenous factors including diet, lifestyle, and exposure to ionising factors and chemicals of natural or synthetic origin" (p.28). Hence, the path of development of the disease occurs "over a long period of time with non-malignant precancerous lesions that only slowly evolve toward cancer" (p.28). This maturation process has three stages or periods: initiation, promotion and progression.

> ...Initiation and promotion each consist of several stages and may involve distinct mechanisms; some of these changes are reversible and some are not, but probably all are susceptible to a variety of modulating factors through which they may be enhanced or inhibited. Also, carcinogenic agents that can induce genetic change are not necessarily the same throughout the neoplastic process and may not act directly on a cell's genetic material. For

instance, dioxin does not change DNA directly, but it is still a potent carcinogen. Some agents appear to act through a receptor mechanism. Even if a carcinogen does not directly damage a cell's DNA, changes in gene expression always occur during carcinogenesis (p.29).

This multi-stage developmental character of carcinogenesis has important implications for occupational breast cancer research. Exposures experienced at a younger age during earlier occupations, may be significant in terms of breast cancer risk.

## 4.3 Breast Cancer overview

Breast cancer is a group of diseases that arises from "the complex interaction between genetics, hormones, and the chemical-physical environment" (Davis, 2001, np). Genetic factors are thought to be responsible for 10 percent of breast cancer incidence (Davis et al., 1998). Breast cancer is the most prevalent cancer among women and overall the second most common cancer. Its incidence has been increasing while in developed Western countries the mortality from breast cancer has declined (Parkin et al., 2001).

The majority of breast cancer cases cannot be explained by known risk factors (Kelsey and Gammon, 1990; Madigan et al., 1995; Henderson et al., 1996, Health Canada, 2001). It is postulated that hormonal and reproductive factors contribute to breast cancer incidence. Key variables include: lifetime exposure to high levels of endogenous oestrogen, resulting from limited parity, early menarche and late menopause, use of hormone replacement therapy and oral contraceptives; age mutations of the genes BRCA1 and BRCA2; and family history of breast cancer (Parkin et al., 2001, Brinton et al., 1998; Enger et al., 1997).

> … Breast cancer is a disease of tremendous significance to women. It is the most common cancer among women in developed countries, and its incidence is rapidly increasing in the developing world. Known risk factors for the disease, such as family history and age at menstruation, explain fewer than one in three cases. While screening and diagnosis has improved in many regions, it cannot completely account for the rate increases. Much research funding has been devoted to treatment of breast cancer rather than its prevention. To date, potential environmental causes of breast cancer have received little attention, even though there is increasing evidence that such links exist (Davis, 2001, np).

Evidence exists regarding the potential adverse effects of persistent organic pollutants (POPs), specific carcinogens, and endocrine disrupting chemicals on breast cancer risk. Many of these chemicals can remain in the environment, bioaccumulate within the food chain, and pose an adverse effect on human and environmental health (United Nations Environmental Programme, 2003), and yet governmental and industry bodies engage in minimal actions to eliminate these exposures or adequately test for their potential risk to human health (Welshons et al., 2003). Little attention has been paid to the potential role of occupational and environmental exposures in the aetiology of women's breast cancer in spite of the toll this disease continues to take (Women's Health Network, 1999; Firth et al., 1997). Early detection through mammography and self-examination is viewed as the best measure to ensure a favourable prognosis from a disease that is deemed to be essentially unpreventable by most Canadian cancer agencies.

There are relatively few epidemiological studies that scrutinise the potential occupational breast cancer risks in general for women (Zahm and Blair, 2003; Gunnarsdottir et al., 1999; Aronson et al., 1994; Zahm et al., 1994). Likewise, tested occupational breast cancer risks are not well studied (Brody and Rudel, 2003). Animal bioassays have identified 200 chemical substances that trigger breast carcinogenesis (Wolff et al., 1996; Brown and Lamartiniere, 1995; Stevens et al., 1994) (*see Appendix E for a partial list of mammary carcinogens*). Although such agents exist, often in high concentrations, in many workplace environments few epidemiological occupational breast cancer studies have been conducted in Canada to investigate their impact. Increasing evidence regarding the genesis of breast cancer is emerging from epidemiological investigations and laboratory animal assays, which point towards an association with endocrine disruptors and breast cancer (Birnbaum and Fenton, 2003). This subject will be explored in greater depth in the next chapter.

Since breast cancer is the most prevalent cancer among women, it presents women and society in general with a serious public health issue. During the 19th and 20th centuries industrial workers have borne the highest exposures to hazardous substances and suffered a corresponding cancer risk. Their excess cancer mortality identified the adverse health risks of exposure to toxins for the whole of society (Infante, 1995). Women's health problems in the 21st century, including breast cancer incidence, might represent for society a similar sentinel event with implications for the whole population and yet minimal interest is given to seriously addressing this issue. The bias of an earlier generation of scientists towards the plight of industrial workers may be reflected anew in the current public health crisis posed by high breast cancer incidence rates.

### 4.3.1 Global insights

Breast cancer, diagnosis and reporting, globally is not evenly distributed across the female population, either temporally or geographically (Brody and Rudel, 2003). Some regions, for example, Europe, North America and Australia, exhibit high-recorded rates while less industrialised countries in Africa and Asia have markedly lower diagnosed and recorded rates (Parkin et al., 2001). More developed countries have a 2.7 times greater breast cancer incidence (based on Age-adjusted Standard Rate (ASR) per 100,000 population) than less developed countries with the highest rates found in Western Europe, Australia/New Zealand, the United States and Canada (Globocan, 2000). Breast cancer is considered a disease primarily of industrialised societies (Solomon, 2003).

While breast cancer is not as prevalent in Japan as in other industrialised countries, it is rising. Between 1975 and 1985 the incidence rates more than doubled in Japan (Kelsey and Bernstein, 1996). While there is still a marked difference in incidence rates between the high risk and low risk countries, the rapid increases in an industrialised country, such as Japan, point to possible environmental contributions (p.48). Japanese women who immigrate to Canada or the United States assume the same breast cancer risk within a short period of time as the host population. The same is true for Canadian women who move to countries like Japan (Epstein, 1997, p.248). Could dietary factors provide greater protection against hormonally mediated diseases even in the face of deleterious exogenous exposures? This is an important question that should prompt additional investigation (Yamamoto et al., 2003).

Asian countries have diets rich in fish and in phytoestrogens, such as soy products, which are oestrogenic compounds that are thought to be protective (Davis et al., 1998). Yet, portions of the Asian population, such as the Japanese, may also have exposure to high levels of pollutants that contain hormonal disruptors and carcinogens that pose a cancer risk and hence one might expect to see higher breast cancer rates unless social, environmental and dietary factors offer some countervailing influence. A very complex picture of varied, competing and perhaps complementary influences on, and possible multiple causation of, breast cancer is beginning to emerge. Environmental exposures to carcinogens and hormonal disruptors in industrialised countries, particularly North America, Western Europe, Australia and New Zealand, may be a strong contributing factor in the elevated breast cancer incidence rate (Kelsey and Bernstein, 1996) as the population does not share the same possible dietary protection as the Asian populations.

The differences in diagnosed and recorded breast cancer incidence between more industrialised and less industrialised countries and the unequal distribution within industrialised countries raise the possibility of exogenous exposures as possible causative factors. The lower breast cancer rate in industrialised countries like Japan appears to raise important questions about the possible protective effect of diet and suggest that it should be included in epidemiological investigations.

## 4.4 Known and suspected risk factors for breast cancer

One of the major concerns in breast cancer research is the role of hormones. Natural oestrogens are now considered to be carcinogenic (Birnbaum and Fenton, 2003). Cumulative lifetime exposure to a constellation of intrinsic and extrinsic oestrogens, such as estradiol, progesterone and other reproductive hormones represent the most widely accepted underlying factor with respect to breast cancer risk (Davis et al., 1998; Kelsey and Bernstein, 1996; Kelsey and Gammon, 1990; Henderson et al., 1996).

Family history of breast cancer, particularly with respect to having two or more relatives with breast cancer and mutation of the BRCA1 and BRCA2 gene represent less than 10 percent of breast cancer cases (Health Canada, 2001, p. 5-6; Sattin et al., 1985; Davis et al., 1998). The tumour suppressor gene p53 mutations may be implicated in breast cancer. This gene is involved in "cell cycle, DNA repair, apoptosis, and other critical functions" (DeBruin and Josephy, 2002, p.119). It appears in about 40 percent of breast malignancies.

Diet, body mass index, obesity and alcohol use are considered risk factors. Being overweight, particularly among postmenopausal women, may increase endogenous hormones, which trigger cell proliferation (Bernstein et al., 2002; Hankin, 1993; Friedenreich, 2001, p. 13-14). Increasing age, lack of physical activity and higher socio-economic status (SES) constitute an additional set of risk factors (Kelsey and Bernstein, 1996; Baquet and Commiskey, 2000; Maxwell et al., 1999). Each of these risk factors relates either directly or indirectly to the cumulative exposure of mammary cells to oestrogen (Kelsey and Bernstein, 1996).

Breast cancer risk is usually found to be elevated among women with higher incomes and education, that is, higher socio-economic status (SES). Income and education are not actual causes but are viewed as surrogates for such factors as age of childbearing and parity (Brody and Rudel, 2003). This group of women with higher socio-economic status, for example, would include women employed in occupations such as health care where they could have exposure to a wide array of carcinogens, including ionizing radiation and anti-neoplastic drugs, in the course of their work. It is also postulated that more affluent women might have increased exposure to certain synthetic chemicals because of their use of dry cleaning and cosmetic pesticide use for lawn treatment (Maxwell et al., 1999).

Statistical models (Gail et al., 1989; Gail and Costantino, 2001) were developed to assist in providing individual risk assessments with regards to breast cancer. These tools have also been used to evaluate medical treatment modalities (Gail et al., 1999; Gail and Rimer, 1998). The Gail model, for example, focuses on factors such as age, age at menarche, age at first birth, and familial breast cancer history. It has been found to limit "discriminatory accuracy at the individual level" (Rockhill et al., 2001). These models do not account for the broader range of exogenous exposures or for the particular timing of exposure. They also focus on the risk factors that can only explain the causality of a minority of breast cancer incidences.

### 4.5 New hypotheses on breast cancer

The new revolution in scientific thinking about endocrine disrupting compounds, generated primarily by animal laboratory experiments and wildlife studies, is critical to the dissertation and its analysis. It is important to explore this issue because one of the few human examples that demonstrate the adverse impact of exogenous oestrogenic exposure and subsequent breast cancer risk is the elevated breast cancer risk among the daughters of women who used diethylstilbestrol (DES) during their pregnancies.

The use of the pharmaceutical diethylstilbestrol (DES) by pregnant mothers led to the development of vaginal adenocarcinoma in their young daughters (Herbst et al., 1971). DES was prescribed for millions of pregnant women between 1941 and 1971 "to prevent spontaneous abortions and stillbirths, to suppress lactation in women who wished to bottle-feed, and as a postcoital contraceptive" (Krimsky, 2000, p. 9). This potent synthetic oestrogen is also found to elevate the breast cancer risk of women who used DES during their pregnancy (Colton et al., 1993; Titus-Ernstoff et al., 2001). A study that examined the sons of women who took diethylstilbestrol during their pregnancy found an elevated risk of testicular cancer (Strohsnitter et al., 2001). These two examples - ionising radiation and diethylstilbestrol - constitute almost the total of human epidemiological evidence regarding developmental exposures and later cancer incidence, although there are suggestions of other possible associations between particular exposures, such as pesticides with childhood cancer (Flower et al., 2003; Colt and Blair, 1998).

> ...Thus, as seen from all the preceding information, industrial chemicals, drugs, and radiation have been associated with an elevated incidence of neoplasms in both experimental animals and in people following early life stage exposures. These studies also suggest that foetal susceptibility (lack of metabolism, protective barriers not formed), sensitive populations (strain differences), and critical periods of target-organ development are key

elements in the response to environmental carcinogens (Birnbaum and Fenton, 2003, p.390).

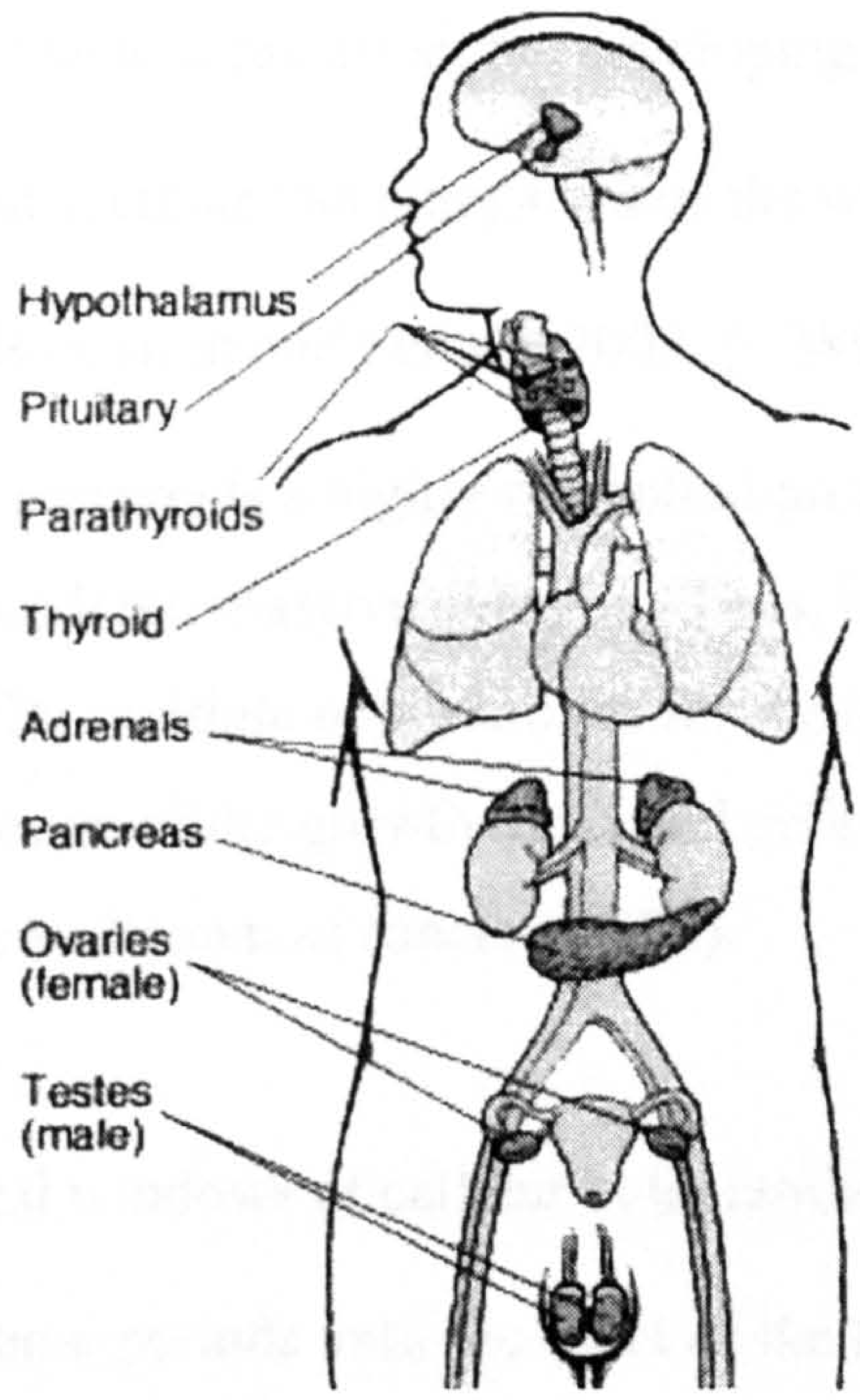
Exogenous chemicals that "mimic" oestrogens (xenoestrogens) may contribute to cellular proliferation and the neoplastic process (Brucker-Davis F et al., 2001; Baccarelli A et al., 2000; Degen and Bolt, 2000; Kennedy, 2000). It is further theorised that particularly prenatal or neonatal exposures can increase the breast cancer risk of women by an "imprinting process that sensitises her to oestrogen exposures" (Coburn et al., 1997, p. 183). There is particular concern about exposures to hormonally modulating substances during periods of rapid cellular growth and differentiation (Birnbaum and Renton, 2003).

Research has shown that, in children, there is rapidity of cell growth and division accompanied by genetic change occur during the embryonic period. This biochemical process offers extensive opportunities for mistakes to arise including gene mutations. The defences of such physiological barriers as the blood-brain barrier are still not fully developed in utero. The detoxifying capacities of the developing organism are not fully matured until after birth (p.389). This perspective provides an essential component to properly designing a questionnaire that examines associations between occupational exposures and breast cancer.

Any of the various exogenous substances may act as an agonist, for example, mimicking hormonal activity; or antagonist, that is a substance that interferes with hormonal activity, or it may alter the way hormones are transported or "bind with more than one hormone receptor" (Colborn et al., 2003, np). There are only a limited number of breast cancer studies that examined occupational exposures that disrupt the endocrine system (Brody and Rudel, 2003).

The model of pathogenesis of breast cancer has recently been revised to account for the role of the endocrine system and the impact hormones have on genetic development and messaging. It is an essential element of the dissertation that this new hypothesis be recognised as providing an insight that may help our understanding of breast cancer aetiology. It is also essential for the developing research initiated in Windsor, Ontario and described later in the dissertation. Figure 4.1 shows the glands that compose the endocrine system. They consist of the thyroid, ovaries and testes, pancreas, adrenals, pituitary, parathyroid and hypothalamus. This set of glands produce hormones that are "signaling molecules" that travel in the bloodstream controlling the growth, development, reproduction and behavior of wildlife, animals and humans (European Commission of Research, 2003).

Figure 4.1: Endocrine System (European Commission of Research)




Oestrogen, a steroid hormone, penetrates the cell membrane and directly interacts with the DNA. It "triggers genes to produce their programmed chemicals" (Schettler et al., 2000, p.4). "Signal disruption" is a complex process in which a chemical or group of chemicals might duplicate the actions of a particular hormone, or interfere with the activity of the hormone. Besides changing the way the hormone is transported, it might also trigger anti-oestrogenic and anti-androgenic cellular activity (Colborn et al., 2003).

These risk factors, mediated by time of exposure in a person's life cycle, as well as, intensity of the dose and thus prenatal exposures, for example, might increase susceptibility for breast cancer risk in later life (Davis et al., 1998). The impact of timing of exposure may induce "more neoplastic transformation of (breast) cells and is thereby more carcinogenic than exposures that occur later in life" (Davis et al., 1998, p. 524). Hormonal factors can affect the developing breast cells' proliferation and differentiation and thus, create "an elongation of the window of sensitivity to potential carcinogens" (Birnbaum and Fenton, 2003, p. 389).

> ...differentiation represents a highly controlled process in which patterns of gene expression undergo massive changes. Thus, both cell division and differentiation offer multiple opportunities for the initiation of lesions as well as the promotion of the growth of altered cells; these are hallmarks of the complex process known as cancer (p.389).

Breast cells have temporal windows of cellular vulnerability that include prenatal, perinatal, prepubescent time periods until the onset of the first pregnancy, and perimenopause (Weiss et al., 1997; Brody and Rudel, 2003). Exposures to elevated levels of hormones during the gestation process may, for example, imprint breast cells and affect their development and susceptibility. This may make them more sensitive to carcinogens or hormonal compounds. Prepubescent exposures "expedite the process of aberrant breast growth and attendant susceptibility" (Davis et al., 1998, p. 525).

Younger women, between the age of menarche and the time of first pregnancy, appear to be particularly vulnerable to genetic damage. The cells in the immature, developing breast are not as yet differentiated and cells are dividing at a greater rate than later in life (Kuller, 1995; Davis et al., 1998). The susceptibility to cell mutation, coupled with the greater propensity of undifferentiated cells to bind with carcinogens and thus trigger DNA damage, means the exposure of younger women to hormonally mediated substances can be crucial causative events (Clark et al., 1997).

For instance, women, whose mothers had exposure to pesticides while pregnant or those who were exposed to endocrine disrupting pesticides as young children, and then decided to delay their first pregnancy until their thirties would be potentially at a higher risk than women who did not share these exposures at an early age and had their first child earlier in life. It is important for the central concerns of the dissertation, however, that the possible impact of endocrine disrupting exposures be recognised and factored into the questionnaire that captures lifetime histories of cancer patients as cited in the case studies. The experience of Windsor in this regard will be described in chapter 9 with the current research study, the Lifetime Occupational and Environmental Histories Record (LOEHR).

These scientific limitations present important challenges to the regulations of these hormonal disruptors. Colborn et al. (2003b) list four important aspects of the endocrine disrupting theory that pose both scientific and political issues about the controls that are necessary to protect the health of the population. First, the effects of these substances occur at levels much lower than is currently being used to test for toxicity. Second, the traditional axiom of toxicology and risk assessment, that is that increasing dose should correspondingly increase the effect, is negated when examining hormonally active substances. Very low levels of exposures may have the most profound effect. Even at extremely low levels of exposure there is an effect that challenges the concept of a safe threshold. Third, this is particularly so when the exposure occurs during a period when the hormonal system is already active.

And finally, mixtures of chemicals, not the single exposures, which are the hallmark of current regulatory testing, can have an additive, synergistic, multiplicative or even cancelling effect.

The non-monotonic Dose Response Curve phenomenon of endocrine disrupting substances poses a challenge to the toxicological axiom that the dose makes the poison and to the way toxic substances are regulated throughout the globe (Colborn et al 2003b). The assumption that a greater exposure, over a longer period of time will increase the risk of diseases like cancer is challenged in animal bioassays experiments (Welshons et al., 2003). Endocrine disrupting substances, even at very low levels of exposure, may have a far greater impact than a greater dose, particularly if linked with the timing of exposure. Vom Saal et al (1997), for example, conducted a series of experiments that exposed mice in utero to bisphenol – A and diethylstilbestrol (DES) and followed the adult mice to determine whether these exposures had an effect on the prostate. Low doses of exposure in the womb caused significant prostate enlargement while higher doses of these substances had no effect.

### 4.5.1 Scientific limitations - epidemiology

This observation has particular meaning for our understanding of hormonally related cancers, including breast and prostate. The traditional epidemiological and toxicological concepts are challenged by these laboratory experiments. The mother's exposure during pregnancy, for instance, might imprint the cells of her female offspring who then in their adult lives might be susceptible to particular exposures that precipitate the neoplastic process. A case control occupational study tests *cause and effect* by examining a particular occupation or exposure. If the study design does not control for these early exposures, then it is missing important risk factors. It is possible that in the case of endocrine disrupting exposures the dose-response curve might not be a viable measure for determining for cause and effect. False negative results can occur when in fact associations do exist if these early exposures are not controlled for. It is important to consider the impact of endocrine disrupting chemicals as one examines the current scientific literature with respect to breast cancer and occupation.

The limitations of epidemiology to detect possible associations between endocrine disrupting chemical exposures and breast cancer are highlighted later in the thesis. There is a need to develop new approaches and standards of proof in evaluating the causal association between synthetic chemicals and breast cancer. Cause and effect in humans may be impossible to decipher with our current scientific tools (Myers, 2002). Animal and laboratory bioassays, not epidemiology, have demonstrated the biological processes that result from early exposures to these xenobiotic substances. Occupational epidemiology attempts to investigate the effects of exposures that occur in the work environment while controlling for other risk factors that may confound possible associations. Epidemiology is constrained by the difficulties in determining prenatal exposures; this creates possible error and bias.

The emerging insights into how the hormonal system functions contradict old assumptions that are cornerstones to occupational epidemiology and toxicology. The notion that the dose makes the poison is shown to be a false premise in the case of xenoestrogenic exposures since timing is an even more essential factor in triggering disruptive outcomes (Axelrod et al., 2001). The non-monotonic dose response curve demonstrates that smaller doses, at crucial moments, might be more important than larger doses. In fact there may not be a safe threshold for activated hormonal systems (Sheehan et al., 1999). How can epidemiology control for events that are unfolding in the womb for a disease of long latency that only appears decades in the future? This scientific challenge may not be resolved for generations as epidemiology, microbiology, and social sciences coupled with the knowledge and experiences of women are incorporated together into a new synthesis. It is within this context that the precautionary principle should be employed in order to reduce harm (European Environment Agency,2001; Davis et al., 1998).

**4.6 Alternative approaches – collaboration with populations at risk**

There is a need to rethink the role that populations at risk must play in generating both research and strategies to prevent such diseases in the future. The women's health movement, for example, is also challenging old presumptions about breast cancer treatment, research and prevention that include greater participation and decision-making power for women (Evans, 2002; Myhre, 2001; Women's Environmental Network, 1999; Bristol, 1992). Breast cancer is viewed, not just as a personal tragedy, but also as a societal "public health crisis" demanding scientific and political action (Evans, 2002, p. VI). These groups are critiquing the old scientific conflict about the avoidable causes of cancer with a holistic perspective that sees the relationship between health and the environment. In the face of scientific uncertainty women's health organisations are promoting the adoption of the precautionary principle; this translates into demands for the reduction of toxic substances in our environment (Women's Environment Network, 1999).

Already there are important perspectives available on the subject that inform the case studies presented in the dissertation. These perspectives are promoted by American non-scientific, grassroots women's organisations (Breast Cancer Action, 2003a, 2003b).

> There is emerging science to suggest that these synthetic chemicals pose risk to the human reproductive system, the endocrine system, and to human growth and development both in utero and after birth. If we fail to properly research the impact toxic chemicals and other environmental contaminants have on our bodies, we close the door on developing potential cures, prevention strategies, and treatments for breast cancer and other serious illnesses (Evans, 2002).

Women, they believe, should be encouraged to reduce their risk through modifiable individual actions and community efforts: "breast cancer is not just a personal tragedy; it is a public health crisis that demands action by society as a whole" (p.vi). They cite the possible risk of breast cancer linked to occupation for women workers in contact with toxic chemicals such as "chemists, clinical laboratory technicians, dental hygienists, paper mill workers, meat wrappers and cutters, microelectronics workers and telephone workers" (p. 18). Also, risks are identified for "white-collar" workers found "generally in higher socioeconomic groups such as school teachers, social workers, physicians, dentists and journalists" (p.18). The groups urge more investigation into potential occupational exposures.

Women's health organizations, like the American Breast Cancer Action, are providing an analysis on breast cancer aetiology that represents an important new perspective in the scientific debate spawned by Doll-Peto and Epstein. While more sympathetic to the general perspective proposed by Epstein, these breast cancer prevention groups challenge a spectrum of scientific and social assumptions. They connect environmental contamination with the power relations within capitalist society. Their analysis challenges the rationality of the economic system that allows the presumption of innocence for 85,000 synthetic chemicals in use today, while demanding the onus of proof of harm be provided by the populations at risk. The assumption that the chemicals are safe until proven otherwise remains as the accepted premise in most industrialised countries. The groups view breast cancer causality within the more general framework of health, which recognises the interconnection of a wide range of adverse disease outcomes, such as reproductive problems and birth anomalies (Steingraber, 2001). The women's groups also recognise the significance of the endocrine disruptor hypothesis (Davis, 2002, pp.159-192). Their ideas represent a clear research agenda in which women would be full partners and not just subjects for investigation. The women's health groups advocate for regulations and social policy changes even when scientific uncertainty exists but the preponderance of evidence indicates culpability and harm. In the case of breast cancer aetiology, as has been discussed, overcoming scientific methodological limitations to establish cause and effect may be a very daunting undertaking. Yet scientific certainty has historically been the cornerstone of regulatory controls. While this debate rages, hundreds of thousands of new breast cancer cases will emerge. Breast cancer groups support strong advocacy and precautionary measures and expect researchers to join them in this quest for a world without breast cancer (Steingraber, 1997b). This perspective strongly imprints on the research that will be described in the coming chapters of the dissertation.

## 4.7 Summary

The chapter has sought to explain briefly the mechanisms of carcinogenicity, especially those pertinent to breast cancer. These mechanisms are highly germane to the thesis as are ;the geographic and temporal distribution of the disease, and the risk factors that have explained, and may explain, the aetiology of the diseases including insights both from scientific and medical groups as well as from women themselves. It is in light of such a knowledge and theory base on insights from non-medical and scientific groups that the case studies that follow have been developed.

# CHAPTER 5: WHAT EPIDEMIOLOGY CAN, AND CANNOT TELL US ABOUT CANCER, BREAST CANCER AND OCCUPATION WITH REFERENCE TO CANADA AND PARTICULARLY WINDSOR

## 5.1 Introduction

The chapter provides new, pertinent and distinctive analyses of critical epidemiological studies that have not hitherto been discussed in the thesis. These studies and the critique of them underpin and inform the development and application of the case studies, which follow and much of the methodological thinking in those case studies. The chapter examines the impact of Canadian cancer studies on, and the inter-relationship with, Canadian occupational health policy and practice pertinent to both Windsor as a geographical entity, and to the two case studies that will follow. Early chapters have explored the international debates on cancer and the significance of scientific toxicological and Non Governmental Organisations (NGO) reports to the study of breast cancer. Now, a much closer investigation of the relevant scientific and governmental literature germane to the research questions is offered.

The first section, therefore, reviews the relevant studies on occupational cancer in Canada and how that research has or has not addressed the needs of employees in the country, provinces and cities. The reasons for deficiencies, successes, and failures on occupational health are scrutinised. The second section naturally progresses to focus in on key epidemiological studies on breast cancer. This section is broken into parts – national studies, the British Columbia example so important to the later Windsor study, and other studies. The third and fourth sections then relate the breast cancer studies to the geographical and occupational profile of Windsor and the surrounding area. In this context, both farming and healthcare work are important employment areas for, or environmental influences on, women. Hence the section looks specifically at farming and nursing epidemiological studies.

## 5.2 Occupational cancer research in Canada

> ...Ontario has no systemic means for generating hypotheses linking cancer incidence and employment, industry, occupation or workplace exposures. This fact stands in the way of reliably estimating the burden of occupational cancers in this province (Marrett and Weir, 1989, pp. 1-2).

Occupational cancer research has been constrained by the limited occupational history data obtained from death certificates or records, which indicate only predominant occupation. There is also no comparable national or provincial exposure assessment such as the United States National Occupational Exposure Survey (NOES) to estimate the number of workers being exposed to carcinogens (Brophy, 1995). It is estimated that over twenty million American workers were exposed to either IARC Group 1 lung carcinogens or probable lung carcinogens based on animal and epidemiological evidence (Infante, 1995). Extrapolating these figures to Canada, which has approximately 1/10$^{th}$ the United States population, would mean that over two million Canadians are being exposed to cancer–causing agents and are bearing some degree of related lung cancer risk. This may be a crude inference since the two economies are not necessarily duplicates. Nevertheless, it does provide a rough measure of the potential extent of the problem. In the European Union (EU) a database was established to document exposure data and record the number of workers exposed to carcinogens (Kauppinen et al., 2000). No such tracking system exists in Canada.

Statistics Canada published a report on Canadian working conditions that polls workers about their work environment (Grayson, 1994). This survey found that 4.9 million workers reported dust and fibres in the air where they work; 3.2 million were affected by poor air quality; and another 2.7 million were exposed to dangerous chemicals and fumes.

> ...A substantial proportion of Canadians exposed to potential workplace hazards believed that their health had been affected...Dangerous chemicals or fumes were perceived as having an effect by about half the workers exposed to them, while more than 40 percent of those exposed to dust or fibres or to loud noise considered them to have been harmful (p.44).

The Statistics Canada study did not record exposure to carcinogens per se but it gives a snapshot of how Canadian workers view their work environment and provides rough estimates of the number of workers that believe they are being exposed to dust, fibres and chemicals with adverse health impacts that can cancer. Yet, scientists and compensation board physicians downplay the existence of such hazards. Cancer Care Ontario estimates that less than five percent of cancer cases are attributable to occupational exposures. Such estimates are misleading and incompatible with our understanding of the multifactoral nature of the disease. As presented in preceding chapters, there is a scarcity of data on occupational histories. Hence, substantial numbers of work-related cancers go unrecorded, and thus the preventable cancer burden sustained by working class individuals is underestimated. The dominant scientific estimates are also at variance with workers' own experiences as demonstrated by the Statistics Canada survey, as well as, in testimony to government commissions and inquiries (Ehring and Roberts, 1993, pp. 110-113).

Studies hitherto based on Worker Compensation Board data have generally had little impact on cancer prevention or workplace conditions. This is not only because of epidemiological methodological problems but also because of an inability to address the systemic barriers that deny the knowledge and experience of workers regarding their own understanding of the work environment and the role it plays in the aetiology of disease, such as cancer. This is a critical barrier to the identification and prevention of occupationally related cancer in Canada (Brophy et al., 2002). The historical experience of occupational cancer prevention demonstrates that it is workers' activity, and not the scientific or medical community alone, that generates the political pressure to ameliorate the work environment and cause governments to regulate toxic exposures (Firth, et al., 1997, p. 1-4; 31-48; Sass, 1986, 1983a, 1983b, 1981).

In 1981 medical consultants with the Ontario Workers' Compensation Board (WCB) estimated that less than 1 percent of cancer cases in Ontario were caused by occupational exposures (Chovil et al., 1981). At that time Ontario had a population of 8.5 million people with a work force of 4.3 million. Since 1947 the compensation board has recognised cancer as a possible disease arising from the work environment. The compensation board physicians argued that since cancer was acknowledged in the Compensation Act and because the Act gives the "benefit of the doubt" to the worker, the actual number of the cancer claims is likely inflated (p.1238). It was suggested "that a proportion of 1% or less -- the lowest level suggested by epidemiologists – is probably a good estimate of the extent to which occupational hazards contribute to the burden of cancer in Ontario at present" (p.1241).

A number of Ontario workplaces were particularly highlighted, such as the uranium mines where 54 accepted claims for work-related lung cancer were awarded by 1981. A Royal Commission, which hundreds of disabled and ill miners and their families attended, generated this recognition. They appeared in order to testify about the high levels of worker exposure to uranium, silica and a host of other carcinogens, as well as, about the prevalence of disease among their co-workers (Firth et al., 1997, pp. 34-35). The medical consultants stated, however, that the exposures were "relatively low" compared to uranium miners in other provinces and "that the highest potential for exposure had existed over a relatively short period during the development of the industry" (Chovil et al., 1981, p. 1239). The Royal Commission had already issued its report with a scathing criticism of the mining conditions which produced "excessive exposure to ionising radiation" causing lung cancer to occur as quickly as five years from the time of first exposure (Firth et al., 1997, p.35). In spite of this information, compensation board consultants continued to discount possible causal associations.

Other reports cited substantial exposures to a wide spectrum of carcinogens in the uranium mines (IDSP, 1996, 1994, 1989, 1987). Recommendations were given to the Workers' Compensation Board regarding the work-relatedness of lung cancer in miners. It was suggested that the legal presumption be extended to a uranium miner who contracted lung cancer. In other words, the disease would be presumed to be work-related unless the opposite could be proven (IDSP, 1994). The Workers' Compensation Board medical specialists concluded, however, the "new cases of occupational cancer are unlikely to develop from exposure to current levels of these carcinogens" (Chovil et al., 1981, p. 1241). This conclusion was challenged by a

Royal Commission report, a government disease advisory panel, epidemiological studies, and of course, by the miners themselves. Wide discrepancies continue to exist between the medical specialists and the workers' own perceptions and opinions of the risk of occupationally related cancer (Brophy, 1995, p. 6). The impetus for the Royal Commission to recognise diseases, particularly cancer, developed out of the activity of the uranium miners in Elliot Lake in the early 1970s. Their struggle to control exposures, to pressure government and employers for protection, and to end the threat of silicosis and lung cancer was to fundamentally change the legal structure in Ontario giving all workers the right to refuse unsafe work and would launch a two decade effort to have occupationally related cancer recognised by the Workers' Compensation system (p.6).

The Ontario Workers' Compensation Board medical consultants provided a clear example of the kind of "science" that protects the vested interest of employers and governments against the demands and protections needed by workers. The mainstream medical profession has likewise followed suit by underestimating and ignoring the extent of harm arising from the workplace, particularly with diseases such as cancer (Sass, 1986).

A challenge to the Ontario Workers' Compensation Board estimates emerged a decade later from other researchers who examined compensation board and cancer registries of individual provinces for the period 1980 to 1989 (Teschke and Barroetavena, 1992). Based on compensation data from British Columbia, Saskatchewan and Ontario, which were the only boards to provide the requested information on occupationally-related cancer claims, researchers found that while occupational attributable risks may be smaller than those associated with smoking and diet, the risks still represent a sizeable cancer burden. Also the Canadian Workers' Compensation system puts the onus on injured workers to recognise the possible connection between their illness and workplace exposures and then to make claims. There were no specific Canadian estimates on risks posed by occupational exposures. However, the researchers estimated that the compensation boards accepted less than 0.25% of all incident cancers among men. This substantial underreporting of occupationally related cancer claims confirms the estimates that less than half of the Ontario workers with asbestos-related cancer claims ever file with the compensation board (Finkelstein, 1989). The number of claims for occupational cancer accepted in British Columbia, Saskatchewan and Ontario represent *less than 10%* of the cases that would be conservatively anticipated based on epidemiological estimates.

The Canadian Unemployment Insurance Commission (UIC) in the 1960s and 1970s collected the Social Insurance number, name, sex, year of birth, and the current occupation and industry of all individuals whose Social Insurance number ended in the digit 4 (Howe and Lindsay, 1983). This data was linked with the Statistics Canada mortality database to record the number of deaths between 1965 and 1973. During this period there were 4,203 cancer related deaths among 415,201 Canadian men with known occupational histories from 1965 to 1969. The researchers found that the cohort demonstrated a "*healthy worker effect*". That is, comparisons between workers and the general population may bias the relative risk and underestimate the true extent of the association. There is generally considered to be a 20 percent difference between the expected mortality of industrial workers and the general population (McMichael et al., 1974; IDSP, 1988).

The mortality rate for the Canadian cohort being studied was 20 % less than in the general population. There were a larger (age-adjusted) percentage of deaths due to lung and bladder cancer within the cohort than within the general population. A number of occupations were identified as having an elevated cancer risk including in the category of "all malignant neoplasms" by occupational divisions, such as clerical, service and recreation, and transportation and communication.

A study used Statistics Canada data to -examine cancer risks faced by women who made up over 40% of the Canadian work force (Aronson and Howe, 1994). Women had been excluded previously from such investigations because they are often listed as "housewife" or "homemaker" on death certificates. Most workingwomen were not included in previous cohort studies. In the 1994 study, statistically significant increased breast cancer mortality was identified among women employed as accountants and auditors (SMR= 207, CI 95% (103-371); in printing and publishing (to the age 64) (SMR = 218, CI 95% (109-391); and in electrical machinery equipment and supplies manufacture (to the age 64) (SMR = 235, CI 95% (107-445). (Standard Mortality Ratio (SMR) refers to the number of deaths observed in a particular population or cohort compared to expected number of deaths in the general population (Last, 2001)).

A further follow-up mortality study of men and women from 1965 to 1991 revealed that many occupational hazards remain undetected with little documented evidence of risks (Aronson et al., 1999). An elevated breast cancer risk was found among female metal fitters and assemblers (less than or equal to 64 years old) ((Relative Risk (RR) =

2.15, CI 95% (1.12-4.15)); secretaries and stenographers (all ages) (RR= 1.83 CI 95% (1.21-2.75); and dressmakers and seamstresses (less than or equal to 64 years old) (RR= 2.02 CI 95% (1.19-3.42).

Such studies share certain limitations that restricted their ability to detect possible associations. These limitations include basing risks on "current" occupation rather than the lifetime occupational history; using occupation as a surrogate for exposure, so that misclassification of exposed and unexposed is likely since the same occupational category can be the aggregate of the two groups; not knowing intensity and duration of exposure; not knowing possible confounding factors, such as smoking history; and using mortality rather than morbidity data, which is more revealing of incidences of cancers such as breast. The studies were the initial efforts to launch a national surveillance system to detect possible occupational risks and generate hypotheses for further study. There is still, however, no national or provincial occupational surveillance system to monitor cancer morbidity or mortality that incorporates occupational histories.

## 5.3 Occupation and breast cancer risks: an epidemiological review

Occupational risk factors and female breast cancer were first reviewed in Canada following a request from the Ontario Occupational Disease Panel (ODP) (1997). The ODP was a quasi-governmental body established by statute to advise the Ontario Workers Compensation Board on the work-relatedness of particular diseases. The ODP had previously focused primarily on the elevated cancer risks of the hard rock miners in northern Ontario, firefighters, and metalworking fluid exposed autoworkers. Each of these groups of essentially industrial workers was overwhelmingly male. As part of the Occupational Disease Panel's effort to provide more gender balance and also to examine the possible cancer risks of a broader range of work environments, the breast cancer review was commissioned[1].

The Panel recognised that women were entering the workforce in greater numbers (Statistics Canada, 1990) and that the continuing increases in diagnosed and recorded breast cancers might be associated with their exposures in the workplace. The review looked at 115 studies comprised of 92 cohort studies, four case-control studies and 19 studies that utilised administrative data in twenty published scientific journals (Occupational Disease Panel, 1997). There was sparse information on lifetime occupational histories, and almost no specific information regarding exposures and non-occupational risk factors. The studies generally had low statistical power with a median number of 19 breast cancer cases. The mean was 64 cases (Labreche and Goldberg, 1997, p.146). Only 10 studies examined specific levels and duration of exposure. This limitation can attenuate the risk and mask possible associations (Dewar et al., 1991). The reviewers noted that the health care workers were a group with potential risk due to their exposure to a wide variety of hazards, including anaesthetic gases and solvents (Labreche and Goldberg, 1997, p.149).

The reviewers also considered there was limited evidence to postulate a possible association between breast cancer and employment in the pharmaceutical and chemical industries and employment as beauticians. Others suggested extremely low frequency electromagnetic fields (EMF) might be linked to breast cancer risk due to

[1] The Occupational Disease Panel was abolished in 1997 as part of alterations to the Compensation Act by the newly elected Progressive Conservative government after complaints from the Ontario Mining Industry about ODP reports documenting the elevated lung cancer risk among hardrock miners (Stang, 1997).

the ability of EMFs to disrupt pineal melatonin, thereby allowing oestrogen and prolactin to increase (Stevens, 1987). Melatonin will stop the proliferation of breast cancer cells in a culture, but when exposed to EMFs the proliferation process begins anew (Blackman et al., 2001). The difficulty of differentiating levels of exposure to electromagnetic fields might hide a possible association to breast cancer (Goldberg and Lebreche, 1997).

Breast cancer incidence findings among solvent exposed workers were not consistent. For example, women employed in dry cleaning and aircraft industries did not show an elevated risk. Some evidence existed, however, of elevated breast cancer risk in administrative studies that examined breast cancer risk among women possibly exposed to solvents while employed in printing, publishing, and mechanics (p.152).

> ...Studies of organic solvents may, however, be beset with health related differential selection into and out of work arising from pervasive early onset toxic effects (dermatitis, hepatic and renal toxicity, central nervous system depression, peripheral neuropathy). Thus there will be a selection bias if susceptible or sensitive workers are at higher risk of developing breast cancer and are more likely to leave exposed jobs early so they are less highly exposed than insensitive people (Goldberg and Lebreche, 1997, p. 153).

Goldberg and Lebreche and recommended population-based case-control studies as a more informative type of study, especially where individual interviews could be conducted to gather lifetime histories, including occupation, and an expert panel could assign likely chemical and physical exposures, which would be factored into the statistical model. As will be discussed in Chapter 8, the Windsor *Lifetime Occupational History Record (LOHR)* was influenced by these recommendations. The *LOHR* questionnaire incorporated a number of these recommendations into its design. It is not, however, until the latest breast cancer study, the *Lifetime Occupational and Environmental History Record (LOEHR)* (*see Chapter 8*) that an expert panel to assign likelihood and intensity of exposures was added to the case control study protocol in Windsor.

Also, epidemiology that examines the possible role of occupational exposures in hormonally–related cancers such as breast cancer might generate false negative associations unless these studies control for the impact of early exposures to hormonally mediated synthetic chemicals. Biological markers are needed to deepen our understanding of the adverse impact of hormonally mediated substances.
It may be that epidemiology has missed the main questions:

> ...Could we be trying to correlate exposure and effect at the wrong time? If it is prenatal or early life stage exposure that is critical to disease susceptibility, why are we measuring environmental chemicals in people once they have developed breast cancer? The critical exposure window may have been much earlier (Birnbaum and Fenton, 2003, p.393).

### 5.3.1 British Columbia cancer registry examines breast cancer and occupation

A population-based case-control breast cancer study utilised the British Columbia Cancer Registry (Band et al., 2000). The study is of particular importance because it is most similar to the Windsor *Lifetime Occupational History Record (LOHR). LOHR* attempted to control for many of the same risk factors including a detailed occupational history.

Beginning in 1982, the provincial government in British Columbia had supported, through the Workers Compensation Board (WCB), research into examining possible occupational cancer risks including carcinogens in the work environment (p.284).

This is unique in the Canadian experience since no other provincial cancer registry had undertaken such an initiative. Perhaps it was possible in British Columbia because British Columbian labour, women, and environmental movements are very influential in the area of occupational and environmental health. Action by the populations at risk is a key ingredient in encouraging cancer agencies to examine such public health issues. Previous British Columbian studies focused essentially on male workers employed in pulp and paper mills, and airline pilots (Band et al., 1996; Band et al., 1997; Band et al., 2001); a population-based case-control study of prostate cancer and occupational risks (Band et al., 1999); and a study of the impact of smoking and occupation among 15,463 male British Columbians (Band et al., 1999).

The Band et al. breast cancer study (2000) sought to investigate occupations while controlling for the known or suspected hormonal risk factors. Women were stratified by pre-and post-menopausal status, and combined as one group. Cases were composed of women 75 years old or younger, who were Canadian citizens residing in British Columbia, spoke English and had no previous history of breast cancer. These women were diagnosed between June 1, 1988 and June 30, 1989. Community controls could not have had a breast cancer diagnosis before June 30, 1989. Cases and controls were given a self-administered questionnaire to record lifetime occupational histories that included duration of job. They were also queried about ethnic origin, educational level, age of menarche, pregnancies, age at first pregnancy, breast-feeding, oral contraceptive use, hormonal replacement therapy, family history of breast cancer, history of breast biopsy, current body mass index, current weight, and alcohol and tobacco consumption. Menopausal status was determined as follows: premenopausal women were defined as those less than 50 years old and either who were still menstruating or had had a hysterectomy. Postmenopausal women were those that had experienced natural menopause or had a bilateral oophorectomy, i.e. removal of one or both ovaries, or had a prior hysterectomy with ovarian conservation (p.286). Canadian Standard Occupational Classification (SOC) codes and the Canadian Standard Industrial Codes (SIC) were employed by an expert coder to assign codes for each occupation and industry.

Among premenopausal women the researchers noted the "very high and significantly increased" odds ratios for breast cancer in "electronic data processing equipment operators, barbers and hairdressers, material processing occupations, and food and transportation industries" (p. 309). Possible aetiologic associations with electromagnetic fields (EMF) and diesel exhaust and pollutants like polycyclic aromatic hydrocarbons (PAHs) were also flagged. A number of administrative occupations had higher than expected risk. The elevation among "white collar" women employed in administrative and clerical positions is a common finding in breast cancer and occupation studies (Goldberg and Lebreche, 1996).

Specific exposures were not identified among this group because occupation was used as a surrogate for particular exposures. This lack of exposure information can conceal possible associations just as the lack of information about lifestyle factors, such as reproductive factors; activity levels and socioeconomic status can influence outcomes.

Due to the small numbers in the British Columbian cohort, pre and postmenopausal women were combined. Their occupational histories were examined while controlling for other possible variables and confounders.

As in the *LOHR* findings (*see chapter 8*), British Columbian nurses were identified as having elevated breast cancer risk. Nurses, Registered, Graduate and Nurses–in-Training who *ever* worked in the profession had an OR= 1.48 90% CI (1.03-2.13); if nursing was listed as their *usual* occupation, the OR=1.54 90% CI (1.05-2.28). In the nursing and medicine categories the confidence intervals were much closer reflecting the greater statistical power of the categories. It would be interesting to stratify the duration of employment into the number of years of work to determine whether there might be an increased risk with years at work such as was found in the nurses' study that examined shift work (Schernhammer et al., 2001). It would also be important to control for exposures that occurred prenatally and during their younger years.

Band et al (2000) study also reported that there was an elevated risk of breast cancer in association with farming, publishing and printing, and motor vehicle repair industries:

> ... Farmers are exposed to pesticides, compounds suspected of being associated with an increased breast cancer risk, whereas the other occupations and industries entail exposure to various solvents and to carcinogenic substances such as aromatic amines in the printing and polycyclic aromatic hydrocarbons in the motor vehicle repair industries (p.309).

Excess breast cancer risk might therefore be related to occupations and industries where pesticides, low-frequency electromagnetic fields, or organic solvent exposure occur (Band et al 2000).

This research provides interesting parallels to the Windsor case studies. It contains many of the same epidemiological strengths and weaknesses. It gathered lifetime occupational histories. It controlled for a wide array of known and suspected breast cancer risk factors. It was a population-based case-control study that used incident cases rather than relying on mortality data. Mortality studies for breast cancer would likely have underestimated the true extent of the disease. The study had sufficient power to detect elevated risks (Checkoway et al., 1989). However, it used *Occupation and Industry* as surrogates for exposure with likely misclassification of exposed and unexposed within the same occupational and industrial categories, which may cause an attenuation of risk. It did not control for confounders such as shift work or for maternal or early childhood exposures. The cohort was not analysed by geographic location within British Columbia and small numbers of cases limited the statistical power. Overall, however, it represents one of the important studies in breast cancer and occupation epidemiology. The use of a provincial cancer registry to explore possible occupational risk factors is unique to the Canadian experience.

As discussed in Chapter 9, on a community level, the Windsor, Ontario two-year breast cancer population-based case-control study, *Lifetime Occupational History Record (LOHR),* gathered analogous information, while sharing many of the Band limitations. Like Band and colleagues, the Windsor study was not able to ascertain the specific exposures but relied on occupation as a surrogate for exposure. It is likely that the Windsor study has exposed and unexposed within the same group, such as farming women or nurses, which may lead to misclassification bias and an underestimation of the actual risk.

This research was also, in part, generated by the activities of the populations at risk. The trade unions in British Columbia have a history of strong health and safety activity and have lobbied for research that examines possible associations between the workplace and disease. The success of the British Columbian unions in securing such research supports the contention of the dissertation that such political action is integral to ensuring that this kind of research be conducted and for the recognition of potential occupational risks.

Workers Compensation Board funding in British Columbia in 2001 included monies to study ovarian cancer and possible occupational risk factors; a case-control study to examine pesticides and their possible endocrine disrupting properties and their possible association with prostate cancer; and a study to examine pentachlorophenol and tetrachlorophenol as occupational carcinogens (Work Safe, 2001).

### 5.3.2 Other epidemiological studies regarding breast cancer and occupation

A number of other studies will be explored in the remainder of this chapter because they help inform the CROME and LOHR case studies in the dissertation. This literature also influenced the development of the LOHR and LOEHR questionnaire. In *Appendix F and G (see* Table 5.2 and Table 5.3), there are Tables that list studies, which examine possible associations between breast cancer and particular exposures, as well as, risks found in specific white-collar work environments. Calle et al. (1992) and Coogan et al. (1996) found a statistically significant breast cancer risk among white-collar workers. Calle and colleagues found a Relative Risk (RR) = 1.14 95% CI (1.01-1.31) for administrative personnel and RR = 1.93 95% CI (1.03-3.62) but not for nurses, librarians and teachers. This United States mortality study controlled for some breast cancer confounders. Coogan et al. (1992) found a statistically significant Odds Ratio = 1.15 95% CI (1.06-1.24) while also controlling for a limited number of other risk factors.

Lack of physical activity in "white collar" occupations may be worth investigating as a potential risk given that physical activity has been shown to provide a protective factor possibly associated with changes in menstrual characteristics, body mass index, and even the immune system (Moradi, et al., 2000; Gammon et al., 1998; Coogan et al., 1997; Pukkala, 1995, p.65). Other possible risks identified included second hand smoke, cleaning solvents, flame-retardants, indoor pesticide use, electromagnetic fields; better diagnosis might also have influenced the results (Spengler, 2000; Dosemeci and Blair, 1994; Coogan et al., 1996).

Shift work studies (Davis et al., 2001; Schernhammer et al., 2001) have found statistically significant increases OR = 1.6 95% CI (1.0-2.5) and RR = 1.36 95% CI (1.04-1.78) respectively. These elevations occurred among women who worked graveyard shifts over long periods. It is hypothesised that melatonin is disrupted, thereby heightening oestrogen production through the disruption of the circadian rhythms (Stevens and Rea, 2001).

Elevated breast cancer risk among organic solvent and pesticide-exposed women would be anticipated by the Epstein analysis regarding the adverse impact of certain synthetic chemicals and has been shown to be a possible risk in later studies (Hansen, 1999).

A 24 U.S. state mortality study to ascertain possible occupational links to breast cancer (Cantor et al., 1995) used a job exposure matrix, while controlling for age and socioeconomic status. White and black women were analysed separately. White and black women with exposure to styrene, several organic solvents, acid mist and metals and metal oxides were identified as having a statistically significant elevated breast cancer risk. Another study noted a twofold excess of breast cancer among women employed as metal plater and coaters (Pollen and Gustavsson, 1999) where exposures to heavy metals and organic solvents were involved.

Polycyclic aromatic hydrocarbons (PAH), benzene, and styrene have been linked to breast cancer (Petralia et al., 1999; Mikoczy et al., 1994; Chiazze et al., 1980).

It is biologically plausible and probable that organic solvents or their metabolites are genotoxic and can adversely impact breast tissue and initiate the pathogenesis of breast cancer (Labreche and Goldberg, 1997). Numerous organic solvents have been detected in breast milk. The majority of breast tumours reside in the ductular system where solvents are found in breast milk. Many of these substances have produced mammary tumours in animal studies. It would be important to determine whether the breast fed children of highly solvent exposed mothers had elevated disease risks including breast cancer later in life.

It is important to note the lack of consistent findings (Goldberg and Lebreche, 1997). Aronson and Howe (1994) in their examination of data from Statistics Canada national labour survey found a statistically significant twofold excess of breast cancer mortality among women employed in the print and publishing industry, while other researchers (Bulbulyan et al., 1999) found below the expected risks for women employed in the printing industry where solvent exposures were identified. Negative studies, however, while informing our knowledge should not be used to discount the possible association since there are many limitations to epidemiological investigations that, due to various reasons, can generate false findings (Watterson and Watterson, 2003a).

The deleterious effect of tobacco smoke exposure may also be important in understanding breast cancer risk (Johnson and Mao, 2000; Morabia et al., 2000; Band et al., 2002). Band and colleagues note that PAHs found in tobacco smoke are not only carcinogenic but also disrupt the endocrine system by transforming oestrogens into genotoxic oestrogen metabolites (p.1048). This accounting for the possible hormonal disruption among younger women represents important insights for our understanding of the aetiology of breast cancer.

In terms of the precautionary principle, there should be a greater societal effort to reduce the potential exposure to these substances and greater effort to consult with workers regarding ways of curtailing their contact with such hazards (Kreibel et al., 2001).

### 5.3.3 Farming Studies and Breast Cancer

The development of our understanding regarding breast cancer risk and farming is an important public health concern given the possible prevalence of pesticide exposure and disease factors in rural communities. It also has direct implications for the dissertation case studies (*see Chapters 8 and 9*) and will be explored, therefore, in some detail. Over 160 chemicals, including a number of organochlorines and related pesticides, have induced carcinogenesis in the breast glands of animals (Wolf et al., 1996). Female farmers and labourers have not been, however, as extensively studied as their male counterparts (Zahm et al., 1997). Many of these substances are particularly persistent and bioaccumulate in the adipose tissue. Certain case-control studies (Falck et al., 1992; Wolff et al., 1993; Krieger et al., 1994; Dewailly et al., 1994) compared the levels of DDE, the primary metabolite of DDT, and PCB residues of women with breast cancer. These studies generally found an elevated risk of breast cancer among women with higher levels of DDE in comparison to controls. More recent studies, however, have not supported an association (Snedeker, 2001). A Canadian study did, however, find an increased breast cancer risk among women with elevated Polychlorinated Biphenyls (PCB) levels in their adipose breast tissue (Aronson et al., 2000).

The populations with the highest levels of chlorinated pesticide concentrations, outside of the pesticide industry, have been identified in agricultural areas (Alavanja et al., 1996; Smith, 1991; IARC, 1991). Over 1500 pesticides are available worldwide. Some of these substances are known human carcinogens, possible human carcinogens and animal carcinogens, while others are without toxicological data (Watterson, 1995b). A large number of these substances are also hormonally active and, therefore, possibly related to breast cancer (Brophy, 2004; Garcia, 2003; Janssens et al., 2001; Allen et al., 1997). The herbicide, atrazine, for example, is one of the most widely used agricultural pesticides (Acquavella et al., 2002; Blair et al., 2001). The triazine pesticides are considered endocrine disruptors and suspected human carcinogens (Dich et al., 1997). Almost sixty percent of the American population has some daily exposure, mostly through food residues. In animal studies, in utero atrazine exposure delays breast gland development and "may also confer an extended window of sensitivity to potential carcinogens after sexual maturity" (Birbaum and Fenton, 2003, p.393).

Pesticides can be both carcinogenic and hormonally disruptive (Ontario College of Family Physicians, 2004). Pesticides are, therefore, important to the study of breast cancer risk and to the dissertation. Traditional toxicology and epidemiology are being challenged by a new synthesis leading to new hypotheses, particularly between prenatal exposures to agricultural chemicals and predisposition to cancer (Colborn et al., 1999). Prenatal and early life exposures may increase the susceptibility to cancer. Epidemiological studies should attempt to control for such risk factors. A further measure might include the identification of biomarkers that would connect the questionnaire data and exposures with biological polymorphisms. New multidisciplinary teams of researchers in collaboration with the populations at risk are needed to address such complex research problems (Susser and Susser, 1996a, 1996b).

Farming populations have an elevated risk of cancers of the brain, breast, leukaemia, lip, lymphoma, multiple myeloma, prostate, skin, soft tissue sarcoma, and stomach (Wood et al., 2002: Blair et al., 1987; Blair and Zahm, 1991; Davis et al., 1992). Among women engaged in farming, excess risks of non-Hodgkin's lymphoma, leukaemia, multiple myeloma, soft tissue sarcoma, and cancers of the breast, ovary, lung, bladder, cervix and sinonasal cavities have been observed (McDuffie et al., 1994; McDuffie, 1994). Particular studies have identified an association " between occupational exposure to phenoxyacetic acid herbicides, specifically 2,4-D and non-Hodgkin's lymphoma" (p. 135). Researchers, however, have generally viewed women in agricultural regions as not directly occupationally engaged in farming and they, therefore, have generally either not examined their exposures or have excluded them due to small numbers (McDuffie, 1994).

The identified excess cancer burden occurs within a population that has generally been viewed as "healthier" given its lower total mortality, lower rates of heart disease and several cancers including lung, oesophagus, colon, and bladder. Their reported lower rates of smoking, greater levels of physical activity and possibly healthier diet have suggested that the aetiologic role of the specific excess cancers may arise from exposures to pesticides (insecticides, herbicides, fumigants, fungicides), solvents, engine exhaust fumes, metals, welding fumes, grain dust, viruses and microbes (Coble et al., 2002; Davis et al., 1992; McDuffie, 1994; Wigle et al., 1990).

Large cohort studies have examined possible associations between breast cancer and farming (Coogan et al., 1996; Cantor et al., 1995; Morton, 1995). None of these studies found an elevated risk among women who farmed.

A recent case-control study was able to control for both traditional breast cancer risk factors as well as exposures among women engaged in farming (Duell et al., 2000; Duell et al., 2001). The findings were complex regarding the association between farming and breast cancer risk in women with and without pesticide exposure. The odds ratio was below that expected for farming women when analysed without controlling for pesticide exposure or the use of protective equipment. However, women who reported being present in the fields during or shortly after pesticide application had an 80% increased risk of developing breast cancer (OR 1.8, 95% CI 1.1 – 2.8). Among those who reported using pesticides without protective clothing, there was a two fold excess breast cancer risk (OR = 2.0, 95% CI 1.0 – 4.3); while women with protective clothing had a lower than expected risk (OR = 0.8, 95% CI 0.4 –1.8). The researchers concluded that while farming may not present an elevated risk per se, farming women exposed to pesticides might have an elevated breast cancer risk (p. 329). This reaffirms the weakness in using occupation as a surrogate for exposure since misclassification of exposure occurs when subjects with less exposure are aggregated with the more highly exposed. Such non-differential misclassification decreases the probability of detecting associations and tends to underestimate the actual risks (Blair et al., 1993; Checkoway et al., 1989). It would also have been interesting to know the ages at which these women first came into regular contact with pesticides, as there is evidence that this can possibly influence breast cancer risk.

The Band et al. (2000) study stratified women by pre-and post-menopausal status as well as by both combined. Among the combined pre- and post-menopausal group, there was a three fold elevated breast cancer risk among women ever employed in fruit and other vegetable farming (OR = 3.11, 90% CI 1.24 – 7.81); there was a seven fold elevated breast cancer risk among women ever-employed in other vegetable farming (OR = 7.33, 90% CI 1.16 – 46.2).

The findings regarding breast cancer among women who ever farmed from the Windsor case control study will be examined in Chapters 8 and 9. The results corroborate the British Columbia study regarding the elevated risks among women employed in agriculture, but also share some of the limitations regarding not being able to differentiate between the exposed and unexposed within the same occupation.

### 5.3.4 Health Care Studies and Breast Cancer

Nurses and other health care workers and their possible breast cancer risk were examined in administrative and cohort studies and case-controls studies (*See Appendix H and I: Table 5.4 and 5.5*). This has relevance to the findings that will be reported in the *LOHR* case study. Between 1990 and 2002 eleven administrative and cohort studies were published. Between 1995 and 2002 six case-control studies were published. These studies examined a wide array of health care professions, including nurses, laboratory technicians, physicians, dental hygienists, pharmacists, radiology technicians, physiotherapists and science technicians to name of few. For the purposes of this review the focus is on the nursing and laboratory technicians epidemiological studies.

Of the eleven administrative and cohort studies eight studies found a positive elevation and in three studies (all cohort) an elevated risk among nurses was not established. Among the case-control studies two found a positive association and four did not (*Table 5.4*). Among the registry based studies few controlled for possible breast cancer risk factors. Rix and Lange (1996), for example, did control for socio-economic status. Breast cancer risk for an array of health care workers has been assessed using the Danish cancer registry and other economically active employed workers as the comparison group to control for the "healthy worker effect". Studies have examined breast cancer risk among registered hospital nurses (Band et al., 2000; Rix and Lynge, 1996; Gunnarsdottir and Rafnsson, 1995; King et al., 1994). Elevated risk is generally noted but these studies often shared methodological limitations due to the lack of controls over known or suspected breast cancer risks.

Seven studies that examined a possible relationship between working as a laboratory technician and breast cancer were reviewed since this group often operates in the same or similar work environment as nurses. Of these, six out of seven found an elevated risk associated with the occupation of laboratory technician (See Appendix I: *Table 5.5*).

### 5.3.5 Strengths and limitations of different epidemiological studies

Administrative studies strongly support a positive relationship between nursing and breast cancer risk, while cohort and case-control studies do not provide strong support for this hypothesis. A number of reasons may explain this observation. The registry-based studies reviewed observed an elevated breast cancer risk for nurses. The strength of these studies is in their statistical power. Mortality studies, however, underestimate the number of cases and thus, underestimate risk, since breast cancer incidence is about three times the rate of death and breast cancer patients have relatively long survival rates. Mortality studies also are unable to control for important variables such as age of menarche and menopause, parity, socioeconomic status, and family history of breast cancer. Thus, risk estimates may be overestimated. Furthermore, most of these studies assign occupation based on death certificate data, which is recognised to sometimes result in misclassification of occupation. Agreement between usual occupation recorded on death certificates and other sources such as next-of-kin interviews, varies from 35-85% (Rubin et al., 1993).

Cohort studies are more likely to be accurate in occupational assignment than registry-based studies, but are much more limited in statistical power. In addition, controlling for potential confounders was limited; Calle and colleagues (1998) study did so, while Gunnarsdottir et al. (1997) controlled for only family history, marital status and null parity.

Case-control studies have a number of strengths. Detailed occupational histories were obtained by questionnaire or interview with living subjects, increasing the reliability of exposure assignment. These studies assess incidence rates rather than mortality rates, which give a more realistic picture of disease burden and greater relevance to aetiology. Adjustment was also made for most known potential confounders. The most robust study reviewed was that conducted by Band et al. (2000) because it had reasonable statistical power, controlled for many potential confounders and was the only study to examine pre-menopausal and post-menopausal cancers separately. Post-menopausal cancers were observed to have higher risk estimates for nurses, while pre-menopausal cancers did not. Collapsing of pre- and post-menopausal breast cancers that are likely to have widely different aetiologies into one group represents a major limitation to most existing research (Weiderpass et al., 1999). No other case-control studies assessed these two demographic groups individually.

All these studies shared a number of important limitations. None controlled for significant exposures such as: shift work (Schernhammer et al., 2001, Davis et al., 2001), ionising radiation, nor other specific chemical exposures. Endocrine disruptors, as a specific focus of study, were not identified in any of the studies, nor were prenatal or parental exposures. It is reasonable to assume that work exposures among nurses differ markedly by department worked in or by specialty (Habel et al., 1996). However, all studies with the exception of Gunnarsdottir et al., (1995), failed to address this. All nurses were grouped into one occupational category assuming that this broad title would be an appropriate surrogate for their exposures. Collapsing all nurses into one group, as though they have like exposures, will produce reduced risk estimates, despite the possibility of a certain subgroup having an elevated risk. This is a major limitation. The case-control study by Gunnarsdotir et al. (1997) is noteworthy as an elevated breast cancer risk was revealed only when the study population was separated into groups according to their specialty (*Table 5.4*). Heterogeneity within occupations must be assessed in conducting future studies about breast cancer and occupation/environment.

Hormonally active chemicals used in medicine and nursing have been suggested to be linked to breast cancer. Epidemiological studies have yet to control for these particular studies. These include: nonylphenol (used in detergents & plastics), bisphenol A (used in polycarbonate plastics), butyl benzyl phthalate and polychlorinated biphenyls (PCBs) (Aschengrau et al., 1998). These substances have been shown to have oestrogenic activity in human breast cell bioassays (Soto et al., 1992). Furthermore, none of the existing studies assess timing of exposure (such as prenatal, pubertal, prior to first live birth, and pregnancy). Gardner et al. (2002) suggest that, "Exposures in-utero, infancy, childhood and adolescence may very well be important missing links to the mystery of this multifactoral disease" (p. 306).

Even with the specific limitations of the various epidemiological study designs there is sufficient evidence to enact precautionary measures to prevent carcinogenic and xenoestrogenic exposures among nurses and laboratory technicians. There is also sufficient evidence generated by occupational breast cancer research to include occupation as a potential risk factor. While scientific certainty may be decades in the future, our current knowledge allows us to make informed inference from current investigations to justify reducing and even eliminating exposure to certain pesticides, organic solvents, polycyclic aromatic hydrocarbons (PAHs) and certain components of plastics. Shift work and its potentially deleterious effects also require important consideration. Finally, the European Union's strategy to minimise exposure to endocrine disrupting substances follows a socially responsible course even as our understanding of their adverse impact on health continues to grow. The European Union's decision comes in the awake of campaigns and political pressure mounted by women's health organisations, trade unions, environmental organisations and other public health groups (WEN, 2003).

## 5.4 Summary

While Canadian studies exist that examine occupational cancer and it causation, this area of cancer research is generally marginalised, ignored or downplayed by the dominant cancer agencies and provincial compensation boards.

In some Canadian jurisdictions, such as the province of British Columbia, trade unionists, environmentalists, and women's health movement advocates have challenged the lack of attention given to exogenous occupational and environmental exposures. Their efforts have triggered research into occupational risk factors for cancer. Of particular relevance to the case studies is the research into breast cancer risk and occupation conducted through the British Columbian cancer registry.

The British Columbian study identified elevated breast cancer among a number of occupations, including farming and nursing. The research employed a method that captured a host of information about lifetime histories. The Windsor case studies similarly attempt to situate cancer risk within a context that can account for numerous risk factors both endogenous and exogenous.

Epidemiology has often not proved sufficiently sensitive to track the impact of hormonally mediated chemicals that act as genotoxins and which increase susceptibility to breast carcinogenesis. Toxicology's assumptions regarding the impact of dose coupled with the timing of exposure is challenged, particularly in animal bioassays of endocrine disrupting substances. The epidemiological evidence of breast cancer and work-related exposure is sparse. Animal bioassays have identified over 200 chemical substances that trigger breast carcinogenesis but many such agents exist in high concentrations in many workplaces, and their influences on breast cancer incidences among exposed workers remain largely unstudied. Cohort and case control studies to date indicate that certain white-collar professionals such as nurses and teachers potentially bear an elevated risk, although the specific aetiologic factors are still unknown. Increasing evidence is emerging about the possible risk of breast cancer posed by pesticide exposure among farming women. The epidemiological evidence requires more precise exposure assessment methodology to accurately categorise exposed versus unexposed people within the same occupational group. The evidence, however, is sufficient to warrant precautionary measures, particularly for younger women who might have contact with pesticides.

While laboratory-based research can identify isolated carcinogenic agents, a population-based study, such as the research described herein, has the advantage of being able to evaluate interactive and cumulative effects in a real world environment. Such information can advance our understanding of cancer aetiology in a practical manner and may ultimately facilitate the formulation of public health interventions.

Women's organisations are challenging the dichotomy between science, which tends to shun the advocacy role, and political action, which is often suspected of distorting science, by demanding their direct participation in knowledge production and decision-making.

The next chapter will contextually situate the dissertation's two case studies by providing health data and indicators of the health risks of the population living in Windsor, Ontario, Canada in the county of Essex. Windsor was the first community to collect the occupational histories of cancer patients at its cancer treatment centre.

# CHAPTER 6: A HEALTH PROFILE OF WINDSOR: THE STATE OF KNOWLEDGE AND THE STATE OF IGNORANCE

## 6.1 Introduction

An assessment of the health profile of Windsor is vital to make sense of what is happening, has happened or what researchers think is happening to the local population in terms of mortality and morbidity. Such an assessment then provides the platform for shaping and guiding the case study interventions.

A brief demographic and geographical snapshot of Windsor opens the chapter as it provides the context to understand the research described herein. The chapter is then divided into four sections moving progressively from provincial health studies that include and compare the health of Windsor's population to smaller more locally generated health studies. The Health Canada studies that examine the health of 17 Canadian communities located in the Great Lakes Basin are analysed insofar as they inform the Windsor picture. Environmental studies that examine the toxic pollutants in this geographic area will also be explored as they add to the understanding of the potential health problems faced by the community. The findings of these environmental studies reinforced the Windsor population's concerns about associations between cancer and exogenous exposures, and influenced the case studies. A detailed analysis is offered of specific Windsor health studies linked to developments within the Occupational Health Clinic for Ontario Workers (OHCOW) and related organisations.

## 6.2 Snapshot of Windsor – Essex County, Ontario Canada

Windsor, in many ways, provides a microcosm of a Canadian industrial community in terms of culture and attitudes towards work and health. Canada is an industrially developed and agriculturally productive nation. Windsor is one of Canada's most industrialised communities with an active trade union movement and therefore, an ideal setting to test the hypothesis of whether the documentation of occupational exposures might reveal possible associations that could ultimately be used to reduce the risk of cancer. The knowledge gained through studies in Windsor may be generaliseable in some respects to the rest of the country potentially having broad policy implications for cancer research and prevention.

The Windsor-Essex area has both an urban and rural population of approximately 350,000 within a small land area in the Great Lakes Basin on the United States-Canadian border across from the city of Detroit. It is the center of the Canadian auto industry hosting operations of all three major North American automakers as well as over 800 other manufacturers, many of them auto-related. The community is located within a day's road travel to 90% of North America's vehicle assembly plants, giving the Windsor-Detroit corridor the highest volume of international trade in the world (Windsor-Essex County Development Commission, 2003). Windsor-Essex county is a highly unionised community, and is one of the centres for the largest private sector union in Canada, the Canadian Auto Workers (CAW). The CAW has over 30,000 members in the area.

In Windsor of the over 157, 000 people employed, forty-six per cent (N = 71,600) are women. In the health care sector eighty-one per cent of the employees are women. In primary industry, which includes agriculture, twenty-seven per cent of the workers (N = 655) are women. In manufacturing of the 24,390 people employed, women constitute thirty per cent (N = 7,375) of the workers (Windsor and Essex County Development Commission, 2001).

Agriculture is also a significant economic activity with over 325,000 acres producing as much as any one of the Canadian Atlantic Provinces (Windsor-Essex County Development Commission, 2003). Windsor-Essex County has field crops, orchards, vineyards and the largest greenhouse (glasshouse) industry in North America covering over 650 acres. It is an area in which a considerable variety and volume of pesticides have been employed throughout the years.

## 6.3 Health Canada Data: Community Health Profile of Windsor, Ontario, Canada: Anatomy of a Great Lakes Area of Concern

The theoretical and practical deficiencies of assessing cancer causality, as outlined in previous chapters, remain unaddressed in Canadian health studies and hence it is necessary here to identify strengths and limitations with data for the empirical section of the thesis. Working populations are not identified or their exposures registered. Some studies, however, while limited, can be used to explore possible relationships between exogenous exposures and cancer. One set of reports stands out as being particularly relevant to the dissertation because it provides morbidity and mortality data where the health outcomes could be related to toxic exposures. This study provides the most significant health assessment of all the previous health studies of Windsor because it works with a large data set composed of morbidity and mortality data and therefore provides adequate statistical power. It is also premised on the possible environmental impact on health and therefore, examines diseases from the perspective of possible exogenous aetiology.

Health Canada's Great Lakes Health Effects Program (Health Canada, 1998) produced reports examining the morbidity and mortality of 17 Ontario communities during the period of 1986–1992 with identified Remedial Action Plans (Environment Canada, 1999). The Detroit River Area, which refers to Windsor-Essex County, was one of the Areas of Concern that examined the health of the population in terms of specific health outcomes that may arise due to environmental exposures (Environment Canada, 1998).

Health Canada chose about 70 categories of health end points (International Classification of Diseases, 1992) from which data would be available. It based its selection of health outcomes on the scientific literature that linked possible associations with exposures to contaminants in the Great Lakes Basin with particular emphasis on occupational and environmental agents (Gilbertson and Brophy, 2001, p. 829). The age-adjusted mortality and morbidity rates were compared with the hospitalisation rates for the rest of Ontario and ratios were calculated comparing the local rates with the provincial rates. Among the 17 Areas of Concern, Windsor was the only location that had a cancer incidence rate for the aggregated age groups in either males or females that was statistically significantly elevated. In the six-year time period of 1986 to 1992 there were 4,275 cases of male cancer and 3,941 female cancers in the Windsor population. The incidence rate for men for the aggregated age groups was 7% above the rate of the rest of Ontario. The female incidence rate for "all cancers" was not statistically significant.

However, there were elevated incidence rates for males and females, aged 45-74; the rates were 10% and 5% higher, respectively, than the provincial rate. There were elevated rates of morbidity and mortality from cancer of the digestive organs, respiratory tract, genitourinary organs and the lymphatic and haematopoietic tissues.

### 6.3.1 Health Canada Data: Limitation of the study's data

The Health Canada reports did not attempt to establish a clear causal relationship between the particular diseases and specific exposures. There were methodological limitations, which were examined in the review of the Windsor data (Gilbertson and Brophy, 2001, p 839). The data points were based on hospitalisation records. It is possible that the figures from the different communities were skewed by factors such as physician availability or differing practices regarding hospital referrals. There were a number of health endpoints related to pollution that were not included. Brain cancers and other more subtle health effects, such as those derived from the endocrine disruptor hypothesis regarding neurologic and immunologic functioning, were missing. Health Canada did not include detailed consideration of either demographic and socioeconomic risk factors or such important confounders as smoking history, alcohol use, and family history of disease. The reports were also weakened by the inability to control for possible occupational risk factors, and therefore, could not adequately differentiate possible higher risk working populations.

Moreover, the study methodology was not able to detect epidemics that are specific to certain sub-populations within the Areas of Concern. Windsor and Sarnia, for example, have had some of the highest rates of asbestos-related disease (Keith and

Brophy, 2004; Mittelstaedt, 2004; Firth et al., 1997, 40-48; Brophy and Parent, 1999; Smith, 2000, p. 85). Asbestosis was not separated from pneumoconiosis and other lung disease caused by external agents (ICD-9: 500-508), and therefore, was diluted in the more general category. Similarly, mesothelioma was not identified independent of respiratory and intrathoracic organs cancer (ICD-9: 160-165). There was likely a loss of some of the sensitivity of the analysis through the aggregation of data and the masking of specific illnesses within larger categories of diseases. Such limitations are the factors that the subsequent case studies are meant, in part, to address.

### 6.3.2 Health Canada Data: The Federal Government suppresses the studies

Relevant to the argument of the dissertation is the institutional reticence of the federal government to share the Windsor findings with the public. The Health Canada studies were not released until a year after their printing. These reports were finally made public after pressure was exerted by a grassroots Cancer Prevention Coalition in Windsor in tandem with the investigative activities of a local Canadian Broadcasting Corporation (CBC) television reporter (Gilbertson and Brophy, 2001; p.828).

These events demonstrate the reluctance, and indeed, the fears of governmental and scientific experts to openly share what is viewed as negative findings with the public.

> ...what's upsetting is the slowness by which we react to our growing knowledge of carcinogens. Not that long ago we thought nothing of smoking in the workplace. Some still see nothing wrong with it.

> Even if we have a good idea that something can be harmful to our bodies, we demand more proof. We are reluctant to distribute the results of tests and experiments (Sarnia Observer, 1998).

This denial of access to health information and possible associated risks is reminiscent of the experience of Ontario industrial workers with regards to studies that found elevated occupational cancer risk (Keith and Brophy, 2004; Brophy and Parent, 1999; Firth et al., 1997. pp. 31-39). The reluctance of governmental officials to share this information has been attributed to:

> ...concern of the costs of cleanup, the reactions of the medical officers of health to the widespread public dissemination of uninterpreted data and statistics and the potential liabilities of governments for exposures of communities to pollutants and for any remedial actions (Gilbertson and Brophy, 2001, p. 828).

Others raise the more systemic barrier to a full disclosure of the prevalence of occupational disease, that is, that corporate control of the production process (Infante, 1995).

### 6.3.3 Using the Health Canada data to compare two industrial communities – Windsor and Hamilton

The Windsor community did not initially understand the importance of the Health Canada hospitalisation data because it was generally uninterpreted data. To examine in more detail the Health Canada findings and methodological approaches with a broader scientific audience and the community at large, a new analysis was prepared, using the same data that compared the health findings in Windsor with another Ontario industrial community, Hamilton (Gilbertson and Brophy, 2001).

While the Hamilton area has a population that is more than twice the size of the Windsor area it shares such common features as similar demographic and socioeconomic measures; the percentage of the population 15 years of age and older; basic education, families and dwellings, as well as average income. These indicators were also similar to the rest of Ontario (p.829).

Windsor had significantly higher rates of mortality among males (8% higher, 613 excess deaths) and among females (5% higher, 366 excess deaths) compared to the rest of Ontario. This increased mortality was especially marked among the 45-74 year age group for both men (14% higher, 496 excess deaths) and women (10% higher, 232 excess deaths). In contrast the mortality rates for men and women in the Hamilton Area of Concern were the same as the rest of Ontario. For males 44 years of age or younger, however, the mortality rate was 10% below the rest of the

**Figure 6.1 Windsor Star Cartoon in response to the Gilbertson and Brophy article**

province and for females under 24 years of age the mortality rate was 14% below the expected. Additional information about cancer incidence in the two communities is found in *Appendix J.*

The Health Canada data lists a number of diseases that are associated with the endocrine system, and the development and functioning of the immune and neurologic systems. These diseases are of importance because they may act as indicators that xenoestrogenic substances could be adversely affecting the health of the Windsor population and consequently, influencing other diseases such as breast cancer incidence. Additional information about hormonally mediated diseases, such as Disorders of the Thyroid Gland, Disorders of other Endocrine Glands, Diseases of the Genitourinary System and Birth Anomalies can be found in *Appendix K.*

Although it was impossible to establish a definitive rationale for the health disparities between the two communities based on the Health Canada data, it is suggestive of a number of possible factors. Hamilton has a more diversified economy with larger numbers of professional workers and therefore, proportionately smaller occupationally exposed population. The occupational exposures are different as are the corresponding working populations. The environmental exposures may not impact the two communities to the same extent. It is only possible to speculate because the data did not control for lifestyle factors, occupation or residential history, which might have allowed for a more in depth analysis. These deficiency further points to the importance of testing the central thesis of the dissertation through the two case studies that critically examine whether controlling for such confounders might reveal causative associations and identify populations at risk.

## 6.4 Transboundry Pollution in the Windsor-Detroit Area

The history of environmental issues, particularly transboundry pollution between the United States and Canada on the Detroit-Windsor axis, provides a rich example of how the health of the population is treated as having lesser importance than the economic interests of the corporate sector. Industrial pollution is tolerated if abatement threatens economic viability. A critical examination of these experiences also provides evidence of how governmental bodies fail to act even in the face of scientific information that should raise alarm.

In 1934 the Canadian federal government lodged a formal complaint with the United States government about sulphur and "smoke" pollution originating in Detroit and crossing the border into Canada. This action arose shortly after farmers in the State of Washington launched an action against the Canadian government due to pollution from the lead and zinc smelter located in Trail, British Columbia (Trail Smelter Arbitration, 1941). The United States demanded compensation and pollution abatement. Sulphur dioxide from Trail, British Columbia was threatening United States forestry and agricultural properties. The International Joint Commission, which arbitrated the dispute, ordered the Canadian government to pay $350,000 (US) in compensation and to control the sulphur dioxide emissions.

The Canadian government argued that the sulphur dioxide pollution levels from Detroit were higher than those from the Trail smelter. The United States government ignored Canada's complaint.

It was not until 1966 that the United States government agreed to allow the International Joint Commission to examine air quality between Windsor and Detroit (Carroll, 1983. p.213). The Commission found that air pollution, primarily from United States sources, was causing harm and agreed to the immediate reduction of sulphur dioxide and that particulates also required urgent action. Both pollutants were in excess of the Ontario level and, in the western part of Windsor, which lies directly downwind from some of the most toxic pollution sources, the level was twice the allowable limits (International Joint Commission, 1972. pp. 93-94).

It is the residents of the more polluted West Windsor, who are generally employed in Windsor's manufacturing industries, potentially constitute a particular population at compounded risk from exogenous causes.

### 6.4.1 International Joint Commission 1992 Report

Of significance to understanding the adverse health outcomes found in the population, which the case studies that follow are designed to address are the environmental studies that examined air pollutants in the Windsor area. Critical synopses of the most important findings are presented. The International Joint Commission (1992) in its report, *Air Quality in the Detroit-Windsor/Port Huron-Sarnia*, states, "information exists...to conclude that there is a significant public health issue which requires the immediate implementation of additional air emission abatement and preventive measures" (p.8). The International Joint Commission had identified 15 carcinogens of concern due to their direct inhalation, which were present in the Detroit-Windsor area. The chemicals benzene, 1,3 butadiene and formaldehyde were of special concern because of the " elevated levels in the ambient air and the strong evidence of their carcinogenicity" (p.8). Arsenic compounds, 1, 4-dichlorobenzene, 1,2-dichloroethane, carbon tetrachloride, perchloroethylene, trichloroethylene, chloroform, benzo(a)pyrene, cadmium, chromium compounds, beryllium and nickel compounds were also identified. Each of these substances is a suspected breast carcinogen (Epstein, 1997, p 275-280; Evans, 2002; Cantor et al, 1995). The United States Environmental Protection Agency (EPA) is currently revising its risk assessment of 1, 3-budadiene based on rodent bioassays in which female mice and rats developed mammary and ovarian tumours. A more severe effect was observed in younger rodent populations (Melnick et al., 1999; National Toxicology Program, 1993). These compounds were cited in the Health Canada report as possibly being associated with the elevated cancer risk within the Windsor population (Gilbertson and Brophy, 2001; Windsor Air Quality, 1994). Unfortunately, air-sampling studies were not conducted in such a way that one could evaluate the air contaminants in particular geographic areas of Windsor-Essex County, thus presenting the misconception that all residents are sustaining similar air-borne exposures when, in fact, certain sections of the community are more polluted than other sections. Furthermore, occupational exposures are virtually ignored.

As the 1992 International Joint Commission report heightened public awareness became more aware of the potential harm environmental toxins might pose to their health, sympathy for the demands of workers for workplace protection increased (Henderson, 2002a, 2002b). Public pressure forced a specific examination of the Windsor air shed (Windsor Air Quality, 1994). The findings of an elevated cancer risk among the Windsor population that was identified in this 1994 report represents part of the tapestry that set the stage for the collection of occupational histories of local cancer patients that will be discussed in the subsequent case studies.

### 6.4.2 Further health studies

A series of health reports provided by local agencies found elevated cancer risks within the population of Windsor, Essex County. These scientific reports confirmed that risks were elevated within the community at large but methodologically were limited by their inability to identify specific occupational groups in which carcinogens might be a factor (Windsor-Essex County District Health Council, 1995). In a provincial cancer report, Essex County men had significantly elevated relative risks in cancer of the lung, bladder, pancreas and kidney, which were cited as having a possible occupational aetiology (Marrett et al., 1995).

#### *6.4.2.1 Breast cancer among sections of the population*

While health studies have generally not found an elevated risk of breast cancer among women in the Windsor area, they did identify elevated risks of disease that indicate that there are exposures or other factors that are influencing the population's health (Abu Zahra, 2002).

The air quality studies documented environmental contaminants identified as breast carcinogens in animal bioassays and could possibly be contributing to a portion of the breast cancer incidences. However, studies of local occupational exposures are needed to help clarify the possible interplay that that potentially exists between such factors as occupation, environment and lifestyle.

In the case of breast cancer, which is the focus of the case studies, it is necessary to investigate whether there are sub-populations (occupational or geographical, for example) within the Windsor area which have an elevated risk while others have a lower risk – thus, statistically cancelling each other out to result in an overall risk that is comparable to the rest of the province. The Windsor breast cancer risk, even if equal to the Ontario average, is still quite high since Ontario and Canada have some of the highest breast cancer risks in the world (Chiarelli et al., 2000, p. 23).

In a study that examined possible connections between environmental pollutants and breast cancer in Windsor, residential mapping demonstrated an elevated risk among women living in the vicinity of local manufacturing facilities (Rizkallah and Mustac, 1995). The authors found a convergence between high breast cancer and lymphoma among women living in an industrial area with "high concentrations of metals" (p.49). The area contained: "...two Chrysler plants (van and mini-van) and two Ford Motor Company plants (Essex Aluminium and Essex Engine). The residential areas are nestled directly between the four manufacturing facilities".

### 6.5 Working class cancer clusters

It is also important to situate the case studies within the context of Windsor workers' own efforts to pressure employers and government to prevent occupationally related cancer. It was their activity rather than that of the local medical community that made occupational cancer a major public health issue. While the recording of the full history of these working class initiatives is beyond the scope of the dissertation, it is important to know that there were numerous cases of occupationally related disease in Windsor that became known in the community; these cases influenced how workers viewed cancer aetiology and the political and social factors that allowed such risks. It also alerted the larger community to the relationship between cancer and exogenous exposures.

The failure of employers and government agencies to adequately protect workers led to grass roots campaigns to publicise the cancer risks of workers due to their occupational exposures. Health and safety activists believed that groups of workers were developing cancer due to occupational exposures but that this relationship was not being recognised medically because of a scientific bias that promoted lifestyle risk factors while ignoring exposures in the work environment. The trade union health and safety activists were able to pressure the provincial government and individual employers to reduce exposures to carcinogens in many Windsor workplaces. These advocates were also able to increase public awareness through their campaigns to prevent occupational cancer. They were not able, however, to convince the provincial cancer agency to establish a mechanism to identify workers with elevated occupational cancer risk.

This process to prevent occupational cancer also led to an awareness among Windsor health and safety trade union activists that they must be directly involved in any process that would define and influence medical research if they hoped to have their concerns addressed. The trade union activists were conscious of the limitations to their own power to confront the cancer agencies regarding their lack of interest in occupational cancer risks. The awareness of the need to collect occupational histories and to have a direct role in the research process eventually led to the precedent-setting labour-supported research discussed in the two case studies.

There are other predominantly working class communities in Canada with elevated cancer rates and serious pollution problems. Similar movements, however, did not emerge beyond Windsor. A number of crucial elements led to Windsor health and safety activism. The founding of a community-wide coalition, Windsor Occupational Safety and Health Council (WOSH) in the early 1980s provided workers with a support system and information resources that most Canadian health and safety activists did not have (Reasons et al., pp. 248-250; Brophy and Jackson, 1982, 1981). The trade union activists also were linked to the wider community through a coalition with community environmental and public health activists, who had organising skills, access to certain knowledge and financial resources. This community coalition provided a political space that functioned as a counter balance to the trade union hierarchy that gave health and safety concerns less prominence than more traditional trade union concerns (Lynd and Lynd, 2000, pp. 187-198). This collaboration also established a sense of trust and common purpose between trade union and community activists, which was to become a crucial factor in the evaluation of the Windsor case studies. And finally, there was a long history of working class activism in Windsor, referred to as social unionism that had imprinted the local culture and supported efforts to mobilise workers as a method to pressure for political and social change (Gindin, 1995).

### 6.5.1 Asbestos in a brake manufacturing plant

The genesis of the Windsor health and safety movement to prevent occupational cancer, which imprinted health and safety activity for the next two decades, began in 1979 with information about exposure to asbestos at the Bendix brake manufacturing facility (Lynd and Lynd, 2000, pp: 191-193; Storey and Lewchuck, 2000; Firth et al., 1997, pp: 42-48). In Windsor, the experience of the Bendix workers facing asbestos-related cancer raised questions about the nature of cancer causality and fundamental political questions about the rights of workers in Canadian society. This experience was of such importance to the development of the research outlined in the two case studies that it will be briefly presented here.

It should be noted that asbestos holds a special place in the annals of occupational health. Globally, the misuse of asbestos represents one of the most glaring examples of both employer negligence and governmental collusion (Keith and Brophy, 2004; Tweedale, 2000; Castleman, 1984). Asbestos can cause cancers in the lungs, larynx, and gastrointestinal system, including a fatal cancer called mesothelioma. It can also cause asbestosis, a non-cancerous but permanent and often fatal scarring of the lungs (Selikoff et al., 1979). For decades, governments, medical professionals and employers knew this and yet such information was not shared with the exposed workers or the public at large (Gee and Greenberg, 2001).

In the summer of 1979, while meeting with WCB representatives, the union representing the Bendix workers was shown for the first time Ontario Ministry of Health inspection reports issued in 1966 and 1970 that had ordered Bendix management to take steps to reduce asbestos exposure. The company had failed to comply with these orders (Firth et al., 1997, p.44).

Workers were unaware of the actual dangers of asbestos but had tied rags around their mouths and noses to keep from choking from clouds of airborne fibres circulated throughout the plants (Keith, 1980).

The danger posed by asbestos was made evident to the Bendix workers and even to the community at large in 1979 when it was announced that a 34-year-old Bendix worker was dying of mesothelioma (Firth et al., 1997, p.44). This announcement triggered a wave of health and safety activity in the community to reduce carcinogens in the workplace. The trauma of occupational disease at Bendix imprinted the perspective of Windsor union health and safety activists regarding the importance of carcinogen identification and cancer prevention (Keith, 1980: p. 38).

> In 1980 the Bendix Corporation announced it was closing its Windsor operations and moving to the United States. For a brief period, union activists occupied the plant and demanded severance and other benefits. Workers in other Windsor workplaces viewed the Bendix experience as a quintessential example of the dilemma faced by workers in capitalist society. One must risk one's health to secure a living. Workers further faced a threat of job loss if they were to challenge the employers' control of the production process (Firth et al., 1997: pp 44-45).

Occupational cancer would remain a prominent public health issue for community and trade union activists in Windsor throughout the 1990s (Brophy et al., 2001, 1999; Brophy, 1998; 1997a; 1997b; 1995).

## 6.6 Occupational Health Clinic for Ontario Workers: community organising continues

During the 1980s there was limited connection between trade union health and safety activists and the medical profession. The lack of professional medical and scientific supports acted as a barrier to identifying occupational cancer risks. The establishment of a Windsor trade union-oriented medical clinic was to function as the bridge to the local cancer centre and help to initiate the process addressing the gap in knowledge about occupational cancer risks factors. It is important to understand this step in the process that facilitated Windsor's precedent setting effort to move beyond the scientific conflict as outlined in Chapter 3 of the dissertation. Without the collaboration of the clinic health professionals, however, it is doubtful that the health and safety activists would have been able to establish the necessary partnership with the local cancer centre.

In the early 1990s the Occupational Health Clinics for Ontario Workers (OHCOW) opened a clinic in Windsor. The worker-directed clinic was to become one of the principal community organisations focusing on cancer causing substances at work (Lynd and Lynd, 2000, pp: 187-198; Brophy, 1995).

The occupational health clinic began to provide the local Canadian Auto Workers (CAW) with information about epidemiological studies being conducted in the United States among American autoworkers. Thirty-five percent of these studies examined occupationally related cancer (Park, 1993). The findings, along with data on elevated cancer among General Motors workers in Michigan who were exposed to metal working fluids (Mirer, 2003; Eisen et al, 1992; Tolbert et al., 1992), caused a renewed interest in preventing occupational cancer among health and safety activists in Windsor (Firth et al., 1997, pp: 50-55). In 1993, the Canadian Auto Workers (CAW) called upon the Ontario Occupational Disease Panel (ODP), a quasi-governmental panel that made recommendations regarding occupational disease to the Workers Compensation Board, to recommend workers' compensation be granted to metalworking fluid exposed workers with cancer (ODP, 1997, 1996, 1995).

The publicity from the ODP consultations further kindled the interest of the oncologists at the cancer centre in Windsor. The cancer physicians were concerned about the lack of data regarding occupational exposures. The Windsor Regional Cancer Centre (WRCC) agreed to a joint proposal from the Occupational Health Clinics for Ontario Workers (OHCOW) clinic, Windsor Occupational Health Information Services (WOHIS), and the Ontario Occupational Disease Panel (ODP) to establish a *cancer registry* at the cancer treatment centre to collect the lifetime occupational histories of all cancer patients. This partnership gave birth to the *Computerized Recording of Occupations Made Easy (CROME),* which is highlighted in the dissertation's first case study.

## 6.7 Summary

Windsor-Essex County is an industrial community coupled with substantial agricultural activity. It is also an area that has had serious environmental pollution that contains contaminants that pose a threat to human health.

Each of the studies presented within this chapter contributed to the shaping of community awareness regarding the need to identify possible occupational risk factors in order to reduce cancer risk. Each of the studies was constrained by the lack of specific data regarding possible confounders, including occupational exposures.

The studies reported have yet to identify causative associations between occupational and environmental exposures and specific diseases. The most informative study was based on Health Canada data that examined the morbidity and mortality of the population of Windsor compared to the city of Hamilton and the province of Ontario between 1986-1992. Mortality and morbidity rates from all causes were higher in Windsor than the rest of Ontario. Higher rates of diseases included various cancers; endocrine, nutritional, metabolic, and immunity disorders; diseases of the blood and blood-forming organs, nervous system and sensory organs, circulatory and respiratory systems, digestive system, genitourinary system, skin and subcutaneous tissue, musculoskeletal system and connective tissues; congenital anomalies; and infant mortality.

Two decades of occupational and environmental activism in Windsor generated awareness within the community in general and within the unions specifically that the high cancer rates could be related to occupational factors. The scientific view that cancer is generally a disease caused by poor lifestyle began to be seen as flawed. This predominant scientific perspective could not adequately explain the health problems in the community. In response to the identification of occupational and environmental exposures and possibly related health outcomes, the worker-oriented health clinic developed a partnership with the local cancer treatment centre to address the gaps in our knowledge about possible aetiological risk factors.

The research question regarding *how and why the dominant medical/scientific view of cancer causation has affected public health policy and practice in Canada* is addressed in the Windsor example as presented in this chapter.

The next chapter will set the stage for examining the two case studies, which make up the central empirical research component of the dissertation.

# CHAPTER 7: SETTING THE SCENE FOR THE EMPIRICAL RESEARCH: GENERAL INFLUENCES, METHODS AND ETHICAL ISSUES ON CASE STUDY DEVELOPMENT AND DESIGN

## 7.1 Introduction

The case studies represent what might be termed as a type of 'action research' and hence they have diachronic and iterative elements, which allow for the refinement of the data collection and categorisation methods used. The methods used in the case studies are informed by the methodological and other weaknesses and limitations of the more traditional studies carried out on the Windsor population analysed in an earlier chapter. This chapter outlines some of the general principles and approaches that cover all the case studies researched in the thesis.

The chapter firstly sets the stage for both the case studies that follow by providing a very brief overview. Secondly the overall context of the research is briefly reviewed to situate the case study work in terms of the debates about cancer causation in Canada and beyond. Thirdly the Windsor setting is discussed with regard to the major institutions and organisations, professional, medical, occupational and lay, that impact and impacted upon the research. In this setting, the roles of women's organisations, trade unions and others were often pivotal. Fourthly a short section provides the history of the research developments with regard to specific case studies: these were the building blocks for the next chapters. Finally ethical approval issues for all the case studies are addressed.

As cited in the Introductory Chapter, community-based action research examines "social, structural, and physical environmental inequities through active involvement of community members, organisational representatives, and researchers in all aspects of the research process" (Israel et al., 1998, p. 173). While it is beyond the scope of this dissertation to fully review the extensive literature on this research approach, it is important, however, to mention that the Windsor case studies employed many of the principles of community-based action research.

This approach is described as "collaboration between community groups and researchers for the purpose of creating new knowledge or understanding about a practical community issue in order to bring about change" (Hills and Mullett, 2000, p.2). It places emphasise on community participation; community capacity building; builds a partnership of learning and ownership over the research; respects the knowledge and wisdom of community members; and recognises the goal of action and change as central to the research process (Isreal et al., 2003). There are advantages and disadvantages to this approach. On the positive side, it provides the community with a mechanism for investigating issues of relevance to them. It give them access to information, including findings, and a process to effect change based on the findings. On the negative side, it can be difficult to coordinate; there may be tensions between community members and researchers regarding goals. It can be time-consuming and emotionally demanding (Stoecker, 1999, pp: 98-112).

In the earlier sections of the thesis the debates about cancer and occupational cancer were explored. The following chapters contain case studies that attempt to address some of the problems revealed by those debates and some of the -shortcomings with those data.

The case studies address aspects of the research questions through the use of epidemiological methods. All are case control studies. Both collect the occupational histories of cancer patients to determine if work might be influencing cancer risk. The case studies also explore the evolution and refinement of the research techniques as the limitations of the methods are analysed and each successive study attempts to address these difficulties. Finally, the two case studies led to another currently ongoing study.

The case studies arose out of the need to contribute to the search for better means to prevent occupationally caused or related cancer. They were initiated with the support of trade union health and safety activists working in collaboration with sympathetic health professionals. The case studies demonstrate the fruitfulness of a collaborative relationship between scientists and populations at risk (Susser and Susser, 1996a, 1996b).

Certainly, the case studies are a challenge to the generalised, systemic barriers to identifying possible occupational risk factors. It was noted almost 25 years ago:

> As Labour Canada indicates, Canadian governments have hesitated to adopt policies, which would help head off occupational cancers. Canadian workers will undoubtedly pay with their lives because of this reluctance to take preventative action (Tataryn, 1979, p. 14).

## 7.2 Overall context of research

Cancer morbidity and mortality remains a serious Canadian public health issue. This group of diseases is generally accepted in the scientific community to be largely environmentally caused and therefore, preventable (Doll, 1977). While there is a long history of scientific concern about the occupational and environmental causes of cancer, as exemplified by Hueper and Carson, their perspective has received limited recognition from the mainstream scientific community, which is either directly or indirectly influenced by industry.

The debate between Drs. Doll, Peto and Epstein contextualises the wider scientific debates that have shaped how cancer agencies in countries like Canada now address cancer prevention. The dominant perspective, which cites lifestyle risk factors as the principle cause of cancer while ignoring or minimising potential environmental risk factors, has particular meaning for women in relation to breast cancer risk. This disease is the most prevalent cancer among women. The suspected or known risk factors for breast cancer cannot explain the majority of cases. While environmental factors would certainly seem to be an important area of inquiry, the scientific focus remains on early detection and aggressive treatment.

The case studies begin to address the institutional disregard for the importance of gathering occupational data. Ten years ago, the Ontario Industrial Disease Standards Panel raised this issue.

> ...The collection of reliable occupation data, in conjunction with accurate medical diagnosis, is essential for health surveys and epidemiological studies on cancers associated with workplace exposures. Although medical information on cancer patients is routinely captured and stored in Ontario, there is as yet no systematic way (nor is there a practice) of collecting occupation data. As a result, there are no means by which the extent of occupationally related cancers in the Province can be directly estimated or monitored (Industrial Disease Standards Panel, 1994b,p.1).

The case studies' tools address the need to capture such data and also begin to explore the possible connection between breast cancer and endocrine disrupting chemicals.

The research grew out of community needs. The awareness of the health problems facing the community, both occupationally and environmentally, helped convince the local oncologists that the cancer centre must respond to the community's concerns. The Windsor researchers willingly collaborated with trade union and community activists. This strategy broke with the more traditional epidemiological methods that might view community participation as biasing the research process (Brown and Mikkelsen, 1990, pp: 132-133). The trade union experience and knowledge, for example, was recognised and sought. Trade union health and safety representatives helped to identify particular areas of the large automobile manufacturing facilities that might not have been recognised as employing carcinogenic agents. This process of consultation allowed for further refinement as the research tools developed. The unions also directly participated in securing funding and building political support that helped maintain the research process.

The literature review demonstrates that new understandings about the role of hormonal disruption plays in carcinogenesis might provide important insights leading to breast cancer prevention. While relatively sparse, occupational breast cancer epidemiological studies have resulted in findings that demonstrate elevated risk among certain occupations like farming and nursing. An array of exposures has also been identified as suspected breast carcinogens including certain pesticides, polycyclic aromatic hydrocarbons, organic solvents, electromagnetic fields and plastics.

## 7.3 The Setting

The community of Windsor brought a particular set of factors together that allowed for this research to emerge. Firstly more than 15 years of activity by Windsor trade union occupational health and safety activists and their community partners in both the workplace and in the broader community had influenced public opinion about cancer causality (Lynd and Lynd, 2000, pp. 187-198; Adkin, 1998, pp. 226-255). Second were the documented health problems and elevated rates of disease arising out of this industrial and agricultural-based economy that employed a wide array of synthetic chemicals while generating environmental emissions. This has been discussed in more detail in Chapter 6. Finally was the interest and support of the Windsor Regional Cancer Centre (WRCC), the Windsor Occupational Health Information Service (WOHIS), the Ontario Occupational Disease Panel (ODP) and the Occupational Health Clinics for Ontario Workers (OHCOW) (Firth et al., 1997, p.89). A resulting collaborative relationship between community activists and sections of the medical and scientific community made this project possible. The OHCOW clinic and the involvement of the Occupational Disease Panel heightened the credibility of the occupational health and safety activists' concerns and gave them access to institutions such as the Windsor Regional Cancer Centre. Each of the groups shared a common concern about the lack of data that might enlighten society about the role of exposures in the workplace with regards to cancer aetiology.

These factors were influenced by the larger global backdrop, which included the upsurge in trade union occupational health activity begun in the 1970s and which complemented the rise of the women's health and environmental movements (Smith, 2000; p. 33; Adkin, 1998, pp. 1–26; Berman, 1978, p. 5). These three movements challenged the corporate, political, and scientific establishments and induced the government and scientific bodies to react differently to their respective communities' concerns.

> ...These movements have significantly advanced public health and safety by pointing out otherwise unidentified problems and showing how to approach them, by organising to abolish the conditions that give rise to them, and by educating citizens, public agencies, health care providers, officials, and institutions. Popular participation brought to the national spotlight such phenomena as DES, Agent Orange, asbestos, pesticides, unnecessary hysterectomies, abuse of sterilization, black lung disease, and brown lung disease (Brown and Mikkelsen, 1990, p.133).

This overall public health movement influenced the collaborative research presented in the case studies.

## 7.4 Genesis of the research

Each case study employed particular data collection methods, which were further refined and improved in the subsequent study. Each case study was influenced by new knowledge and improved epidemiological approaches. As *CROME*, for example, shed light on breast cancer and farming, the *LOHR* questionnaire was designed to capture known or suspected breast cancer risk factors. As further evidence emerged from *LOHR* about breast cancer and farming, the new *LOEHR* questionnaire further developed so as to better capture the possible impact of endocrine disruptors and to minimise exposure misclassification.

In 1994, plans to collect occupational histories were initiated. A year later a data collection project, *Computerised Recording of Occupations Made Easy (CROME)* began to collect occupational histories at the Windsor Regional Cancer Centre (WRCC). *CROME* was developed through a process that involved occupational health professionals, medical specialists, including an occupational health physician, a respirologist, an oncologist, a researcher familiar with farming methods in Essex County, and a panel of trade union health and safety representatives from the automobile and related industries. Dr. Ethan Laukkanen, a Windsor oncologist and research team member, stated:

> ...I feel very positive about this project because it gives me the assurance that the valuable information that these patients carry is being put into a context that can be helpful. I think that when one looks at one patient at a time one simply has the question: and when one has a framework in which to put that information it has a greater value. I recall quite vividly, one of my first experiences as a medical student was to attend an autopsy of a gentleman in his early thirties who had died of leukaemia and the chart showed that he was a rubber tire worker and what struck me most was that observation was not given any type of attention, even when the association was one that was understood. I think when we contemplate cancer in our particular region and we consider the relative excess of upper and lower airway cancers and cancers of the GI tract that one has difficulty simply explaining those on the basis of lifestyle choices of the population and one is hopeful that we'll be able to drive a more solid explanation which ultimately can lead to a preventive strategy that can be owned by the community collectively (Laukkanen interview, Keith et al., 2000).

Arising from the *CROME* findings (Chapter 8), a team of local researchers, including community representatives from the Occupational Health Clinic for Ontario Workers (OHCOW) and the Windsor Occupational Health Information

Service (WOHIS), partnered to investigate more specifically the possible association between breast cancer and agricultural work. A grant from the Ontario Workplace Safety and Insurance Board (WSIB) Research Advisory Committee (RAC) facilitated collection of lifetime histories of women with breast cancer over a two-year period. A case-control study, *Lifetime Occupational History Record (LOHR)*, compared 564 women with breast cancer to 599 women in the community of similar ages but who did not have breast cancer (Chapter 9). The ensuing and currently ongoing case control study, *Lifetime Occupational and Environmental History Record (LOEHR)*, will be discussed in Chapter 9 as well. The *LOEHR* study, which intends to interview 1000 breast cancer cases and 1000 community controls over a three year period, has a number of methodological enhancements.

The case studies will address the debate that anchors the dissertation regarding the importance of controlling for a multiple set of cancer risk factors including occupation. Both *LOHR* and *LOEHR* collect not only occupational history data but also such lifestyle data as smoking and residential history along with medical, reproductive, and other potential confounders.

## 7.5 Research Ethics

Appropriate university ethical approval was obtained for the studies. The Windsor Regional Cancer Centre's (WRCC) Ethics Review Board approved the *CROME* project (*see Chapter 8*). During the initial pilot project to check the validity of the questions, the Windsor Regional Cancer Centre (WRCC) patients were interviewed at the Occupational Health Clinic for Ontario Workers (OHCOW). At that time OHCOW staff administered an informed consent process. Once the full study began, participants completed consent forms administered by WRCC staff prior to data collection. No personal identifiers were ever utilised in the course of the analysis or published results.

The University of Windsor served as the host institution for the *LOHR* study (*see Chapter 9*). The University and the WRCC Ethics Boards both approved the *LOHR* research. All participants completed signed informed consent forms prior to data collection. No personal identifiers were utilised in the course of the analysis or reports. All research team members and staff, which had access to patient names, signed a pledge of confidentiality. Records were maintained in a secured, locked location.

The new *Lifetime Occupational and Environmental History Record (LOEHR)* research (*see Chapter 9*), which is an enhancement of *LOHR*, has undergone ethics approval at the University of Windsor and the WRCC. It is following protocols for ethical research conduct in accordance with the Canadian privacy legislation and Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (Interagency Advisory Panel on Research Ethics, 2003).

## 7.6 Summary

The chapter has provided a crosscutting perspective on the background and selection of the case studies and the methods to be used. The perspective is, within limits, generalisable to all the case studies. The chapter also provides the ethical background to those studies. The thesis now moves on to look in detail at the case studies.

# CHAPTER 8: COMPUTERISED RECORDING OF OCCUPATIONS MADE EASY (CROME)

## 8.1 Introduction

The chapter begins with a description of the development of the data collection process. Secondly methods are explored with particular references to the different industrial and occupational groups that are set up within the *CROME* database. Thirdly the method of data collection is described and discussed. Fourthly, the *CROME* findings are presented while describing the assembling of the study cohort. Finally the *CROME* approach is analysed for its strengths and limitations.

### 8.1.1. The background

The chapter examines the first of two case-control studies that form the core empirical work of the dissertation. These studies represent the first time that a local community in Canada met the challenge posed by Doll and Peto (1981), a decade and a half earlier to collect occupational histories of cancer patients (Occupational Disease Panel, 1997). The initial case study examines the use of a general occupational history registry whose purpose was to identify possible associations between workplace exposures and elevated cancer risk and therefore, generate possible hypotheses (Brophy et al., 2002; Brophy, 2004, 2000b, 1999a, 1999b, 1998b, 1997; Brophy and Keith, 2000c; Firth et al., 1997). The chapter examines a case control study that arose from the initial finding of an increased breast cancer risk among women who were 55 years of age or younger and had ever farmed (Brophy et al., 2004a). The *CROME* questionnaire and other material produced during the research can be found in the *Appendices L, M, N, O, P, and Q*.

## 8.2 Data collection begins

A feasibility plan was developed in 1994 (IDSP, 1994c). The author of the dissertation, on behalf of the Occupational Health Clinic for Ontario Workers (OHCOW) in Windsor suggested that the Windsor Regional Cancer Centre (WRCC) involve the Industrial Disease Standards Panel (IDSP) in a collaborative process to design a database that could be used to collect the occupational histories of local cancer patients. The IDSP was keenly interested in such an initiative because it had already identified the lack of occupational history gathering as a major obstacle in identifying work-related cancer in Ontario. The IDSP joined with the Windsor Occupational Health Information Service to develop a pilot database whose primary functions would be:

> ...to store, retrieve and compare data which are 1) down-loaded from the Ontario Cancer Treatment and Research Foundation (OCTRF) Lotus "Approach" Database (physician and/or self-administered information); 2) collected from questionnaires completed and returned by cancer patients based on hygienist interviews and assessment of cancer patients" (Carlan, 1994, p.1) (*see Appendix L* ).

It was planned that the WRCC and OHCOW in Windsor would develop a "touch screen" computer program. OHCOW and IDSP staff would administer an interview-based questionnaire to a subset of patients (N=50) that had completed the "touch screen" programme to verify the responses and gather additional information about exposures. It was the intention of the IDSP to also involve the Cancer Treatment Centre and Occupational Health Clinic for Ontario Workers in Sudbury, Ontario. Sudbury was a centre for mining and, therefore, it was hypothesised that the Windsor-Sudbury project would capture two industrial communities that had been identified as having industries of interest and evidence of elevated cancer incidence (p.2). The Sudbury cancer centre, however, did not proceed with the project. Windsor was alone in this process, perhaps due to the more organised community-based lobby that planned and supported it (*see Chapter 6*).

Research team members developed the "touch screen" computer programme with the assistance of a group of Canadian Auto Worker (CAW) health and safety representatives. Thus a collaborative process gave rise to the first project to collect occupational histories of Ontario cancer patients:

> ...the programme was developed by three groups of people who will ultimately use it and benefit from it. In the normal course of events these types of projects are conceived and developed by researchers and scientists. In this case a treating physician, Dr. Laukkanen was responsible for much of the programme development. The staff of the Occupational Disease Panel, an agency with a primary focus on research of occupational sources of disease, and the OHCOW clinic ensured that the data being collected was organized in a fashion that would allow it to be matched with other similar databases. Finally representatives of the workers, specifically CAW Health and Safety Representatives... helped us to develop a programme which hopefully will be easy to use and will properly capture the jobs in this community. I am convinced that this cooperative approach to scientific research will be mandatory in the future (Carlan, 1995, p.3).

This project received widespread media attention and community support, which improved patient involvement (Workers Health and Safety Centre, 1995; Rennie, 1998; *see Appendix M*). The Occupational Disease Panel (ODP) highlighted it as a major achievement:

> ...In conjunction with the Southwestern Regional Office of Cancer Care Ontario (previously the Ontario Cancer Research and Treatment Foundation) and the Occupational Health Clinic for Ontario Workers (Windsor) the ODP created a computer programme to allow workers to electronically record their occupational histories. The programme was designed to create a complete work history that would be electronically retrievable and easily matched with other electronic databases. The occupations are recorded in accordance with the standardized occupational codes for wider access.
>
> The system is currently in use at the Regional Cancer Centre in Windsor, the first cancer centre in the province to include occupation as a standard entry in the patient's history. In the best of all worlds the other regional cancer centres will also adopt this approach and begin to include occupation in their history taking. This would be the first step to an improved ability to identify work-related sources of cancer (ODP, 1997).

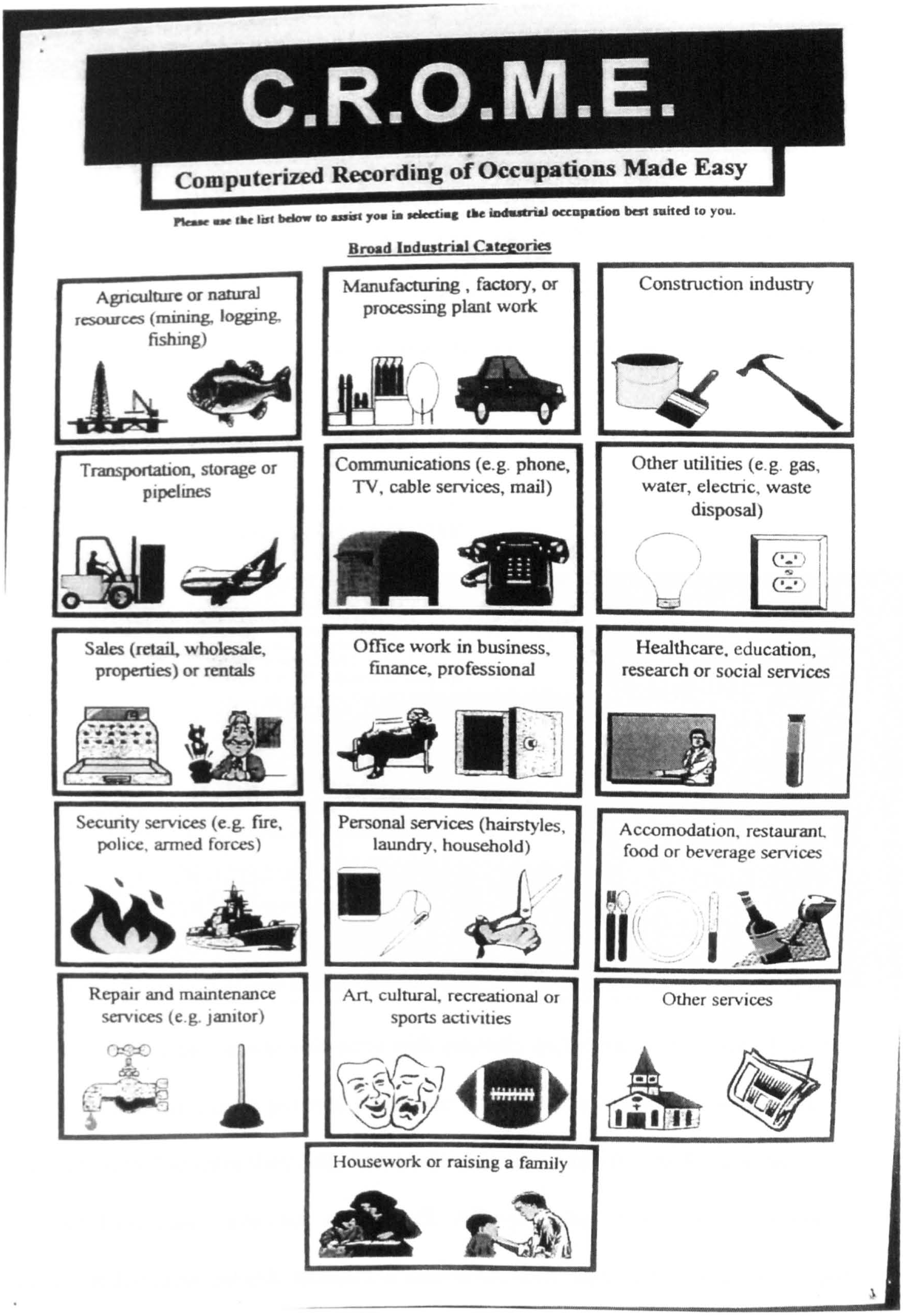
The Occupational Disease Panel was dissolved in 1997 by the newly elected Progressive Conservative provincial government leaving the *CROME* data collection project in the hands of the Windsor Regional Cancer Centre and the Occupational Health Clinic for Ontario Workers.

## 8.3 Methods

The design of *CROME* was not based upon any previously developed occupational history gathering measure. Rather, it was designed to fulfill a broad research mandate -- to screen for possible associations between any occupations and any cancers without an *a priori* hypothesis.

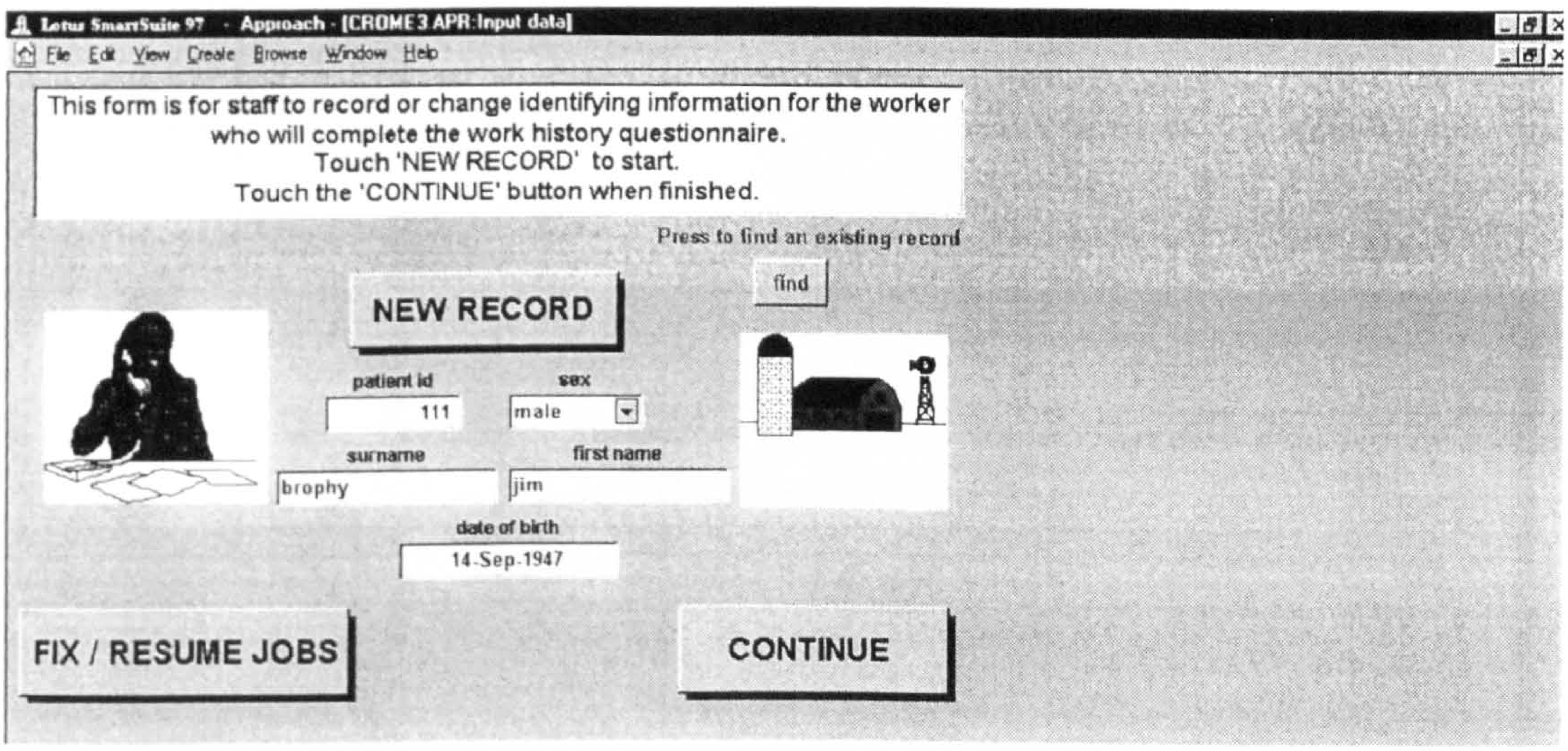
The consulting panel created an abbreviated list of industrial and occupational categories using their own knowledge of the most locally prevalent industries and occupations. Sixteen (16) major industries and three hundred (300) occupational categories were included in the list (*see Figure 8.1*). These categories were then matched to Health Canada's Standard Industrial Classification (SIC) and Standard Occupational Classification codes (SOC) (Ontario Cancer Treatment & Research Foundation, 1995).

Figure: 8.1 CROME poster with list of industrial categories:



Rather than attempt to create a questionnaire to capture a detailed exposure history that would adequately address all potential exposures in every possible occupation, occupation was treated as a "surrogate" for exposure within the *CROME* construct (Rothman and Greenland, 1998; p. 142-143). Exposure within recorded industries and occupations was assumed based on available industrial hygiene literature. *CROME* captured length of employment (duration) and time of employment to onset of disease (latency) but not intensity of exposure. The *CROME* database also captured age, and such key socioeconomic status (SES) variables as residence area, income level, and educational status.

**Figure 8.2: Initial Screen of the CROME**




The *CROME* database was enhanced with graphics and menus (*see Figure 8.2*). It was intended that cancer patients would use this user-friendly, touch-screen data collection tool to enter their full chronological work histories with little or no support from cancer treatment center staff. After an initial pilot, however, it was apparent that most patients required at least some staff support to adequately record their work histories.

Following a pilot phase, an evaluation was initiated to test the reliability of the data collected. An occupational health nurse and occupational hygienist interviewed 50 cancer patients who had completed recording their occupational histories utilising *CROME*. The pilot and evaluation helped to refine the computer system and modifications were made (*see Appendix O for copy of medical release form*).

For the next four years trained clinic staff conducted computer-assisted interviews with cancer patients who volunteered to participate in the project (*see Figure 8.3*).

**Figure 8.3: Patient being assisted with CROME database**

Interviews took, on average, between 20 to 30 minutes to complete and were conducted whenever the staff could accommodate them into their clinic schedules. Patients who were awaiting treatment would be invited to document their occupational histories. Copies of their histories were made available to them (*see Appendix P*). No attempt was made to select one group of cancer patients over another. However, due to such circumstances as treatment availability and waiting times, the largest group of cases recorded into *CROME* was females with breast cancer. This group slightly exceeded the category of women with other cancers.

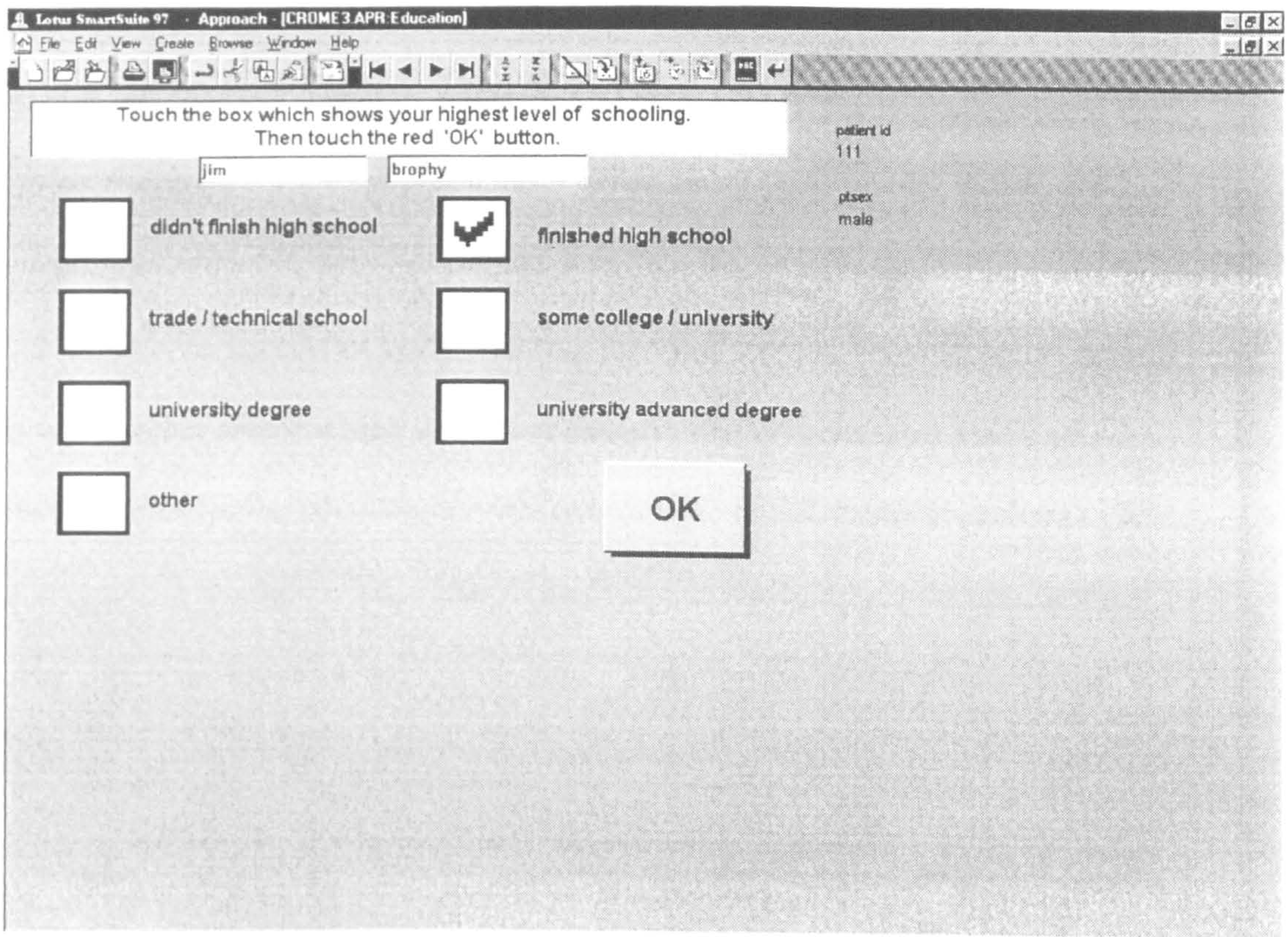
This selection method likely yielded a representative sample. Since the generation of the hypothesis followed the data collection process, the specific hypothesis of the case-control study did not: (1) influence the manner in which the data was collected, or (2) influence the decisions of the clinic staff regarding which cases were selected for recording occupational histories.

The structured interviews completed by the cancer patients included a detailed occupational history of the following: major industry; occupational category; duration of employment; age; level of education; and years starting and ending each job during the course of the patients' entire adult working lives. *CROME* was matched with the patients' medical charts, which provided additional data regarding potential key co-variates such as age at diagnosis, and lifetime cigarette smoking pack-years.

## 8.4 Patient in-put

The programme for each patient would begin with a computer screen that asked for their name, gender, birth date and an identification number. There was also a question on educational level as a surrogate for socioeconomic status. The choices were "didn't finish high school", "finished high school", "trade/technical school", "some college/university", "university degree" "university advanced degree", and

**Figure 8.4: Educational Screen**

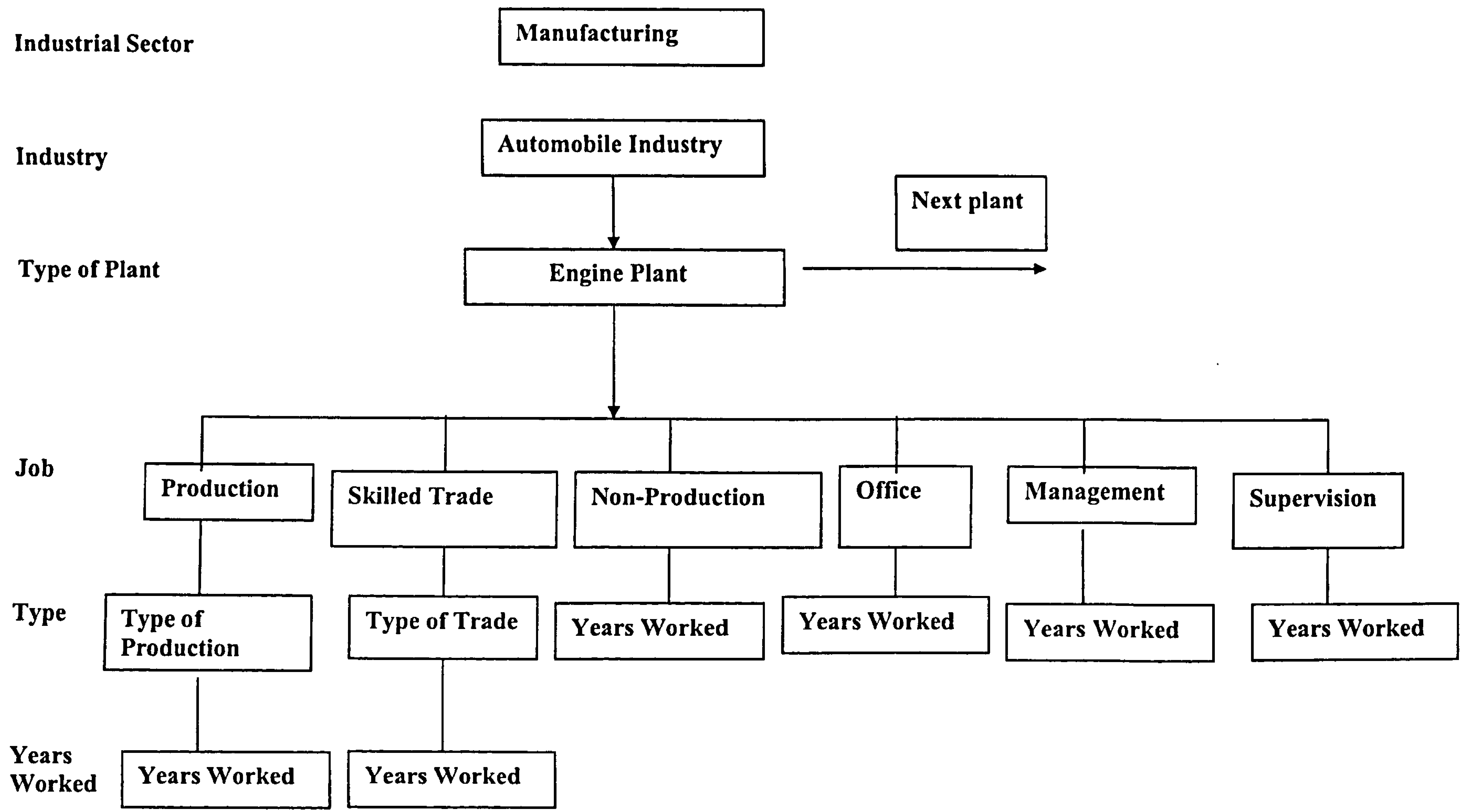



The next set of screens would permit the selection of the Industry (*see Figure 8.1*). There were 16 choices. The cancer patient was encouraged to begin by thinking about the general industry that described each of his or her jobs, rather than the particular job while employed in that specific industry. If, for example, the patient worked in an office position for an auto company, he or she would be instructed to indicate automobile industry. The particular job within that industry would be identified later in the process.

To give a specific example, the patient would be asked to begin by listing every job at which he or she had worked for at least a year. If the first job was working as an *electrical apprentice* in a automobile engine plant, the first job would be categorised as *manufacturing*, which would be selected by touching the "Yes" button under the manufacturing choice from the 16 possible choices *(see Figure 8.5: Schematic of CROME job choices)*. The next screen would list a variety of choices including *auto or other transport equipment production*. After choosing the "Yes" button, the programme would then move to another set of choices that would include *auto or truck manufacturing*. After again selecting the "yes" button, the programme would move to another screen which listed such automotive facilities as *assembly plant, foundry, engine plant, trim plant or transmission plant*. After choosing *engine plant*, the next screen would provide a list of possible jobs including *production, skilled trades, office, management and supervision*. Selecting the *skilled trades* button would then move the programme to the next screen with choices such as *electrician, mechanic, millwright, sewing mechanic, maintenance, carpenter, welder and other*.

After selecting *electrician*, for example, the programme would move to another screen where the patient would select the number of years worked and her age when she started and completed this job. The programme would then allow the patient to return again to choose one of 16 industries to begin the process over again for their next job. It would continue for each job of at least one year's length until the occupational history was completely documented.

Figure 8.5: Schematic of CROME Project
(Source: J. Brophy.)



## 8.5 Results

The original intention of the project was not to study breast cancer and occupation, but rather to collect data on the occupational histories of all cancer patients. As it turned out, following four years of data collection, the breast cancer cases made up the largest proportion of the participating cohort providing an adequate sample size from which to conduct data analysis. As this study was designed to capture limited data from a wide range of cancer patients, data regarding a few of the risk factors specifically identified with breast cancer were unavailable (Brophy, 2004). This will be discussed in greater detail in this chapter and in the following chapter on *LOHR*.

In 1999, the data collected using *CROME* was analysed by a contracted epidemiologist in consultation with the author of the dissertation and the CEO of the cancer centre. The largest single group of patients in the sample was women with breast cancer. Possible occupational factors were then examined by comparing women with breast cancer to a comparison group composed of women in the database with cancer other than breast. There was no *a priori* hypothesis. In *Table 8.1* descriptive comparisons are made of the two groups. There is considerable similarity in characteristics such as age, socioeconomic status and smoking pack-years.

Socioeconomic status (SES) is an important variable in breast cancer research, itself a predictor of breast cancer. Because this study's personal-level SES proxy—educational achievement--was not available for nearly half of the study sample (this did not differ significantly between cases and controls), an ecological measure of SES was also included based on area of residence (*see Table 8.1*) (Baquet and Commiskey, 2000; Gorey et al., 1998; Kelsey and Horn, 1993). This information was collected from the patients' medical charts.

The case study group was the 299 primary malignant female breast cancer patients (ICD Code = 174) (Percy et al., 1990), selected by convenience from the WRCC patient treatment roster between January 1, 1995 and December 31, 1998. The comparison (control group) consisted of 237 women with cancer other than breast who were receiving treatment at the WRCC during the same time period. The control group represented 28 different types of cancer; none of which accounted for more than 15% of the sample. The controls, with variability in age and residence, allowed for the construction of a stable logistic regression model.

*Table 8.1* shows that substantial proportions of this study's aggregate sample farmed (13%) for at least a year of their adult working lives. A tentative hypothesis was tested to determine whether the occupation of farming might pose a breast cancer risk. Because of consistently observed associations with pesticide exposures, lymphoma cases were excluded (Checkoway et al., 1989; Williams et al., 1977).

The calculation of descriptive statistics among cases and controls, including stratification and adjustment, employed standard epidemiologic and biostatistics techniques (Checkoway et al., 1989). Logistic regression odds ratios (OR) were created. The logistic model regressed the key dependent variable (women 55 years old or younger with breast cancer) on the key occupational independent variable (farming) adjusting for key confounders that were available (Kleinbaum and Kupper, 1978). Covariates included age, education and smoking history. Cigarette smoking was not shown to be a confounder of this study's findings. In this study's database smoking pack-years were not significantly associated with farming, or with breast cancer. In the interest of both parsimony and statistical power, it was removed from all of the logistic regression models.

Associations with breast cancer are displayed in *Table 8.2*. The table's left column displays hypothesised farming-breast cancer Odds Ratio (OR) point estimates and their associated 95% confidence intervals that were age-adjusted. These three models systematically replicated null findings across the following different samples: all ages; women 55 years of age or younger; and women 56 years of age or older, who had ever farmed. These null associations are consistent with most other of this field's studies that have not accounted for critical confounders such as socioeconomic status. Of greater interest are the table's centre and right columns that display socioeconomic-adjusted models, respectively, adjusted for personal (educational achievement) and ecological (census tract median household income) measures of socioeconomic status.

The point-estimates of increased breast cancer risk among farmers ranged from three to nine-fold, albeit within rather broad confidence intervals. Even granting its limitations, the consistency and size of this preliminary study's breast cancer - farming association strongly suggests that this relationship ought to be treated as a successfully tested hypothesis that warrants future examination with more rigorous epidemiologic methods.

**Table 8.1: Descriptive Profiles of 299 Breast Cancer Cases and 237 Other Cancer Controls**

| | Breast Cancer | | Other Cancer * | |
|---|---|---|---|---|
| Characteristics | N | % | N | % |
| **Age at Diagnosis** | | | | |
| 25- 46 | 22 | 7.4 | 28 | 11.8 |
| 46-55 | 58 | 19.4 | 42 | 17.7 |
| 56-65 | 84 | 28.1 | 60 | 25.3 |
| 66-75 | 101 | 33.8 | 72 | 30.4 |
| 75 and older | 34 | 11.4 | 35 | 14.8 |
| **Education °** | | | | |
| Less than high school diploma | 45 | 27.4 | 43 | 29.7 |
| High school diploma | 44 | 26.8 | 39 | 26.9 |
| Some post high school education | 44 | 26.8 | 37 | 25.5 |
| University degree | 31 | 18.9 | 26 | 17.9 |
| **Median Annual Household Income »** | | | | |
| $15,000-37,999 | 72 | 24.1 | 68 | 28.7 |
| $38,000-45,999 | 79 | 26.4 | 56 | 23.6 |
| $46,000-59,999 | 68 | 22.7 | 58 | 24.5 |
| $60,000-89,999 | 80 | 26.8 | 55 | 23.2 |
| **Smoking Pack-Years** | | | | |
| None | 208 | 69.6 | 157 | 66.2 |
| 1-24 | 52 | 17.4 | 46 | 19.4 |
| 25 or more | 39 | 13.0 | 34 | 14.3 |
| **Farming Person-Years ϕ** | | | | |
| None | 257 | 86.0 | 212 | 89.5 |
| 1-19 | 24 | 8.0 | 15 | 6.3 |
| 20 or more | 18 | 6.0 | 10 | 4.2 |

° Proportion of missing data did not differ significantly between cases and controls (c2 test).
» Ecological measure; based on 70 Essex County, Ontario census tracts in 1996.
ϕ Includes field crop production, crop spraying and dusting, vineyard or fruit farming, greenhouse or nursery operations, livestock farming, other agricultural jobs, and other farm services.

**Table 8.2: Logistic Regression Estimated Odds Ratios of The Ever Potentially Pesticide Exposed-Breast Cancer Association by Age Groups**

| | Estimates Adjusted for the Following Variables | | | | | |
|---|---|---|---|---|---|---|
| | Age | | Age and Education | | Age and Income | |
| Exposure<br>Age Groups | N | OR (95% CI) | N | OR (95% CI) | N | OR (95% CI) |
| Ever Farmed | | | | | | |
| All Ages | 536 | 1.34 (0.81, 2.34) | 309 | 1.38 (0.67, 2.83) | 536 | 1.36 (0.74, 2.51) |
| Fifty-Five or younger | 150 | 2.57 (0.75, 8.85) | 89 | 9.05 (1.06, 77.43) | 150 | 2.81 (0.94, 8.40)* |
| Fifty-six or older | 386 | 1.18 (0.65, 2.13) | 220 | 0.88 (0.44, 1.92) | 386 | 1.14 (0.57, 2.28) |

Notes. OR = odds ratio, CI = confidence interval.

* 90% confidence interval of (1.12, 7.05).

## 8.6 Discussion

The *CROME* case-control study had a number of strengths and limitations. They are discussed in the following sub-sections.

### 8.6.1. Strengths of *CROME*

The *CROME* study used data regarding lifetime occupational histories of study participants. It controlled for the potentially confounding influence of such socioeconomic factors as education and income status. As shown in *Table 8.2*, for women 55 years and younger, who had ever engaged in farming, there was an OR = 9.05, 95% CI (1.06 - 77.43) albeit with a wide confidence interval. The wide confidence interval was the result of missing SES data that reduced the power of the sample. Among all such women, the age and socioeconomic status-adjusted rate of breast cancer was tentatively observed to be an almost three fold excess OR = 2.81; 95% CI (0.94 - 8.40).

*CROME* demonstrated its potential scientific utility by being able to successfully collect the occupational histories of cancer patients. Its purpose was to act as a mechanism for hypothesis generation regarding occupational associations with cancer risk. The elevated breast cancer risk among women fifty-five years old and younger who had ever farmed was consistent with other epidemiological studies that suggested possible breast cancer risk among women employed in agriculture as delineated in the literature review.

### 8.6.2 Limitations of *CROME*

The *CROME* study had a number of limitations. It was not able to control for known breast cancer risk factors such as family history and oestrogen-related factors, such as use of oral contraceptives or hormone therapy, and reproductive history. Consequently, the research team could not say with a high degree of confidence what role these factors might have had on the breast cancer risk of women employed in agriculture. The sample size was small and the use of a comparison group made up of women with cancers other than breast raises potential confounding issues.

For example, while the lymphoma cases were eliminated because they share possible common aetiologic risk factors with breast cancer, there may be other cancers that are similarly influenced, and yet, were left in the control sample.

The *CROME* generated-data was limited by its reliance on the Windsor Regional Cancer Centre (WRCC) patient medical chart to provide additional life history information to control for possible factors that might confound the findings. The *CROME* database collected data on occupational history and socioeconomic status. During the *CROME* data collection phase of the process, the research team did not have access to patient medical charts. The researchers believed that the clinic charts would provide information from each patient regarding lifestyle factors that might influence cancer risk. The *CROME* database was not designed to examine any particular cancer, but rather to collect the occupational histories of all cancer patients. The work histories would then be added to the overall information from the patient chart in order to examine the impact of occupation on cancer risk while controlling for other risk factors.

> Cancer treatment centres collect a significant amount of information but a lot of it has not really been prevention oriented. And the difficulty is that because of the funding of the treatment centres, even if they do get some information it is not sent centrally where it is analysed....Each cancer centre focuses on different areas and we really need to get a template where all of them are giving the same

information and collecting the same data (Dr. Deborah Hellyer – Keith et al., 2000).

Another limitation is that *CROME* relied on the occupational category as a surrogate for exposure. The process assumed that, for example, welders were exposed to welding fumes and asbestos insulators had asbestos exposure. Most researchers engaged in case-control or even cohort epidemiological studies find it difficult to retrospectively capture occupational exposures. Length of employment in a particular occupation will often be substituted for actual exposure. There was no information about specific exposures, or their intensity. Length of time on the particular job acted as a surrogate for duration of exposure. While the approach did not capture specific exposures, it captured the effect of real life mixed exposures through the comparison of occupations.

*CROME*, therefore, operated on the assumption that all workers in the same occupational category shared generally the same level of exposure. Production workers in auto assembly plants would be clustered together as if they shared the same set of exposures. But in such an environment there were departments that had certain kinds of exposures such as metalworking fluids and welding, while other departments did not. These workers would, however, be grouped together which could possibly underestimate the risk of an exposed sub-set of workers. Misclassification of exposed and unexposed can bias the results and underestimate the risk (Checkoway et al., 1989). This sort of limitation could have very real consequences on the determination of breast cancer risk among a farming population in that some women might have worked with certain pesticides while other women did not. This variability in exposure is not accounted for in the *CROME* cohort.

A further limitation was the small sample size. There were only 299 women with breast cancer compared to 237 women with cancer other than breast. The small population does not yield enough statistical power to confidently establish associations. When controlling for numerous variables statistical power is further reduced.

Despite these limitations, the *CROME* data collection process demonstrated its ability to gather occupational information and generate hypotheses. The research team envisioned that the next step would be to conduct population based case-control studies to examine, with greater specificity and with larger numbers, the hypotheses generated from *CROME*.

The limitations of this preliminary study were addressed in a follow-up study designed to test the breast cancer-farming hypothesis. This new study, *Lifetime Occupational History Record (LOHR)* is described in greater detail in the following chapter of the dissertation.

## 8.7 Conclusion

The *CROME* project represents a step in the development of a standardised occupational history questionnaire that could be employed at cancer centers across Ontario. In an interview, Dr. Laukkanen stated:

> ...Our first objective is to look at new cancer cases in Essex County. We want to identify these occupations in our patients. We want to put occupational histories into the broad context of what is known about cancer in our area...Once patterns are identified and compared to patterns in the general population, we can investigate specific work categories and attempt to identify and remove the cause of the disease (Workers Health and Safety Centre, 1995, p.5).

There were also hopes that the trade unions in Ontario would carry this initiative to their own communities.

> It is also important to recognize that this has been largely a labour initiative. Worker involvement in developing public health policy ensures that the right questions are asked, which is necessary if we are to get the right answers. Labour councils around the province will be encouraged to bring this project to their district health councils (Workers Health and Safety Centre, 1995,p.5)

If such data were to be collected, the resulting data set would provide many opportunities to screen other cancer-occupation-exposure hypotheses, such as the breast cancer-farming hypothesis. Findings of elevated risks and the identification of causal agents would encourage occupational cancer prevention strategies to emerge. By bringing to light this possible association in the Windsor context it validated the project's primary goal, which was to see if the collection of occupational histories might identify populations at risk.

This case study also demonstrates that a community driven occupational cancer research initiative can yield useful results. It also has implications for prevention:

> Gathering occupational data is ultimately relevant to prevention. Firstly, if we define a contributory association between a particular workplace or workplace exposure it becomes possible to take steps to take away that exposure and thus, enable other people to carry out that occupation without that element of risk. The second point to make is that an awareness of cancer prevention in its various, multiple approaches will likely be a way to change cancer management most significantly. We can accomplish only so much with established cancers and a focus like this enables us to explore a territory that offers a great many opportunities. It requires something quite different than the management of an established cancer. It requires a set of attitudes and a set of commitments from a

very big population but I believe that it's an area where the rewards will be great (Interview with Dr. Ethan Laukkanen – Keith et al., 2000).

The following chapter will describe the two-year case-control study, *the Lifetime Occupational History Record (LOHR)* that emerged from the *CROME* process. The *LOHR* study was to test the *CROME* findings regarding breast cancer risk and farming.

# CHAPTER 9: LIFETIME OCCUPATIONAL HISTORY RECORD (LOHR)

## 9.1 Introduction

This chapter presents the case study of *the Lifetime Occupational History Record (LOHR)* findings, and examines possible future initiatives based on its strengths and limitations (Brophy et al., 2004, 2000a, 2000d; Brophy and Keith, 2002a, 2002b, 2002c; Brophy 2001b).

The chapter begins by critically assessing a number of the data collection issues encountered in the *CROME* phase of the research. Secondly the political barriers that influenced the development of the case studies are outlined. Thirdly the *LOHR* methods and tools are presented and analysed. (The *LOHR* questionnaire and other research-generated material can be found in Appendices R, S, T, U, V, W,X, Y, Z, AA and BB. Fourthly the results of the research are given. Fifthly the strengths and limitations of the *LOHR* approach are explored. Finally, the new Windsor study, *the Lifetime Occupational and Environmental History Record (LOEHR)*, is presented as part of the further development of the case studies' process with an enhanced questionnaire and improved method for capturing exposures. (The new *LOEHR* questionnaire, its specific occupational modules and other research-generated material can be found in Appendices CC, DD, EE, FF, GG, HH, II, KK, LL, MM, NN, and OO).

## 9.2 Data collection problems

The *CROME* finding of an association between women with breast cancer, 55 years of age or younger, who had ever farmed, changed the process of occupational data collection in Windsor, Ontario. The original objective behind the *CROME* research was to collect the occupational histories of *all* local cancer patients. *CROME* was meant as a simple registry that would be linked to the patient's medical chart. The combination of these two data sources would potentially contain a rich source of information that would detail multiple aspects of each cancer patient's life. Such a registry would also address the systemic failure to control for possible risk factors attributable to work and better comprehend its impact on cancer causality (Doll and Peto, 1981, p. 1239).

In order to introduce this data collection process it was necessary to find an inexpensive mechanism to gather the information since the provincial cancer agencies were not prepared to financially support such an undertaking (ODP, 1997,1997). The *CROME* touch screen was meant to address this lack of financial resources at the Windsor Regional Cancer Centre (WRCC), which could not afford to allocate staff to assist all cancer patients in documenting their occupational histories. So in spite of the strong support from within the WRCC, not every patient was able to participate. It was recognised by all of the community partners, such as the occupational health clinic and WOHIS that financial resources would have to be found in order to designate a full time person to be responsible for such information gathering. Cancer Care Ontario (CCO) has not viewed occupational factors as a major cause of cancer (Do, 2004), and therefore, as argued in earlier chapters of the dissertation, was not prepared to allocate the necessary resources for such an undertaking. Other funding sources were needed if this process was to continue.

Given Windsor's industrial nature, it was first conjectured that the *CROME* registry would document cancers among male industrial workers who were exposed to carcinogens in the auto plants or auto-feeder plants. The exposure of particular interest was metalworking fluids as they were previously identified as responsible for elevated cancer risk among United States autoworkers (Eisen et al., 1992; Tolbert et al., 1992). The Canadian Auto Workers (CAW) had raised their concerns about work-related cancer to the Occupational Disease Panel in 1993 and demanded recognition and compensation for a host of cancers they believed to be associated to metalworking fluids (ODP, 1995a).

There were a number of reasons this did not occur. The *CROME* touch screen was not as accessible as initially believed. Cancer patients found it onerous. Many cancer patients were not computer literate and found even this supposedly accessible method of data entry too difficult.

Perhaps a more problematic factor was the desire of the patients to talk with someone about their life and perceptions of what might have contributed to them having contracted cancer. When a WRCC staff person was made available, many work histories were collected. If staff was unavailable, then the number of participating patients declined.

Another factor was that each type of cancer had its own treatment schedule. Appointments for lung cancer patients almost always ran on time with little waiting, so the individual patients would receive treatment and then leave the centre. Breast cancer patients, on the other hand, tended to have a much longer wait, allowing many of them time to participate in *CROME* before their treatment began. Women with breast cancer were available and also were very interested in speaking about their concerns. These women were also, as a group, less ill than, for instance, lung cancer patients and therefore, were better able and more willing to participate.

There was not, however, any attempt to select either just women or women with breast cancer. The *CROME* cohort was assembled of whosoever was available at any given time without prejudice and was willing to participate in an interview.

### 9.2.1 Moving away from the registry

*CROME* was a tool to help generate hypotheses regarding occupational causes of cancer. Once a population at risk was identified, further analysis and research would be conducted. With the finding of elevated breast cancer risk among women who farmed the project had reached a point where a decision had to be made on how this research should proceed. The breast cancer finding clearly required further investigation. There were additional risk factors, such as family history and oestrogen load factors, which were not properly controlled for and which might contribute to the observed elevated risk. There were also limited resources available at the WRCC to provide necessary staffing. These factors led the research team to submit a proposal to the Workplace Safety and Insurance Board (WSIB) for a grant to conduct a case-control study to test the breast cancer – farming hypothesis (Gorey, Brophy et al., 1999). This choice to procure research monies for a specific examination of a particular type of cancer had the consequence of the overall registry being abandoned. The outcome of this decision was to sustain in some form the collection of occupational histories of cancer patients. The only option, if any occupational cancer research was to continue in any form, was to access funding sources available for more traditional epidemiological studies.

### 9.2.2 Political background

A number of political factors also influenced the choices made by the researchers. When *CROME* began in 1994, the New Democratic Party (NDP) was in power in Ontario. The NDP is historically a social democratic party with close ties to the Ontario trade unions. For example, the government supported expanding the occupational health clinics and the Occupational Disease Panel (ODP). By 1999, the Progressive Conservative party had replaced the NDP as the provincial government. The new government was less supportive towards the occupational health clinics and had abolished the ODP (Keith, 1996). There was no money available to continue *CROME*. Cancer Care Ontario (CCO) was generally unsupportive of the assertions made by labour groups such as the Ontario Federation of Labour about occupational cancer and the need for cancer registries to capture occupational histories (Rennie, 1999). Also efforts to expand the registry to other Ontario cancer centres had not proven successful (Brophy, 1995).

By 1999, however, the influence of the Ontario trade unions had been substantially reduced after almost four years of struggle against the conservative provincial government (Moore, 2001). The Canadian Auto Workers (CAW) was less interested in pursuing research regarding metalworking fluids and cancer as it had responded to the initial findings on metalworking fluids by negotiating its own5-fold lowering of the exposure standard at the Canadian Ford, Chrysler and General Motors operations (Firth et al., 1997, p. 92). The CAW had also developed a national cancer prevention campaign (CAW, 1998) and, with the exception of the former Holmes foundry workers in Sarnia, was not vigorously pursuing compensation on behalf of autoworkers who developed occupationally related cancer (Keith and Brophy, 2004).

The changes in the global economy and the fear of job loss also reduced the levels of challenge and confrontation, and directed the attention of the unions away from health issues such as occupational cancer (Keith and Brophy, 2004; Brophy and Keith, 1998a).

In spite of the above-cited limitations there had developed significant political, community and local labour support for examining the possible contribution of workplace exposures to cancer incidence. The decision was made to apply for funding to follow-up specifically on the breast cancer findings. The following quote from a local resident helps to explain the development:

> I have some personal history with cancer. My mother, who worked in an auto plant in the city of Windsor for some twenty years was diagnosed with cancer at the young age of 49 years old and in a year's period had a radical mastectomy and eventually lost her battle with cancer and died at the age of 50. And you can't help but think that those twenty years in the workplace must have had some impact on her health and that disease that she was diagnosed with. Again, we can't buy the notion that she made all of her mistakes in lifestyle choices. There has to be something there and *CROME* would be able to provide any information to show whether there was a relationship between her occupation and cancer (Interview with Ken Bondy, CAW – Keith et al., 2000).

The District Health Council, the Women's Incentive Centre, the Windsor and District Labour Council and Essex County Medical Society provided support letters for the continuation of this research (*see Appendices Y, Z, AA and BB*: Martel, 1999; Greene-Potomski, 1999; Parent, 1999; Barnard, 1999). The research proposal was accepted and the interview process of women with breast cancer and a corresponding number of community controls began in January,2000. The research was called the *Lifetime Occupational History Record (LOHR).* The rest of this chapter will critically examine the methodology and findings of *LOHR*. There will also be a discussion about the research generated from this study.

## 9.3 Methods

Over a two-and-a-half year period (2000-2002), all female patients of the Windsor Regional Cancer Centre (WRCC) diagnosed with histologically confirmed new incident primary breast cancer (International Classification of Diseases, 9th edition; ICD-9 code = 174) (Percy et al., 1990) were invited to participate in a population-based case-control study. After an in-service training session to explain the purpose of the *LOHR* study and to identify the work instructions applicable to each department, staff in Radiation, Chemotherapy, Medical Records, New Patient Referral, Supportive Care, and Computer Services participated in patient recruitment. The medical records department screened all new breast cancer patients to confirm pathology and date of diagnosis and then forwarded a letter (*see Appendix S*) outlining the *LOHR* project to all eligible incoming patients. A follow up telephone call was made by project staff to the patient to schedule an interview at the patient's convenience (*see Appendix U*). Of the eligible breast cancer patients, 564 participated in the study. Only 3 patients declined participation, resulting in *a better than 99% response rate* (*see Table 9.1*).

**Table 9.1: Female Breast Cancer Patients**

| | Participated in Study | Refused Participation | No. Of Patients out of Sampling Frame | Ineligible for other reasons |
|---|---|---|---|---|
| **Female Patients** | 564 | 3 | 95 | 14 |

All of the breast cancer cases were diagnosed between January 1, 2000 and May 31, 2002. The interviews took place between June 1, 2000 and July 4, 2002. During the study period, a total of 29 patients were sent to neighbouring Detroit, Michigan area hospitals for treatment due to long treatment waiting times in Ontario, which was not resolved until June 26, 2000. These patients were eventually seen post treatment at follow-up appointments at the WRCC. There were 95 women with histologically confirmed breast cancer who were deemed ineligible to participate because, while they received treatment at the Windsor Regional Cancer Centre, they resided outside of Essex County. Also, there were 11 women who died before an interview could be arranged; one woman was handicapped and unable to participate; and 2 interviews were discarded due to incomplete information.

Community controls were chosen at random using POLK City Directory (1999) software and were recruited by letter (*see Appendix T*) and a scripted follow-up telephone call (*see Appendix U*). *See Table 9.2* for the demographic breakdown of the community controls. The controls were matched to reflect the proportion of the urban and rural residency of the breast cancer patients. The response rate for controls was: Windsor - 52.2%, Windsor Suburban - 53.2% and Leamington -51.8% (all communities in Essex County).

**Table 9.2: Female Community Controls**

| | No. of Interviews Completed | No. of Letters Sent to Controls | No. Who Refused Interview | No. of Letters Returned to Sender | No. of Controls out of Sampling Frame |
|---|---|---|---|---|---|
| **Windsor Female** | 367 | 1090 | 80 | 96 | 287 |
| **Windsor Suburb Female** | 173 | 442 | 29 | 39 | 78 |
| **Leamington Female** | 59 | 145 | 14 | 14 | 17 |

All subjects, cases and controls, signed informed consents (*see Appendix V*) and each was given a $20 stipend. Subjects were informed that their participation was completely voluntary and that they had the right to withdraw themselves and/or their data from the project at any time. To protect confidentiality, participants were identified by study code only in the database.

Included in the analysis were 564 female breast cancer cases and 599 female controls (*see Appendix W*). There were 247 cases (44%) interviewed by telephone and 317 (56%) interviewed in-person. There were 420 (70%) female community controls interviewed by telephone and 179 (30%) interviewed in-person.

A comprehensive lifetime history questionnaire (*see Appendix R*) was administered to each subject by trained interviewers. Interviews were conducted in either a private office at the WRCC, at another location convenient for the patient, or by telephone. Data gathered included known or suspected risk factors along with a complete occupational history of all jobs ever worked. The questionnaire gathered data regarding height and weight (body mass index), marital status, income, education, age at menarche, menstrual history, pregnancy and breast-feeding history, menopausal status, hormone use, family breast cancer history, residential history by 3-digit postal codes, hobbies, and occupational history including age at the start and end of each job. Jobs were categorised using the National Occupational Classifications (NOC) (Human Resources Development Canada, 1992) and the North American Industrial Classification System (NAICS) (Statistics Canada, 1998b). The NOC codes, which provided more specificity than the NAICS, were used in the analysis. Because there were relatively few subjects within each of the NOCS, they were grouped together with similar or related occupations to provide adequate statistical power (*see Appendix X*).

The Canadian Auto Workers (CAW) health and safety co-coordinators for Ford, Chrysler and General Motors joined the researchers for a series of meetings to further refine the NOC codes. The five major local auto manufacturing facilities included the motor engine plants, the car assembly plant, the transmission and trim plant, and the foundry. Departments from these operations were added to the NAIC list. This refinement of the NAIC codes better reflected the actual areas of auto work in Windsor. This is a further example of the role that populations at risk can play in such research if their knowledge and experience are recognised.

The questionnaire also included questions on a range of occupational exposures: asbestos, man-made mineral fibers, dusts, second-hand tobacco smoke, engine exhaust, other smoke or particulate, metal-working fluids, solvents, paints, strippers, pesticides. Subjects were asked whether they were exposed to "none", "a little", "some", "a lot" of each of the exposure agents. Agricultural workers were also asked about pesticide/herbicide exposure. Unfortunately, subjects' recall about previous pesticide/chemical exposures proved to be limited and much of the exposure data was deemed unreliable by the interviewers or was missing. Therefore, exposure data was not ultimately included in the analysis.

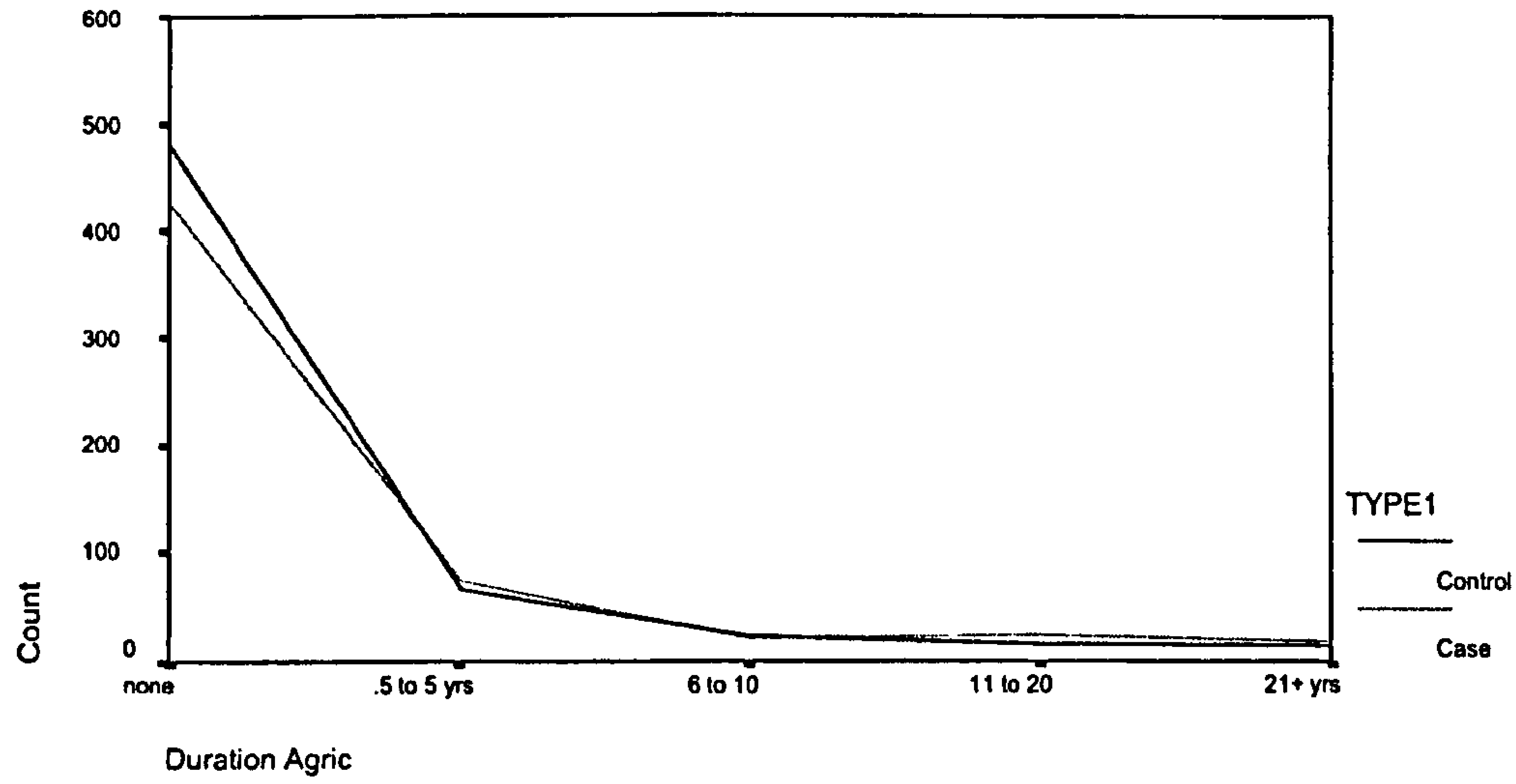
On average the interviews were completed within thirty to forty-five minutes. However, interview length depended on the number of residences and jobs the participant had held.

## 9.4 Findings

The statistical programme, Statistical Package for Social Scientists (SPSS) (Version 10), was used to conduct a three-step multivariate analysis to test the hypothesis about the possible association between breast cancer risks and work in agriculture. The calculation of descriptive statistics among cases and controls, including stratification and adjustment, employed standard epidemiologic and biostatistics techniques (Checkoway et al., 1989). A conditional logistic regression model was used to calculate adjusted odds ratios (OR) and 95% confidence intervals. The logistic model regressed the key dependent variable (breast cancer) on the key occupational independent variable (farming) adjusting for employment duration along with other confounders (Kleinbaum and Kupper, 1978).

In the initial step, cases and controls who were ever employed in agriculture were compared while controlling for duration of employment (five category ordinal variable, None, .5 to 5 years, 6 to 10 years, 11 to 20 years and 21 or more years). As shown in Figure 9.1, the two groups were very closely matched in terms of years of duration of employment.

**Figure 9.1: The distribution of cases and controls by years employed in agriculture**




As shown in *Table 9.3* among the breast cancer cases there were 154 women who were ever employed in agriculture and 133 community controls who were ever employed in agriculture.

**Table 9.3: Cases and Controls Employed in Agriculture**

| Type | Grouping of Agricultural NOCs | | Total |
|---|---|---|---|
| | Yes | No | |
| Case | 154 | 410 | 564 |
| Control | 133 | 466 | 599 |

The Odds Ratio (OR) for women ever employed in agriculture was 1.35 (CI 95%, 1.01 - 1.79) with a significance of 0.04. Duration did not reach statistical significance for any of the specific periods.

Step 2 in the logistic regression (See *Table 9.4*) inserted the following ordinal co-variates into the model: Age at diagnosis (mean age of cases = 60.33, mean age of controls = 58.64); education level; annual household income; body mass index; number of pregnancies; years of oral contraceptive use; months of breast feeding; years of cigarette smoking; alcohol use and marital status.

**Table 9.4: Descriptive Profile of 564 female Breast Cancer Cases and 599 female Community Controls**

| | Breast Cancer Cases | | Community Controls | |
|---|---|---|---|---|
| | No. | % of Total | No. | % of Total |
| **Age at diagnosis (years)** | | | | |
| age less than 40 | 30 | 2.60% | 42 | 3.60% |
| 41-50 years | 109 | 9.40% | 140 | 12% |
| 51-60 years | 145 | 12.50% | 165 | 14.20% |
| 61-70 years | 134 | 11.50% | 120 | 10.30% |
| 71-80 years | 100 | 8.60% | 93 | 8.00% |
| 81 years > | 46 | 4.00% | 39 | 3.40% |
| **Education** | | | | |
| some elementary school | 6 | 0.50% | 8 | 0.70% |
| completed elementary school | 29 | 2.90% | 29 | 2.50% |
| some high school | 84 | 7.20% | 92 | 7.90% |
| finished high school | 248 | 21.30% | 207 | 17.80% |
| some college/university | 54 | 4.60% | 89 | 7.70% |
| college graduate | 69 | 5.90% | 94 | 8.10% |
| university graduate | 63 | 5.40% | 70 | 6.00% |
| advanced postgrad degree | 11 | 0.90% | 10 | 0.90% |
| **Household Income Level** | | | | |
| less than $20,000. | 43 | 4.00% | 33 | 3.10% |
| $21,000 to $40,000 | 109 | 10.20% | 127 | 11.80% |
| $41,000 to $50,000 | 83 | 7.70% | 72 | 6.70% |
| $51,000 to $75,000 | 192 | 17.00% | 182 | 17% |
| $75,000 plus | 97 | 9.00% | 134 | 12.50% |

| | Breast Cancer Cases | | Community Controls | |
|---|---|---|---|---|
| **Body Mass Index[1] (Kilograms) at Interview** | | | | |
| Missing Values | 31 | 2.70% | 34 | 2.90% |
| 37 to 51 Kilograms | 32 | 2.80% | 36 | 3.10% |
| 52 to 65 Kilograms | 189 | 16.30% | 203 | 17.50% |
| 66 to 80 Kilograms | 189 | 15.50% | 189 | 16.30% |
| 81 Kilograms> | 132 | 11.30% | 137 | 11.80% |
| **Number of Pregnancies** | | | | |
| Never | 68 | 5.80% | 69 | 5.90% |
| 1 to 3 | 333 | 28.60% | 364 | 31.30% |
| 4 to 6 | 135 | 11.60% | 146 | 12.60% |
| 7 to 9 | 25 | 2.10% | 15 | 1.30% |
| 10> | 3 | 0.30% | 5 | 0.40% |
| **Years of Oral Contrceptive Use** | | | | |
| Missing Values | 274 | 23.60% | 264 | 22.70% |
| Never Used | 34 | 2.90% | 35 | 3% |
| 1 to 5 years | 121 | 10.40% | 152 | 13.10% |
| 6 to 10 years | 76 | 6.50% | 79 | 6.80% |
| 11 years> | 59 | 5.10% | 69 | 5.90% |
| **Months of Breast Feeding** | | | | |
| Missing Values | 378 | 32.50% | 370 | 31.80% |
| 1 to 12 months | 143 | 12.30% | 172 | 14.80% |
| 13 to 24 months | 31 | 2.70% | 33 | 2.80% |
| 25 to 36 months | 4 | 0.30% | 12 | 1% |
| 37 months > | 8 | 0.70% | 12 | 1% |
| **Years Smoked Cigarettes** | | | | |
| Did not Smoke | 316 | 27.20% | 328 | 28.20% |
| 1 to 5 years | 29 | 2.50% | 25 | 2.10% |
| 6 to 10 years | 24 | 2.10% | 26 | 2.20% |
| 11 to 20 years | 36 | 3.10% | 63 | 5.30% |
| 21 years > | 159 | 13.70% | 157 | 13.50% |
| **Alcohol Use** | | | | |
| Never Used Alcohol | 123 | 10.60% | 88 | 7.60% |
| Past User of Alcohol | 138 | 11.90% | 54 | 4.60% |
| Occasional Alcohol Use | 182 | 15.60% | 300 | 25.80% |
| Current User of Alcohol | 121 | 10.40% | 157 | 13.50% |
| **Marital Status** | | | | |
| Married or Common Law | 391 | 33.60% | 429 | 36.90% |
| Separated or Divorced | 39 | 3.40% | 48 | 4.10% |
| Single | 31 | 2.70% | 29 | 2.50% |
| Widow | 102 | 8.80% | 93 | 8% |

[1] Body mass index = weight(kg)/height2 (m)

This step also included the following dichotomous co-variates (See Table 9.5): *mother ever had cancer* (yes or no); *ever pregnant* (yes or no); *ever used hormones* (yes or no); *ever smoked tobacco* (yes or no); *ever breast fed* (yes or no); *ever used oral contraceptives* (yes or no); *and ever resided on a farm or lived within a mile of a farm* (yes or no). *Years lived in Essex County* was a continuous variable within the model. Ever worked in agriculture had an OR = 1.24 (CI 95%, .92 - 1.7) with both *age* OR = 1.01 (CI 95%, 1.0 - 1.02) and *alcohol use* (1) OR = 1.9 (CI 95%, 1.2 – 3.0).

**Table 9.5: Descriptive Profile of 564 female Breast Cancer Cases and 599 female Community Controls**

| | (Dichotomous Variables) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Breast Cancer Cases** | | | | **Community Controls** | | | |
| | **Yes** | **%** | **No** | **%** | **Yes** | **%** | **No** | **%** |
| **Mother Ever Had Cancer**[1] | 125 | (10.9%) | 431 | (37.5%) | 146 | (12.7%) | 447 | (38.9%) |
| **Ever Pregnant**[2] | 495 | (43%) | 65 | (5.6%) | 527 | (45.8%) | 64 | (5.6) |
| **Ever Use Hormones** | 261 | (22.4%) | 303 | (26.1) | 263 | (22.6%) | 336 | (28.9%) |
| **Ever Smoke Tobacco** | 249 | (21.4%) | 315 | (27.1%) | 273 | (23.5%) | 326 | (28%) |
| **Ever Breast Feed** | 378 | (32.5%) | 186 | (16%) | 370 | (31.8%) | 229 | (19.7%) |
| **Ever Used Oral Contraceptives**[3] | 289 | (25%) | 273 | (23.6%) | 339 | (29.3%) | 256 | (22.1%) |
| **Ever reside on a farm or live within a mile of a farm**[4] | 253 | (22.2%) | 305 | (26.7%) | 247 | (21.6%) | 337 | (29.5%) |

1 Missing Cases = 14 (1.2%)
2 Missing Cases = 12 (1%)
3 Missing Cases = 6 (.5%)
4 Missing Cases = 21 (1.8%)

The final step in the conditional logistic model added the major NOC groups (*auto related manufacturing; clerical -computer- writer; communications; dry cleaning; education and library; petrochemical; finance and insurance; food processing; food service; hair dressing; manufacturing-engineering managers; other managers-*

*lawyers- paralegals-architects; policy- skilled sales; health care including dental; janitorial; other manufacturing; plastics; printing-painting- construction; retail social service; textile; transportation-gas station-customs- security; unemployed outside the home; animal care; sports-arts; pest control; postal; mining-logging; landscaping; and home care*). In the third step conditional forward model all the occupations interacted with age.

At this stage there were 1026 cases (N = 506) and controls (N = 520) with 137 missing (11.8%) (see *Table 9.6*). The odds ratio for *ever worked in agriculture*, controlling for duration and the above listed co-variates interacting with the remaining occupations, was OR = 2.80 (CI 95%, 1.6 – 4.8). If one ever worked in agriculture and then was employed in auto-related manufacturing, the odds ratio was OR = 4.0 (CI 95%, 1.7, 9.9). If one ever worked in agriculture and then was employed in health care, the odds ratio was OR = 2.7 (CI 95%, 1.1 – 4.6). *Age* ((OR = 1.0 (CI 95%, 1.0 – 1.02)) confirmed the generally observed trend that breast cancer incidence increases with age. There was a statistically significant two-fold increase of breast cancer incidence in this logistic model among women *who were past users of alcohol.*

| Table 9.6: Logistic regression-estimated odds ratios (ORs) of women ever employed in agriculture | | |
|---|---|---|
| | Odds Ratio (ORs) | 95.0% C.I.) |
| Ever Worked In Agriculture | 2.8 $^{\phi}$ | (1.6 - 4.8) |
| Worked in Agriculture and then Auto-related Manufacturing | 4.1 $^{\pi}$ | (1.7 - 9.9) |
| Worked in Agriculture and then in Health Care | 2.3 $^{\Psi}$ | (1.1 - 4.6) |
| Age | 1.0 $^{*}$ | (1.0 - 1.03) |
| Alcohol Use | 2.0 $^{**}$ | (1.3 – 3.2) |

$^{\phi}$ Sig. = .000
$^{\pi}$ Sig. = .002
$^{\Psi}$ Sig. = .02
$^{*}$ Sig. = .005
$^{**}$ Sig. = .003

## 9.5 Discussion

The findings of the case study point to increased breast cancer risks from farming exposures. From a practical standpoint, the development of knowledge on such hazards as those which may be more prevalently experienced in certain workplaces (for example, increased risk of breast cancer due to pesticide and herbicide exposure among farmers) is extremely important for the development of appropriate public health efforts on prevention. It is well known that most cancers (breast and others) are probably the result of complex interactions of genes and environments. The more we know about one of these factors, the better able we will be to design preventive strategies. It should be noted that if a particular cancer were caused by the interaction of a gene and a particular environmental carcinogen, then removal of the offending substance from the environment would help to reduce the risk of cancer from occurring, even though one causative component is genetic. It is also important to account for timing of exposure, since from our understanding of the possible deleterious role of endocrine disrupters this factor could be significant.

The steady increase in the incidence of breast cancer in Canada suggests exposure to occupational and environmental agents plays a role in the genesis of this disease (Davis et al., 1997b). The majority of breast cancer cases cannot be explained by the widely accepted list of attributable risks (Kelsey and Gammon, 1990; Madigan et al., 1995; Henderson et al., 1996; Welp et al, 1998). Therefore, there is a need to test for other potential risk factors (Brophy, 2004). There is more good evidence that exogenous chemicals are contributing to the overall incidence (Aronson et al., 2000; Wolff et al., 1996; Krieger, 1989). One area that should receive particular attention is the family of synthetic substances that "mimic" estrogens (xenoestrogens). This group includes organochlorine pesticides, polycyclic aromatic hydrocarbons, organic solvents and plastics (Welp et al., 1998; Allen et al., 1997; Davis et al., 1997a; Epstein et al., 1997; Johnson-Thompson and Guthrie, 2002; Goldberg and Labreche, 1996; Millikan et al., 1995; Petralia et al., 1999a; Teppo, 1998).

The findings of the *LOHR* study are also in keeping with the findings of other studies. Duell et al. (2000) presented a complex picture of the association between farming and breast cancer risk in women with and without pesticide exposure that supports the *LOHR* study's conclusions. The Odds Ratio was below that expected for farming women when analysed without controlling for pesticide exposure or the use of protective equipment. However, women who reported being present in the fields during or shortly after pesticide application had an 80% increased risk of developing breast cancer (OR = 1.8, 95% CI 1.1 – 2.8). The authors concluded that while farming may not present an elevated risk per se, farming women exposed to pesticides may have an elevated breast cancer risk (p. 329) (*see chapter 5*).

*LOHR* findings are also consistent with a Canadian study conducted in British Columbia that reported a possible elevated breast cancer risk among farmers (Band et al., 2000). The researchers sought to investigate occupations while controlling for known or suspected hormonal risk factors. Though women were stratified by pre- and post-menopausal status as well as by both combined, it was with the combined pre- and post-menopausal group, that a three fold elevated breast cancer risk among women ever employed in fruit and other vegetable farming (OR = 3.11, 90% CI 1.24 – 7.81) was found. There was a seven fold elevated breast cancer risk among women ever employed in other vegetable farming (OR = 7.33, 90% CI 1.16 – 46.2). Although the British Columbia study had greater statistical power, the methodology was quite similar. The researchers controlled for many of the same breast cancer risk factors, again having to rely on occupation as a surrogate for actual exposures (*see chapter 5*).

Biological and toxicological evidence also help to explain the *LOHR* findings. While 2,3,7,8-tetrachlorodibenzo-*p*-dioxin has anti-estrogenic properties and is protective of adult animals for breast cancer from carcinogen exposures, there is evidence from animal testing that prenatal exposure to dioxin may increase the susceptibility to mammary cancer (Brown et al., 1998). This research poses a new hypothesis that may help to further clarify the possible biological dimension of prenatal exposure to endocrine disruptors and the occurrence of breast cancer in humans *(see Chapter 4).*

The scientific literature suggested that female breast tissue may be more susceptible to tumour initiation and progression during periods of great morphological and biochemical change, that is, from puberty to time of first pregnancy and possibly continuing throughout the reproductive years. The cells in the immature, developing breast are not yet differentiated and cells are dividing at a greater rate than later in life (Kuller, 1995). The susceptibility of cell mutation, coupled with the greater propensity of undifferentiated cells to bind with carcinogens, and thus trigger DNA damage, means the exposure of younger women to exogenous toxins can be crucial (Clark et al., 1997). Furthermore, later reproductive factors, which will influence estrogenic load, can influence this risk (*see Chapter 4*).

### 9.5.1 Limitations of LOHR

The first case study (*CROME*) and second case study (*LOHR*) primarily found and then tested associations with specific occupations, such as farming, but neither of these studies could adequately control for specific exposures. *CROME* relied on the general occupation to represent exposures. The *LOHR* study did control, unlike *CROME*, for other breast cancer risk factors, such as family history and oestrogen load. While *LOHR* attempted to gather much more detailed information through the interview process about specific exposures, it was not able to identify actual causative agents by relying on the historical recollection of the interviewees regarding possible exposures and their intensity. Unfortunately, many of the patients and community controls were not aware of their specific exposures. There were so many gaps in the data that this exposure information could not be utilised in the analysis. It is possible that the actual breast cancer risk among the women in the *LOHR* cohort who had ever worked in agriculture and had exposure to pesticides is even higher because the unexposed are aggregated with the exposed, and thus, may be statistically diluting the risk. Such non-differential misclassification decreases the probability of detecting associations and tends to underestimate the actual risks (Blair et al., 1993). Neither method reliably captured exposure information.

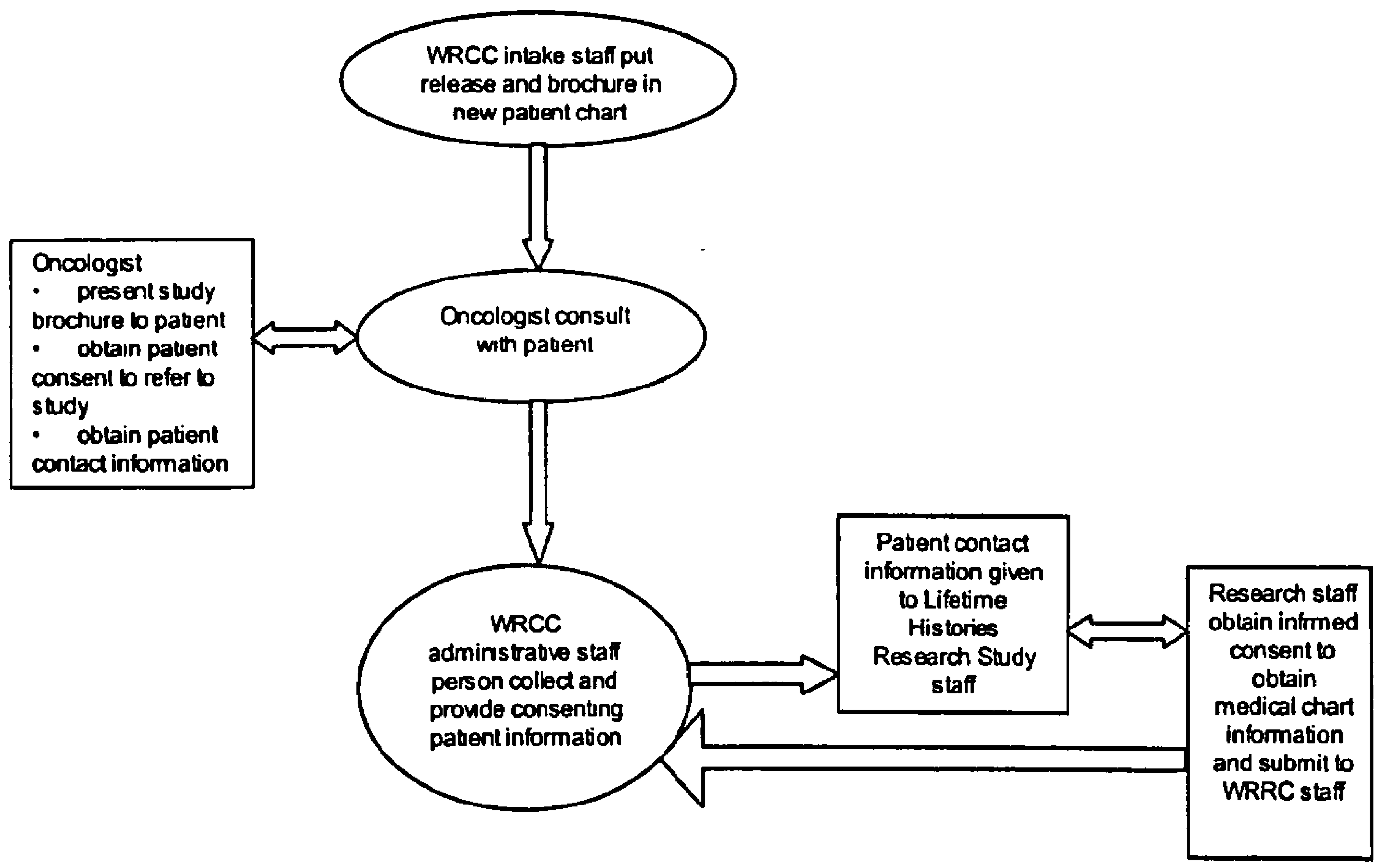
Another limitation of the *LOHR* case control study was the limited sample size. A minimum sample size of 1,000 is recommended for such a study to be meaningful (Siemiatycki, 1995).

## 9.6 Revised new study: Lifetime Occupational and Environmental History Record (LOEHR)

A new research team (see Acknowledgements) was assembled to continue the process of collecting the occupational histories of women with breast cancer. The new study, the *Lifetime Occupational and Environmental History Record (LOEHR)* received three funding grants to cover the costs of a new three-year case control study (Brophy et al., 2004c, 2003a, 2003b, 2003c) *(see Appendix B, NN).*

*Each year* for three years beginning in September 1, 2003, 335 women with breast cancer and 335 community controls (for a total of 2010 subjects over three years) will complete the *LOEHR* questionnaire assisted by fully trained interviewers. The estimated number of participating cases is based on the projected annual WRCC catchment area caseload of approximately 353 new incident cases and an expected 95% response rate or better (*LOHR* achieved a 99% response rate).

Figure 9.2: WRCC study recruitment process




An in-service session was held with WRCC oncologists and administrative staff to explain the purpose of the research and their role in the recruitment process. WRCC oncologists will seek, from their newly diagnosed female breast cancer patients, written consent to be referred to the study (*see Figure 9.2*) (*see Appendix HH*). A WRCC administrative staff person will screen all new breast cancer patients to confirm pathology and date of diagnosis. Research staff will then forward letters of information outlining the study to all eligible patients. Follow-up telephone calls will then be made by project staff to the patients to schedule interviews at the patients' convenience after obtaining written informed consent (*see Appendix HH*).

Community controls will also be recruited using methods that proved effective in the *LOHR* study. Letters, inviting recipients to participate in research exploring "risk factors for breast cancer," will be sent to randomly-selected households obtained through the generation of random telephone numbers linked to addresses (*see Appendix II*). The letters will not specifically target occupational or environmental risk factors in order to minimise selective recruitment and reporting bias. The letters will then be followed up with telephone calls by project staff inviting the recipients' participation (through past experience, it is estimated that approximately 2,400 randomly mailed letters will be required to recruit 335 valid controls each year). Cases and controls will sign letters of informed consent and will be offered remuneration of $20 to offset parking, travel costs and inconvenience. Subjects will be informed that their participation is completely voluntary and that they have the right to withdraw themselves and/or their data from the project at any time (*see Appendix JJ*). To protect confidentiality, participants will be identified by study identification code only in the database. Both the University of Windsor (the host institution) and the WRCC Ethics Committee have approved this procedure (*see Appendix KK*).

The *LOEHR* questionnaire (*see Appendix CC*) is an enhancement of the questionnaire used in the *LOHR* study with adaptations based on questions and approaches from other validated occupational cancer questionnaires (US Department of Health and Human Services, 1998; Stewart et al., 1996; Siemiatycki, 1991). In consideration of the limited stamina of patients undergoing treatment, the questionnaire has been designed to gather only data pertinent to the focus of this study or those factors, which may act as potential confounders. The *LOEHR* questionnaire will capture traditional risk factors (Gail and Costantino, 2001; Gail et al., 1989), such as intrinsic and extrinsic oestrogen load; parity; lactation (Enger et al., 1997); menstrual and menopausal history; use of hormone replacement therapy and oral contraceptives (Lippman et al., 2001; Brinton et al., 1998; Malone et al., 1993; Brinton et al., 1988); family history data (Sattin et al., 1985; King, 1990; Sasco et al., 1993; Thomas, 1993); indicators of socioeconomic status (SES); physical activity; weight and body mass index (BMI) (van den Brandt et al., 2000; Carpenter, 1999; Coogan and Aschengrau,1999; La Vecchia et al., 1997; Huang et al., 1997; Franceschi et al., 1996; Mannisto et al., 1996; Taioli et al., 1995); alcohol use (Goldberg et al., 2001, pp: 11- 14); detailed lifetime occupational history (which will provide data for the assessment of exposures, including duration, dose, age when first exposed); residential history by three-digit postal code for mapping of cases and spatial analysis (Besag and Newell,1991); shift work and night work history (Davis et al., 2001; Schernhammer et al., 2001; Hansen, 2001); parental occupations and other indicators of prenatal and perinatal exposures (Vatten et al., 2002; Brown et al., 1998; Kristensen et al., 1996); childhood exposures (Davis et al., 1998; Weiss et al., 1997; Clark et al., 1997; Kuller, 1995); smoking history (including second-hand smoke) (Manier et al., 2001; Johnson et al., 2000; Morabia et al., 2000; Morabia et al., 1996); Great Lakes fish consumption (Daly, 1993; Jacobson and Jacobson, 1993; Swain, 1991); household exposures; hobbies; and oestrogen and progesterone receptor status of the tumour (the latter to be extracted from patient medical record) (Zheng et al., 2000; Petralia et al., 1999a; Dewailly et al., 1994). Key variables, such as occupational histories, are placed near the beginning of the questionnaire, followed by questions regarding moderating and intervening factors. Less taxing questions are placed at the end under the assumption that increasing fatigue may influence recall.

### 9.6.1 Addressing the issue of exposure

An expert panel will assess and classify each job and designate likely exposures. This study employs an improved method for assessing past occupational exposures. There are three approaches commonly used in community-based occupational cancer case-control studies to assess past exposures: 1) self-reported exposure data; 2) job-exposure matrix; and 3) assessment by an expert panel (Fritschi et al., 2003; Teschke et al., 2002; Benke et al., 2001; Weston et al., 2000; Kauppinen et al., 1998; McGuire et al., 1998; Siemiatycki et al., 1997; Fritschi et al., 1996; Cantor et al., 1995; Siemiatycki, 1995; Kauppinen, 1994; Dosemeci et al., 1994; Messing et al., 1994; Plato and Steineck , 1993; Goldberg et al., 1993; Kauppinen et al., 1992; Gilks and Richardson, 1992; Sieber et al., 1991; Siemiatycki et al., 1989).

Elements of each approach are being incorporated into *LOEHR* (*see Appendices DD, EE, FF, and GG)*. Self-reported data is gathered through structured interviews with open-ended, probing questions by a fully trained interviewer. The interview elicits a complete work history. Detailed exposure characterisations, particularly for endocrine disruptors, are sought for local industries (automotive, plastics, pharmaceutical, distilleries, and agriculture) and industries which have traditionally employed women, such as health care, sales, service, clerical and education. An expert panel will make exposure assessments. The expert panel will be comprised of several members of the research team and staff from the Occupational Health Clinics for Ontario Workers (industrial hygienists, occupational physicians, and researchers). The panel will be "blind" as to whether data relates to cases or controls. It will review data, evaluate job histories (coded by industrial classification North American Industrial Classification System (NAICS) (Statistics Canada, 1998) and occupational classification National Occupation Classification System (NOCS) (Human Resources Development Canada, 1992) and will classify exposures using compiled information. Dose will be estimated and recorded as a gradient of 0 to 4. Duration of exposure will be determined from interview data regarding the length of time on a specific job and the subject's recollection of time spent in the actual exposure, in conjunction with expert panel assessment. This process will be streamlined as time goes on -- assessments made and information gathered for previous jobs will be useful in the assessment of subsequent jobs.

Particular effort will be made to examine agricultural exposures. Focus groups of men and women with experience working on farms in Essex County will be convened to help develop exposure profiles and hazard maps for different historical periods (Keith et al., 2003a.2003b; Keith et al., 2002; Keith and Brophy, 2003a. 2003b). The scientific literature on effective risk assessment and pesticide reporting will also be analysed (Acquavella et al., 2002; Coble et al., 2002; Wood et al., 2002; Dosemeci et al., 2002).

## 9.7 Conclusion

*The Lifetime Occupational History Record* (*LOHR*) evolved from the initial *CROME* finding of elevated breast cancer risk among women who were 55 years of age or younger who ever farmed. The *CROME* findings were not able to control for numerous risk factors that might have impacted on the results. *LOHR* would address for some of the limitations in the *CROME* design. *LOHR* would test the hypothesis regarding breast cancer risk and farming, while controlling for a wide array of potential lifetime risk factors. The *LOHR* study provides evidence of an association between farming and breast cancer risk, as well as a possible interactive effect between occupational farming exposures and subsequent exposures in other occupational environments. It might be extrapolated that exposure to pesticides or other farm exposures initiate the breast cancer process and subsequent exposures to agents in auto-related industry, health care or other industries act as promoters. This interactive effect requires further study and consideration. Moreover, we need a clearer understanding of the effects of farming exposures during the early periods of life when breast tissue is most vulnerable. This would fill a glaring gap in our occupational cancer knowledge base and aid our general understanding about the causes of breast cancer.

This chapter described the *LOHR* study that constitutes one of the two central research case studies of the dissertation. Both studies found associations between breast cancer risks for women who were employed in agriculture. These finding are consistent with other epidemiological reports (Duell et al., 2000; Band et al., 2000). The research was meant to address a gap in society's efforts to prevent cancer by identifying possible working populations that were at "elevated risk" due to exposures at work. Such knowledge would lay the framework for a cancer prevention strategy.

The *CROME* and *LOHR* grew out of a convergence of occupational health activity, community pressure, and the willingness of a portion of the medical staff at the Windsor Cancer Treatment Centre and at the Occupational Health Clinics for Ontario Workers in Windsor to explore possible occupational associations and cancer aetiology.

The next chapter will evaluate the research questions and objectives posed by the dissertation.