A B S T R A C T

Occupational cohort studies conducted to study cancer incidence and mortality require extensive data gathering about workers' job histories, exposures, and health outcomes. Although this process is expensive, the database created can be looked upon as a resource for broad investigations of the relationship between work and health. This paper presents the example of a retrospective cohort study which began in the traditional way, examining the link between a specific pesticide exposure and mortality and cancer incidence. The cohort register has since been used to investigate whether infertility, adverse reproductive outcomes, and childhood cancers might be associated with this exposure. It is also being used as the basis for studying other sawmill exposures including noise and wood dust, as well as socioeconomic factors including job strain, job mobility, unemployment, and retraining. This approach allows both the efficient use of occupational cohorts as well as providing the opportunity for investigators to develop a more comprehensive perspective on the determinants of the health status of workers and their families.

A B R É G É

Les études de cohortes professionnelles menées pour étudier la mortalité par cancer et l'incidence de cette maladie exigent que l'on rassemble un très grand nombre de données concernant les antécédents professionnels des travailleurs, leurs expositions aux risques, et les résultats en termes de santé. Bien que cela soit coûteux, on peut voir la base de données ainsi créée comme une ressource utile pour mener de vastes enquêtes sur les rapports qui existent entre le travail et la santé. Cet article présente le cas d'une étude de cohorte rétrospective qui a eu recours aux méthodes traditionnelles pour examiner le lien entre l'exposition à un pesticide spécifique et les taux de mortalité et d'incidence du cancer. Le registre de la cohorte a depuis servi à voir si l'infécondité, les issues défavorables en termes de reproduction et les cancers des enfants pouvaient être associés à cette exposition. On s'en est également servi pour étudier les risques posés par d'autres éléments auxquels on est exposé dans une scierie comme le bruit et la sciure de bois, ainsi que des facteurs économiques comme le stress dû au travail, la mobilité professionnelle, le chômage et le recyclage professionnel. Cette approche permet un meilleur recours aux cohortes professionnelles en plus d'offrir aux chercheurs la possibilité de développer une perspective plus complète sur les déterminants de l'état de santé des travailleurs et de leurs familles.

Opportunities for a Broader Understanding of Work and Health: Multiple Uses of an Occupational Cohort Database

Kay Teschke, PhD, Aleck Ostry, MSc, Clyde Hertzman, MD, MSc, Paul A. Demers, PhD, Maria C. Barroetavena, MD, MHS, Hugh W. Davies, MSc, Helen Dimich-Ward, PhD, Helen Heacock, MSc, Stephen A. Marion, MD, MHS

An often cited disadvantage of cohort studies is that they are very expensive compared to other study designs used in occupational epidemiology.¹ This is especially so in studies of rare diseases which require large cohorts. The major components of the cost are abstracting the personal identifiers and job histories of employees, determining exposure for each job, linking the employee register to the relevant health outcome database, and tracing individuals who are lost to follow-up.

Despite the cost, the majority of retrospective cohort studies investigate outcomes with respect to a single exposure agent, type of agent, or industrial process, e.g., asbestos,² formaldehyde,³ dioxins,⁴ furniture making,⁵ aluminum smelting.⁶ Although cohort studies allow investigation of multiple health outcomes, they are most commonly limited to mortality and cancer incidence which are routinely recorded by national statistical agencies.

Cohort studies do present other opportunities which may not be recognized. They can be used to develop a broader understanding of work-related health issues within a cohort population, by extending the data gathering and analyses to additional

outcomes and exposures. The data may also be useful for social science objectives, for instance studying the effects of technological change on job structure and work force mobility, or reconstructing the economic history of an industry. Bridging the health and social science domains allows investigation of socioeconomic determinants of health within cohort communities.

This paper demonstrates how data from a traditional retrospective cohort study can be more fully utilized. We present the example of a study of sawmill workers which was initiated to investigate the association between exposure to chlorophenates fungicides and mortality and cancer incidence. By linkage to other health databases, the cohort register has been or will be used to study outcomes such as non-cancer morbidity, fertility, birth defects, and childhood cancer. The effects of other exposures, including wood dust, noise, job strain, unemployment, and safety measures are now being examined. The data have also been used to describe historical employment patterns in the industry, and to examine the economic and ecological impact of technological changes in resource-based communities. Most of these studies required new funding, but at considerably reduced expense since one or more of the usual cohort study costs had been borne by the initial study.

EVOLUTION OF THE COHORT DATABASE

The original study

The cohort consists of 26,500 male workers employed in 1 of 14 British

Department of Health Care and Epidemiology, University of British Columbia
Correspondence: Dr. Kay Teschke, Department of Health Care and Epidemiology, University of British Columbia, 5804 Fairview Avenue, Vancouver, BC, V6T 1Z3, Tel: 604-822-2041, Fax: 604-822-4994, E-mail: teschke@unixg.ubc.ca

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TABLE I
Overview of Exposures and Outcomes Under Investigation in the Sawmill Cohort

Study Cohorts	Data Linkages Used	Exposures	Health Outcomes
The Original Study			
A. Sawmill workers employed 1950-1985 (n = 26,000)	BC Cancer Registry, Canadian Mortality Data Base	Chlorophenate fungicides as estimated for jobs by worker raters	Cancer incidence, mortality
Fertility and Birth Outcomes			
B. Offspring of sawmill workers born 1952-1988 (n = 19,700)	BC Marriage and Birth files, BC Health Surveillance Registry	Chlorophenate data from study A	Prematurity, low birthweight, stillbirths, neonatal mortality, birth defects among offspring
C. Cohorts from studies A and B	Birth files from study B	Chlorophenate data from study A	Fertility of sawmill workers
D. Cohort from study B	Birth files from study B, BC Cancer Registry	Chlorophenate data from study A	Cancer incidence among offspring
Additional Exposures			
E. Cohort from study A	Canadian Cancer Registry, update of Canadian Mortality Data Base	Softwood dust exposures of jobs as estimated by measurements and reconstruction of conditions	Cancer incidence, mortality
F. Cohort from study A	Mortality files from study E	Noise exposures of jobs, as estimated by measurements and reconstruction of conditions	Heart disease and injury mortality
G. Cohort from study A	Mortality files from study A, vital statistics from study B, coroner's records of traumatic fatalities, morbidity data from study J	Personal and job history data from studies A and B, machine guarding, safety training, protective equipment	Mortality from external causes, injury morbidity
Socioeconomic Determinants of Health			
H. Cohort from study A	Mortality files from study A	Job strain, as estimated by experts using demand-control model	Heart disease mortality
I. Cohorts from studies A and B	Mortality files from study A, birth files from study B	Job mobility, skill level of job, job security, reason for leaving sawmill job	All cause, traumatic, cardiovascular, alcohol-related mortality; birthweight, prematurity
J. Subset of sawmill workers from study A employed in 1979 (n = 11,200) and their offspring from study B	Mortality and cancer incidence files from study E, birth files from study B, BC Linked Health Data Base	Employment status, retraining	Mortality, physician and hospital service utilization cancer incidence, fertility, birthweight, prematurity

Columbia sawmills (11 on the coast, 3 in the interior) for at least one year between 1950 and 1985.⁷ Job histories and personal identifiers from personnel records were abstracted at each mill. Workers with at least 5 years of seniority were interviewed to estimate the fungicide exposures of each job at each mill over the entire period of chlorophenate use.⁸⁻¹⁰ In order to carry out this task, a history of fungicide use and technological change had to be reconstructed for each mill.¹¹ Outcomes were ascertained by probabilistic linkage of the cohort register to the Canadian Mortality Data Base and the BC Cancer Registry. Additional linkages with the pension, driver's licence, and income tax records were conducted to reduce the number of person-years in which vital status was unconfirmed.

Table I outlines the exposure, outcomes, and data linkages involved in this initial study, and in a similar way, describes the subsequent studies.

Fertility, birth outcomes, and childhood cancer

The literature suggested that chlorophenates and other dioxin-contaminated products might be linked to infertility in exposed workers and to birth defects in their offspring,¹²⁻¹⁵ therefore we developed means to ascertain the offspring of the sawmill cohort. Births are registered by the provincial Vital Statistics Division, allowing probabilistic linkage of fathers' names and birth dates on birth certificates to the cohort file. Mothers are more consistently reported on birth records than fathers, therefore we also linked the cohort register

to the provincial marriage files to allow more complete birth ascertainment. In this way, we identified 19,700 births to cohort members between 1952 and 1988.

Establishing the birth cohort allowed analyses of fertility among the sawmill cohort,¹⁶ as well as examination of certain birth outcomes routinely recorded in the Physician's Notice of Birth: gestational age; birthweight; stillbirth; and neonatal mortality.¹⁷ These outcomes were analyzed using the established job history and chlorophenate data to look for risks associated with exposure.

To determine whether specific birth defects were associated with paternal chlorophenate exposure,¹⁷ an additional data linkage was required, to the British Columbia Health Surveillance Registry. This unique data source was established in

TABLE II
Outcome and Exposure Information in the Sawmill Cohort Database

	Sawmill Workers		Workers' Offspring born 1952 to 1988 (n=19,700)
	Full Cohort employed > 1 yr 1950 to 1985 (n=26,500)	Sub-Cohort still employed in 1979 (n=11,200)	
Outcomes			
Mortality	✓ ¹	✓ ¹	
Cancer incidence	✓ ¹	✓ ¹	✓
Fertility	✓	✓	
Birthweight			✓
Gestational age			✓
Stillbirths			✓
Neonatal mortality			✓
Birth defects			✓
Physician services		~	→
Hospital services		~	→
Workers' compensation claims		~	→
School performance			→
Exposures			
Work history at 14 sawmills	✓ ¹	✓ ¹	✓ ^{1,2}
Chlorophenate fungicides	✓	✓	✓ ²
Substitute fungicides		→ ³	→ ²
Wood dust	~	~	→ ²
Noise	~	~	→ ²
Marital status	✓	✓	
Factors related to injury fatalities	✓	✓	
Machine type and guarding	~	~	
Safety training	~	~	
Personal protective equipment	~	~	
Job strain	~	~	→ ²
Job skill level	✓	✓	✓ ²
Job mobility within mills	✓	✓	✓ ²
Mill location	✓	✓	✓ ²
Reason for termination	✓	✓	✓ ²
Employment status	✓ ¹	✓ ¹	→ ²
Retraining		~	
Post-sawmill employment		~	

✓ Data gathering complete, analysis complete or in progress
~ Data gathering in progress for planned analyses
→ Data under consideration for use in future analyses
1 Update in progress
2 Paternal exposure
3 Data would be collected for a smaller sub-cohort still employed in 1989

1952 and uses over 60 registering sources to "ascertain, record, and classify handicapping conditions, congenital anomalies, and genetic defects in the population."¹⁸ These files are directly linked to the provincial birth files using a unique identifier.

Finally, cancer incidence in the offspring is currently being ascertained by linking the birth cohort file to the BC Cancer Registry, as was done previously for the sawmill workers cohort. Analyses will determine whether there are associations with chlorophenate exposures of the fathers.

Additional exposures

In 1995, the International Agency for Research on Cancer classified wood dust as a known human carcinogen, but the strongest evidence was from workers

thought to be exposed to hardwoods, and very little exposure-response data were available.¹⁹ The sawmills whose employees were enrolled in this cohort cut only softwoods, therefore the cohort provided an ideal opportunity to investigate cancer and mortality outcomes associated with these woods. To allow a quantitative exposure-response analysis, each mill will be revisited to reconstruct its technological history pertinent to wood dust exposure, and about half the mills will also be involved in an extensive inhalable and thoracic wood dust monitoring program. The exposure data gathered will be attached to job titles, so that each cohort member's cumulative exposure can be reconstructed through the existing job history. Mortality and cancer incidence data will be updated five years beyond the records used in the

chlorophenate study. The cancer incidence data will also be extended nationwide, using the Canadian Cancer Registry.

At the same time as the wood dust data are being collected, historical noise exposure will also be reconstructed, using similar methods. The objective of this study will be to examine the association of noise exposure to non-auditory health outcomes. In particular, increases in cardiovascular disease risk have been described, but the findings remain equivocal.²⁰ This study will address and overcome many of the methodological weaknesses which have hampered earlier studies (e.g., cross-sectional design, poor characterization of exposure, use of blood pressure or hypertension as the outcome)^{21,22} and should provide a better understanding of the putative link. The association between noise exposure and accident mortality²³ will also be examined.

In another study, the existing cohort mortality data have been used to identify those workers who died from external causes (traumatic injuries), both at work in the sawmills and off the job. The British Columbia Coroner's Service and Workers' Compensation Board records have been accessed to retrieve information about factors associated with these deaths. Comparison of rates will be possible for age, calendar year, marital status, number of children, sawmill jobs, and duration of sawmill employment, variables available from the original personnel records and the Vital Statistics linkages. Factors available only from the Coroner's or Compensation records will be examined descriptively since comparable data will not be available for denominator person-years. In addition, the data about sawmill operations being gathered for the wood dust and noise studies will include machine type, machine guarding, safety training, and personal protective equipment to allow future analyses of these potential determinants of injuries.

Socioeconomic determinants of health

During the years in which the cohort was developed and analyzed for cancer and reproductive outcomes, new concerns were raised regarding the long-term health impact of working conditions *per se*. In particular, job strain (i.e., the combination

of high-paced work with low levels of control over decision making and skill utilization) has been associated with heart disease.²⁴⁻²⁶ A panel of union and industry experts who evaluate sawmill jobs for the purpose of wage adjustment and adjudication will be asked to rate the strain associated with each of the jobs held by cohort members using a model which combines information on three dimensions: psychological demand; control; and social support.²⁷ This study will investigate the effect of job strain on coronary heart disease mortality.

An epidemiologist in our study group who is also a historian by training (AO) pointed out that the cohort register provided a useful source of data on the economic history of the sawmill industry in British Columbia, including patterns of employment, unemployment, and within-mill job mobility; changes in the industry job structure between production jobs and support and maintenance functions; and changes in the demography of the workforce.²⁸ Two studies were then initiated to examine whether there were health impacts related to these changes in the economic structure of the industry.

The first was designed to use existing data to look for variations in alcohol-related, smoking-related, accidental, violent (including suicide), and cardiovascular death rates among the sawmill workers, as well as variations in prematurity and low birthweight among their offspring. The exposures examined were length of time worked at each job, number of jobs held per unit time, skill level of the jobs held (i.e., management, maintenance, skilled production, unskilled), direction of job mobility, type of job security (i.e., permanent, casual, part-time), and reason for leaving sawmill employment (i.e., voluntary or not). We also examined systematic differences in mortality between individual mills; between mills and their local community; between groups of mills in urban versus rural settings; and between mills in established communities versus single-industry "boom towns".

A second study was designed to examine a sub-cohort of 11,200 workers who were employed in 1979. This group was subject to dramatic changes in the industry in the

early 1980s, when many sawmill processes were automated, log supplies were reduced, and the provincial economy was undergoing a recession. By 1985, only 5,300 of these workers were still employed in the 14 cohort sawmills. The objectives of this study are to compare the mortality, morbidity, and health care services utilization of those who remained employed versus those who were laid off and then permanently reemployed or who were laid off and since have been chronically underemployed. Cancer incidence and fertility among the sub-cohort members, and birthweight and prematurity of their offspring will also be examined.

In order to study the morbidity and health care utilization outcomes, a new probabilistic linkage will be required, to another special database recently developed in British Columbia. The Linked Health Data Base includes data about all physician visits and hospitalizations charged to the provincial medical insurance fund, which covers virtually all persons resident in the province for at least three months. To retrieve the exposure data, we will update the sawmill register from personnel files for the period 1986 to 1996. In addition, each of the 11,200 sub-cohort members will be mailed a questionnaire to ascertain their employment and retraining history in the period from 1979 to the present.

Our completed and planned analyses have not exhausted the possibilities for examining the determinants of health of the sawmill workers, using either the current data set or additional data yet to be collected or linked. For example, we are considering using morbidity data from the Linked Health Data Base to study acute and sub-chronic effects of fungicides which were introduced in 1989 as substitutes for chlorophenates (Table II).

DISCUSSION

Table II summarizes the outcome and exposure information held or being developed for the sawmill cohort database. Although some of the outcomes investigated among the sawmill workers and their offspring are likely to be exceptional because of special data resources available in British Columbia, many were made pos-

sible by linkages to birth, marriage, and death files which are available in most jurisdictions. Cancer registries are becoming more common and hospital discharge data are increasingly accessible. It is also likely that in some other areas of the world, there are unusual data resources which may allow extension of outcome analyses previously unforeseen.

Unlike many other studies, our focus has included not only exposures specific to the industry such as wood dust and fungicides, but also more ubiquitous ones such as noise, job strain, job mobility patterns, job skill level, employment status, and demographic characteristics of the workforce. Although not all the exposures currently under investigation were included in our original vision of the study, most are based on the job history gleaned from personnel files in the original cohort ascertainment. Wedding the job history to each additional exposure under consideration has required significant new expenditures for exposure assessment, using established methods. In retrospective cohort studies, where exposure measures are linked to employees through the intermediary of their job titles, jobs are often grouped where exposures are expected to be similar. In studies where multiple exposures are to be assessed, groupings may not be appropriate for every exposure, therefore information transcribed from personnel files must be retained in such a way that each discrete job title may be identified.

A concern that may arise is the issue of multiple comparisons using the same dataset. Assuming that there is a legitimate *a priori* reason for interest in the exposure and the outcome, the additional analyses described here should be no more or less valid than those carried out to test the original study hypotheses, provided they are done with equal care. Interpretation of the results should be as in any epidemiological study, that is within the context of all the evidence, considering in particular the strength of association and consistency with the literature. However, it would not be acceptable to browse the data for associations, use this information to develop hypotheses, elaborate the exposure or disease in more detail, then confirm the hypothesis using the same dataset.

There are ethical considerations in mounting a series of studies of the same cohort. In Canada at least, historical cohort studies which use employment records as a sampling frame do not require consent from individual cohort members. Instead, they require consent from their employment representatives, including unions and company managers, and from the guardians of the health outcomes databases with which the personnel data is linked. This requires assurances that individual identifying information will not be published, and in fact will be destroyed once no longer required for data linkages. Studies such as those described here require that the personal identifiers be held for considerable lengths of time, therefore data management procedures should be reviewed by investigators at each new stage of the study.

There are many benefits of diversifying the uses of occupational cohort data. Greatly reduced costs of subsequent studies is one. It may be of interest to compare the relative costs of the various components of the sawmill cohort study. Fertility and birth outcomes were added for about one-quarter the cost of the original study. Studies of all the additional exposures combined (wood dust, noise, job strain, and injury determinants) will cost about one-half as much as the original study, as will the studies of the socioeconomic determinants of health.

More importantly, adopting a broader vision offers the opportunity to study processes other than carcinogenesis which have long latent periods, or are associated with long-term exposure. In addition, these studies allow researchers to develop a much more complete picture of the demographics and health of the workforce they are studying. A more thoroughly examined cohort may allow us to understand the relative importance of specific worksite exposures versus more prevalent exposures, such as unemployment or job strain, informa-

tion which would be extremely valuable for policy making. Such investigations merge interdisciplinary interests within one study population. Even within occupational health, it is not uncommon for reproductive epidemiologists to examine different populations than cancer or cardiovascular disease epidemiologists. Here, studies of multiple outcomes and exposures have evolved from the same cohort, promising a more comprehensive model of the determinants of health and well-being among workers and their communities.

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