Case Studies in Occupational Epidemiology

Edited by

Kyle Steenland

Case Studies in Occupational Epidemiology

This page intentionally left blank

Case Studies in Occupational Epidemiology

Edited by

KYLE STEENLAND

New York *Oxford*
OXFORD UNIVERSITY PRESS
1993

Oxford University Press

Oxford New York Toronto
Delhi Bombay Calcutta Madras Karachi
Kuala Lumpur Singapore Hong Kong Tokyo
Nairobi Dar es Salaam Cape Town
Melbourne Auckland Madrid

and associated companies in
Berlin Ibadan

Published by Oxford University Press, Inc.,
200 Madison Avenue, New York, New York 10016

Oxford is a registered trademark of Oxford University Press

Library of Congress Catalog-in-Publication Data
Case studies in occupational epidemiology / edited by Kyle Steenland.
p. cm. Includes bibliographical references and index.
ISBN 0-19-506831-9
1. Occupational diseases—Epidemiology—Case studies.
2. Occupational diseases—Epidemiology—Examinations, questions, etc.
I. Steenland, Kyle, 1946– .
[DNLM: 1. Epidemiologic Methods—problems.
2. Occupational Diseases—epidemiology—problems.
WA 18 C337]
RC964.C285 1993
614.4'0722—dc20 DNLM/DLC
for Library of Congress 92-6175

1 2 3 4 5 6 7 8 9

Printed in the United States of America
on acid-free paper

Preface

The purpose of this book is to provide material for teaching epidemiology. Thirteen case studies are arranged in four parts (cohort studies, case-control and proportionate mortality studies, cross-sectional studies, and surveillance and screening studies). Each part begins with a description of the general study design. The case studies are based on actual epidemiologic studies and have been written by the respective principal investigators. It is hoped that they preserve the flavor of the practical problems confronted by the working epidemiologist.

A broad range of etiologic studies is considered, and all major study designs are well represented. In addition, the chapters on surveillance give the reader practical examples of how public health practitioners can use surveillance data to develop effective interventions. The case study on screening illustrates the issues involved in screening a population at high risk of bladder cancer due to occupational exposure.

The book deals with a wide variety of disease outcomes, including spontaneous abortion, carpal tunnel syndrome, kidney dysfunction, cytogenetic changes, ischemic heart disease, dermatitis, chronic renal disease, and several types of cancer. The exposures of interest are equally diverse, including VDT use, repetitive hand-wrist motion, heavy metals, carbon monoxide, diesel exhaust, lead, vinyl chloride, pesticides, solvents, silica, and acid mists. These outcomes and exposures represent many of the current topics of interest in occupational health.

While the case studies are occupational in nature, the principles involved are the same as for any type of epidemiologic study. Thus, the book can be used in general courses on epidemiology as well as in higher-level courses on occupational epidemiology.

Each case study, arranged in the same format, attempts to take the reader through the same steps that the investigator took when conducting the actual study. The student is asked to solve the same problems that the investigator solved in the course of the study. Each case study includes questions regarding

study design, identification and measurement of exposure, problems of data collection, analytical issues, and issues of interpretation. Answers are provided at the end of each chapter. Many of the cases also include analytical exercises suitable for classroom use.

The book is designed so that most calculations can be done with a pocket calculator. Measures and statistics required for answering analytical questions in the text are presented in the Appendix. Optional questions based on multivariate analyses using either linear or logistic regression (requiring a computer) are also offered in several of the case studies.

Data sets are attached to five of the case studies. For three others the data sets were too large to include in the text. However, course instructors using this text may obtain all eight data sets as ASCI files on diskette from the editor.

This book is a collaborative effort. Seven of the case studies have been written by other investigators, albeit with some editing by myself. I bear sole responsibility for six of the studies, as well as for the introductions and the Appendix. Alberto Salvan and Deanna Wild kindly helped check some of the calculations.

Cincinnati, Ohio K. S.
May 1992

Contents

Contributors

MICHAEL O'MALLEY, MD, MPH
California Environmental Protection Agency
Department of Pesticide Regulation
Sacramento, California

ANA OSORIO, MD, MPH
California Department of Health Services
Berkeley, California

TERESA SCHNORR, PhD
National Institute for Occupational Safety and Health
Cincinnati, Ohio

KYLE STEENLAND, PhD
National Institute for Occupational Safety and Health
Cincinnati, Ohio

FRANK STERN, MS
National Institute for Occupational Safety and Health
Cincinnati, Ohio

MICHAEL THUN, MD, MS
American Cancer Society
Atlanta, Georgia

ELIZABETH WARD, PhD
National Institute for Occupational Safety and Health
Cincinnati, Ohio

This page intentionally left blank

Case Studies in Occupational Epidemiology

This page intentionally left blank

Part I Cohort Studies

In a cohort study the investigator defines a cohort of nondiseased, exposed individuals and a cohort of nondiseased, nonexposed individuals (the comparison or referent population) and follows them over time to determine disease incidence. Cohort studies can be either prospective or retrospective. In a prospective study the subjects are identified in the present and followed into the future. For example, a sample of the population of Framingham, Massachusetts, free of heart disease and aged 30–59, was enrolled in 1950–1952 in a now famous prospective study (Dawber et al., 1951). A variety of risk factors for heart disease were measured at that time (enabling investigators to divide the population by "exposure" status, such as high blood pressure versus low blood pressure). The population has since been followed to determine the incidence of heart disease.

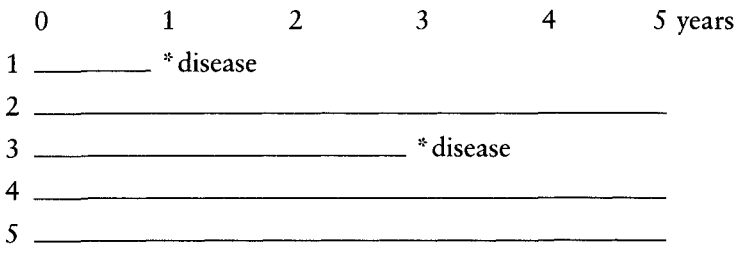
Retrospective cohort studies identify exposed and nonexposed populations at some point in the past and then determine who among them has developed disease. For example, to determine the association between carbon monoxide and heart disease, workers exposed to carbon monoxide while working in tollbooths outside the entrances to tunnels of Manhattan before 1965 were identified by government investigators in the mid-1980s (Stern et al., 1988). Their heart disease mortality through 1984 was subsequently determined and then compared to the general population of a similar age, race, and sex distribution. Retrospective cohort studies are often advantageous because the investigator does not need to wait many years for an appreciable number of individuals to get the disease of interest. On the other hand, in retrospective cohort studies investigators are often unable to obtain precise information on level of exposure or other risk factors (e.g., blood pressure or smoking) since the exposure occurred in the past, and since the cohort may now be dispersed and difficult to contact.

Cohort studies are most useful in the study of rare exposures and common diseases. Rare exposures can be studied by choosing the specific group that has been exposed, even if the exposure is uncommon in the general population. For

example, exposure to vinyl chloride gas is uncommon in the general population, but one could study one or several manufacturing plants where vinyl chloride is produced to obtain a fairly large population. Rare diseases are a problem in cohort studies, because even if a large cohort is assembled only a few cases may occur, limiting the ability of the investigator to detect a difference between exposed and nonexposed groups. Suppose, for example, that one wanted to study end-stage renal disease among workers exposed to solvents. A cohort of solvent-exposed workers might have to number in the hundreds of thousands for many cases of end-stage renal disease (male incidence about 10/100,000) to be observed.

Cohort studies also have the advantage that more than one disease can be studied, so that the possible association of the exposure of interest with a given disease can be evaluated for a multitude of diseases simultaneously. Even though a particular exposure–disease association has been hypothesized a priori, a posteriori data analysis may uncover unexpected exposure–disease associations.

Cohort studies may address either the proportion of the study population exposed over time (cumulative incidence) or the rate of disease among the study population (incidence rate, or incidence density rate). The former measure is based on "count" data while the latter measure uses person-time data. Consider the data for the five hypothetical individuals below:



Cumulative incidence is defined as follows:

$$\text{C.I.} = \frac{\text{Number of new cases of disease during a defined period}}{\text{Total number of people at risk of disease}}$$

The incidence rate is defined as follows:

$$\frac{\text{Number of new cases of disease during a defined period}}{\text{Person-time at risk}}$$

In this example, the cumulative incidence is 2/5, or 0.40, while the incidence rate is 2 cases/19 person-years at risk, or 0.11. With incidence rates individuals can enter the study at any time, can contribute unequal numbers of person-years, and can also be lost to follow-up before the study end. Cumulative incidence, on the other hand, is often calculated in situations where everyone is

followed for the same length of time with minimal or no loss to follow-up. Cumulative incidence is most appropriate for studies with short follow-up periods. When considering the disease incidence in an exposed and versus a nonexposed population, relative risks may be calculated from cumulative incidence data while rate ratios may be calculated from incidence rates.

Three cohort studies are described in Part I. The first is a retrospective cumulative incidence study of spontaneous abortion among women working with video display terminals (VDTs). The follow-up period in this study is only a few years. The second is a retrospective cohort mortality study of workers exposed to carbon monoxide, focusing on heart disease as the outcome of interest. The third is a retrospective cohort incidence study of larynx cancer among men exposed to sulfuric acid. Both the second and the third studies involve long follow-up periods and are based on person-time data.

References

Dawber T, Meadors F, Moore F. Epidemiologic approaches to heart disease: the Framingham Study. Am J Public Heath 41: 279–286, 1951.

Stern F, Halperin W, Hornung R. Heart disease mortality among bridge and tunnel officers exposed to carbon monoxide. Am J Epidemiol, 128, 6: 1276–1288, 1988.

This page intentionally left blank

Chapter 1 Video Display Terminals and Adverse Pregnancy Outcomes

TERESA SCHNORR

Video display terminals (VDTs) were first associated with adverse reproductive outcomes in 1980, when a cluster of birth defects was observed among women using VDTs at the Toronto *Star* newspaper. This report was followed by a number of other adverse pregnancy outcome clusters, primarily spontaneous abortion, but including other adverse outcomes such as stillbirths, low birthweight, and preterm birth (Berquist, 1984).

Three different hypotheses were proposed as possible explanations for the clusters: (1) physical stress (defined as prolonged sitting), (2) psychological stress due to the demands of the work environment, and (3) electromagnetic energy emissions (Tell, 1990). As of 1984, no epidemiologic studies of VDT and pregnancy outcome study were underway in the United States, and the literature contained little information on the potential hazards of VDTs. While physical stress, defined as heavy lifting, had been associated with an increased risk of preterm birth (Mamelle et al., 1984), the association with work posture (sitting versus standing) had not been studied. There was little information about the potential effect of workplace psychological stress on reproductive function, although two studies had shown an association between a measure of occupational mental stress and premature birth (Mamelle et al., 1984; Naeye and Peters, 1982). No animal or human studies had been conducted of the potential reproductive hazards of electromagnetic fields produced by VDTs. These electromagnetic fields were of two types, ELF (extra-low frequency) and VLF (very low frequency). These two frequencies are in the lower end of the electromagnetic spectrum, below radio waves or microwaves. ELF fields are also produced by common 60 Hz wiring in houses and appliances. Studies of the reproductive effects in animals exposed to ELF and VLF were just beginning.

Because of the large number of women using VDTs in the workplace and the public concern, the National Institute for Occupational Safety and Health

(NIOSH) decided to conduct a study to determine if VDTs posed a risk for pregnant women. The focus was to be on spontaneous abortions, but researchers wanted to investigate other possible adverse outcomes as well (low birthweight, birth defects, stillbirth, and preterm birth).

QUESTION 1. What would be the most appropriate design for a study of spontaneous abortion and other outcomes among VDT users: case-control, prospective cohort, or retrospective cohort? How would you determine the outcome(s) for each type of study?

QUESTION 2. What would be your principal definition of exposure for a study of spontaneous abortions among VDT users? How would your study design take into account all the hypothesized exposures of interest (electromagnetic fields, physical and psychological stress)?

QUESTION 3. How would you calculate the estimated number of women needed in the exposed and nonexposed populations (assume a 1-to-1 ratio) for the proposed study design? Sketch out an approach to the answer; you do not need to do actual calculations.

QUESTION 4. What are the important confounders to consider in such a study?

Materials and Methods

The investigators decided to conduct a cohort study in a population of telephone operators. Reproductive histories were to be obtained via telephone interview. Medical confirmation of reported spontaneous abortions would be sought.

One type of operator, the directory assistance operator, used a VDT for the entire work day. The comparison group was made up of general operators who did not use VDTs. Both groups shared the same degree of physical and psychological stress.

Directory assistance operators used the VDT to locate telephone directory information and provide it to customers who called in. A computer automatically routed incoming calls to the next available operator, so the time between calls was brief. Operators usually had less than a second between calls. Operators were monitored by the computer, which recorded their number and length of calls. They were also monitored by their supervisors.

The general operator, the operator reached by dialing "0," had duties similar to those of the directory assistance operator. General operators assisted customers in placing long-distance calls, among other duties. General operators

did not use a VDT; they used a light-emitting diode (LED) or neon glow tube (NIXIE tube) screen. Like the directory assistance operators, the general operators were monitored by a computer and by their supervisors, and calls were automatically routed to the next available operator so that the time between calls was usually less than a second.

Both jobs required the same education and skills, and salaries were similar. Both operator groups had duties that required that they sit for seven hours a day in front of their respective equipment. Both groups also had jobs that included customer contact and both machine and human monitoring. While there may have been some differences in work practices between the two groups, the primary difference was the presence or absence of the VDT.

Two companies with both exposed and nonexposed operators were tentatively identified for the study. A study period was defined as 1/1/83–7/1/86.

There were 5,544 operators (exposed and nonexposed) employed between these dates at the two companies. To maximize the number of pregnancies, women were required to have been between 18 and 33 years of age during the study period. To be eligible for the study, a woman had to have been employed and married at some point during this period. Furthermore, the operator had to have been pregnant and employed for at least one day during the first 28 weeks of gestation, and the pregnancy had to terminate between January 1, 1983, and December 1, 1986 (the follow-up period). The date of the last menstrual period, obtained during interview, was considered the beginning date of each pregnancy.

Addresses and telephone numbers of potential study participants were obtained from company records. Addresses were checked against post office and IRS records to obtain updated addresses. A letter describing the study and requesting participation was sent to each potential participant. This letter was followed up by a phone call in which it was determined whether the woman had been married during the study period, and if she had been pregnant while employed at the company. If so, a 25-minute home telephone interview was conducted, in which a reproductive history during the study period was obtained.

Unfortunately, approximately 50% of the cohort had outdated telephone numbers. Locating current phone numbers was hampered by two factors: (1) women tended to list their phone numbers under their husbands' names, and (2) a benefit of working for the phone company was receiving an unlisted phone number at no extra charge. Investigators found 40% of the missing phone numbers through directory assistance, often using information on the husband's first name which was received in the IRS verification process.

QUESTION 5. How would you go about obtaining phone numbers for the remaining 30% of the cohort.

QUESTION 6. How would you define a spontaneous abortion? What would you do about induced abortions? Ectopic pregnancies? Twins?