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Accounting for Measurement Errors in Epidemiological Studies

by

Ranjeeta Mallick

A thesis submitted to the Faculty of Graduate Studies and Research
in partial fulfillment of
the requirements of the degree of
Master of Science

Department of Mathematics & Statistics

Carleton University

Ottawa, Ontario

October 15, 1996

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ISBN 0-612-19542-2

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Accounting for Measurement Errors in Epidemiological Studies

submitted by

Ranjeta Mallick

in partial fulfillment of the requirements
for the degree of Master of Science

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Carleton University
October 15, 1996

Abstract

Numerous cohort mortality studies of underground miners exposed to radon daughters in the air of mines have shown an increased risk of lung cancer in comparison with nonexposed populations. Case-control studies of the potential lung cancer risks associated with radon gas in homes, where exposures are much lower than in mines, have provided less consistent results. These epidemiological studies have inherent limitations due to errors in exposure assessment. Both errors in exposure measurement and incomplete measurements contribute to inconsistencies of current residential radon studies.

In this thesis, we focus on measurement error and its effects on risk assessment in epidemiological studies. We review recent statistical methods that deal with the measurement errors in epidemiological data. Through a simulation study on Colorado miners data, we evaluate the properties of the distribution of the dose-response parameter in two cases: (i) when exposure error is not accounted for, and (ii) when exposure rate is taken into account. We also analyze the robustness of a suggested approach for accounting for measurement error in this context. Next, dealing with residential radon concentrations in homes in Winnipeg, Canada, we determine correction factors to account for seasonal variation in radon measurements. We compare two models (the seasonal correction factor model and the multiplicative model) to predict yearly radon concentrations based on observations for the first six months only.

Acknowledgement

First and foremost, I wish to express my sincere thanks and appreciation to my thesis supervisor, Professor Daniel Krewski, whose continued guidance, support and patience made this thesis a manageable effort.

I am very much grateful to Dr. Jan Zielinski of Health Canada for all the time he has spent working with me throughout my thesis work and his valuable guidance.

I am grateful to my family members who showed their support in my efforts with continued interest and encouragement.

Finally, I would like to thank Mr. Ed McMullen of Health Canada for helping me with my computer related problems.

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Chapter 1

Introduction

1.1 Background and Motivation

Measurement error is one of the important causes of bias in epidemiology. Errors in measurement are introduced during almost all phases of a study, data collection being one of the most vulnerable phases. The method chosen does not always provide maximal accuracy within the bounds of the investigator's resources and other practical limitations. Another source of error in exposure measurement is faulty instrumentation. Results can vary not only between two instruments which measure the same exposure, but also for a single instrument depending on the conditions of use. Errors can occur during data entry and analysis.

In epidemiology, past exposures are important, and there are often no ideal records that can provide the data required. The person providing subjective data may either be the subject of the study or a proxy respondent. Subjective responses are prone to different sources of error. Data on exposure provided by proxies are prone to all the errors of data provided by the subjects themselves and perhaps some additional ones. Sometimes, records that have not been collected specifically for the purpose of measurement of

exposure may be used in the study. The records are themselves prone to error. A record may be incomplete or in error, or perhaps not even made. Records may be lost or altered.

Because of measurement error, both the mean and variance of the measured exposure differs from the true exposure mean and variance. Measurement errors also have an effect on the observable mean and variance of an exposure variable within a population. Of greater concern, however, is the effect of exposure measurement error on the measure of association between an exposure and an outcome in a study. Differential measurement error can have an effect on correlation or regression coefficients.

Although both natural and man-made alpha-emitting radionuclides in our environment can pose a risk to human health, natural sources account for the largest contribution to human exposure. Among the natural sources, inhaled radon and radon decay products are the largest contributors to population exposure and might be responsible for a large number of lung-cancer deaths each year [28]. For estimation of risks associated with exposure to the alpha-emitting radionuclides, the most important human populations examined are the underground miners who are exposed to widely different concentrations of radon-222 progeny. Numerous studies of underground miners exposed to radon daughters in the air of mines have shown an increased risk of lung cancer in comparison with nonexposed populations [28]. Research in the United States and other countries has also provided data on concentrations of radon and radon progeny in homes. A few exploratory epidemiological investigations of the lung-cancer risk associated with radon daughter exposure in homes have been carried out, but the study populations have been small and the results inconclusive.

Epidemiological studies reported to date have not clearly shown an association between residential exposure to radon and its decay products and lung

cancer risk, even though studies of underground miners exposed to radon, as well as experimental studies in animals, have shown that radon causes lung cancer [28]. Some have interpreted this seeming inconsistency as evidence that (1) exposure to radon progeny at the levels typically found in homes does not cause lung cancer, (2) exposure to radon progeny in homes causes lung cancer, but not to the extent estimated from risk models based on miners, or (3) risk among miners is dominated by smoking or other exposures in mines and risk models based on miners are therefore not applicable to residential exposures.

Many epidemiological studies of environmental radon and lung cancer are currently underway worldwide [22, 29]. The epidemiological studies have inherent limitations due to errors in estimates of exposure to indoor radon. These errors take on special significance because the level of residential risk predicted from studies of underground miners is relatively low and possibly at the limit detectable by current epidemiological methods [22]. Errors in exposure assessment and incomplete measurements contribute to inconsistencies of current residential radon studies. The presence of random errors in dose estimates often cause systematic biases in estimates of risk, thus causing underestimation of radiation effects in dose-response analyses.

1.2 Contributions of the Thesis

The primary focus of this thesis is on measurement error and its effects on risk assessment in epidemiological studies. The epidemiological studies we consider are the ones which deal with risk assessments in subjects, especially uranium miners, who are exposed to occupational exposure to radon daughters. Also because radon gas is found in indoor air, some studies dealing with residential radon exposure are also considered. The main contributions

of the thesis are summarized below.

- 1.) Apart from reviewing the sources of measurement errors, their effects on measurement, and ways to reduce their impact, we analyzed three recent methods (Mitchell *et al.* (1993) [25], Lubin (1996) [23], and Thomas (1994) [38]) that deal with measurement errors in the estimation of radiation dose exposure in underground miners.
- 2.) Colorado miners data are analyzed to study the effect of errors on the estimation of the radiation dose-response relationship. Through a simulation study, we evaluate the properties of the distribution of the dose-response parameter in two cases: (i) when exposure error is not accounted for, and (ii) when exposure rate is adjusted for measurement error. Furthermore, we also analyze the robustness of a suggested approach for accounting for measurement error.
- 3.) Radon levels in homes in Winnipeg, Canada were monitored using two six-month periods integrated readings in which significant differences were found among measurements taken during different seasons of the year. In order that the measurements can be comparable among each other and be able to reflect average annual concentrations, some corrections are required. Dealing with residential radon concentration in homes in Winnipeg, we estimate correction factors to account for seasonal variation in radon measurements and to predict yearly observation using only six months of data. We compare two models (the seasonal correction factor model and the multiplicative model) to predict yearly radon concentration using only six months period of observation.

1.3 Organization of the Thesis

The organization of the thesis is as follows. Chapter 2 gives an overview of measurement errors in epidemiology. Various measurement error terminologies taken from the epidemiological literature are defined. Sources of errors in measurement, introduced in all phases of a study, are discussed in considerable detail. Later in this chapter, a basic regression model is given to describe measurement error. Finally, impacts of measurement errors on exposure measurement are briefly discussed along with the ways to reduce the impact of measurement errors.

Chapter 3 describes three recent methods that deal with the estimation of radiation dose exposure in epidemiological studies. The first method, suggested by Mitchell *et al.* [25], estimates occupational radiation dose to individuals using weekly dosimetry data at Oak Ridge National Laboratory. The second method, suggested by Lubin [23], considers the effects of exposure measurement error in the underground miner data on the estimation of excessive relative risk and the identification of age, time since exposure and the inverse dose rate effect. The third method, suggested by Thomas [38], characterizes the relevant features of the distribution of true radiation exposure for a miner given his/her measured dose.

In Chapter 4, we study the effect of errors on the estimation of the radiation dose-response relationship using data in Colorado miners. For this purpose, we conduct a simulation study to evaluate the properties of the dose-response parameter in two cases: (1) when exposure error is not accounted for, and (2) when exposure rate is adjusted for measurement error. We use an approach, recently suggested by Lubin (1996) [23], to account for measurement error in the original exposure data. We also analyze the robustness of the suggested approach of adjusting for measurement error.

Chapter 5 deals with residential radon and lung cancer cases in Winnipeg, Canada. Radon levels in homes were monitored using two six-month periods integrated readings using CR-39 alpha track detectors. Significant differences were noted among measurements taken during different seasons of the year. In order that the measurements are comparable among each other and are able to reflect average annual concentrations some corrections are required. In this chapter, based on a similar approach by Pined *et al.* (1994) [32] to deal with indoor radon measurement in the United Kingdom, we estimate correction factors that will seasonally adjust measurements taken over other periods for the Winnipeg data.

Chapter 6 summarizes the thesis and lists some of the issues and limitations encountered during the analysis. Areas for future work are also identified.

Chapter 2

Measurement Errors: An Overview

2.1 Introduction

The main objective of this chapter is to give a comprehensive review of measurement errors in epidemiology. This chapter begins with an overview of cohort and case-control studies and outlines some of their fundamental differences. Various measurement error terminologies taken from epidemiology are then defined. Sources of error in measurement, introduced in all phases of a study, are discussed in detail. Later in this chapter, a basic regression model is given to provide a statistical basis for the evaluation of measurement error. Finally, impacts of measurement errors on exposure measurement are briefly discussed, followed by the ways to reduce the impact of measurement errors.

2.2 Epidemiological Studies

There are two basic approaches to investigating the causes of disease. One that works from cause to effect is called the *cohort study*; the other that proceeds from effect to cause is called the *case-control study*.

2.2.1 Cohort Studies

In a cohort study, individuals are selected for observation and followed over time. Selection may depend on the presence or absence of certain characteristics that are thought to influence the development of disease, or it may be at random within some target population, effectively yielding a sample of individuals who vary with respect to their exposure to one or more risk factors of interest.

2.2.2 Case-Control Studies

In a case-control study, individuals with a particular condition or disease (the *cases*) are selected for comparison with a series of individuals in whom the condition or disease is absent (the *controls*). Cases and controls are compared with respect to existing or past attributes or exposures thought to be relevant to the development of the condition or disease under study.

2.2.3 Cohort vs Case-Control Studies

The major difference between the cohort and the case-control studies is in the selection of study subjects. A cohort study selects subjects who are initially free of disease and follows them over time to determine the rates of disease in the presence or absence of exposure. By contrast, the case-control study selects subjects on the basis of the presence or absence of the disease under study. Both approaches allow one to estimate the effect of exposure on the

risk of disease in terms of relative risk parameter.

The case-control approach is useful in the study of rare diseases. In such situation, a cohort study is inefficient, because virtually all of the effort is devoted to follow-up of individuals who remain free of the study disease.

The case-control study is also most appropriate for studying diseases with long latency. An investigator using the case-control approach studies persons who have already developed the disease of interest, so that there is no need to wait for time to elapse between an exposure and the manifestation of disease.

2.3 Measurement Error Terminologies

Measurement error is one of the important causes of bias in epidemiology. It is obvious that any deviation from the actual measurement can sometimes produce misleading results about the relationship between exposure and disease.

In order to understand the measurement error properly, we now define certain terms, *exposure*, *measurement*, *measurement procedure*, *exposure measurement error*, as used in the epidemiological literature. Detailed discussions on these terms can be found in [2].

2.3.1 Exposure

The term *exposure* denotes any of a subject's attributes or any agent with which he/she may come in contact that may be relevant to his/her health. In other words, exposure may consist of the agent that may cause a physiological effect or that may cause or protect from disease. Exposure also includes agents that may confound the association between another agent and a disease or physiological effects or may modify the defects of other agents.

Exposure sometimes consists of agents that may determine the outcome of the disease. Exposure may also include certain host factors, whether solely genetic or resulting from the interaction between genetic and environment factors, and measures such as socio-economic status.

Exposure is often given a quantitative rather than a qualitative connotation. It may designate the amount of an agent with which the subject has come in contact.

2.3.2 Measurement

In general, *measurement* is regarded as a classification of objects and events in which a certain indicator (e.g., numeral, letter, or word, etc.) is assigned to each defined class according to a specified rule.

One cause of instability in the collected data is the failure of field workers to follow operational methods of measurement. A method of measurement is considered operational if instructions for use of the method is understandable to other investigators who may wish to follow, and if there is a demonstration (at least a pilot study) to show that measurements resulting from this method are reproducible.

When the variable of real interest, the true exposure, is not directly measurable, some of its indirect indicators are measured.

2.3.3 Measurement Procedure

The term, *measurement procedure*, refers to a procedure or set of procedures designed to measure one or several of the variables of interest in an epidemiological study. Hence, sometimes the term, measurement method, is used. This includes

- self-administered questionnaires,
- personal interviews,
- biochemical analysis of biological specimens (e.g., blood), and
- physical or chemical analysis of the environment

The measurement method involves all aspects of the measurement process involving individual subjects, including

- instructions for application of the main measurement method,
- the method itself, and
- specification of procedures that follow application of the main method for analysis.

A measurement method with all the procedures outlined above should be written down in such detail that any investigator should be able to reproduce the measurements obtained by another using only this written description.

2.3.4 Exposure Measurement Error

The *exposure measurement error* for an individual can be defined as the difference between the measured exposure and the true exposure. The true exposure is the agent of interest and includes a specified time period in which the exposure could have caused the disease. Measurement error can be random or systematic. If the errors of measurement are in some sense systematic and not random, one would expect some sources of bias each time a measurement is taken. *Validity* refers to the capacity of an exposure variable to measure the true exposure in a population of interest. Measures of validity represent the measures of exposure measurement error in a population. When exposure measurement error differs according to the disease or outcome being studied, it gives rise to *differential exposure measurement error*.

2.3.5 Assessment of Risk

An assessment of the risk of disease is best made in terms of the number of new cases that occur during a specified period of time - the *incidence*. To adjust for the size of the population at risk and the duration of time at risk, two distinct measures of disease occurrence may be calculated, both commonly referred to as the *incidence rate*. The first, sometimes termed the *incidence rate*, or the *attack rate*, is the proportion of persons in a subgroup, initially free of disease, who develop the disease within a specified time interval. The second measure of disease occurrence, variously termed the *incidence rate*, the *person-time incidence rate*, the *instantaneous incidence rate*, is the number of new cases divided by the population-time (e.g., person-years of observation) over which they occur.

Relative risk represents how many times more (or less) likely disease occurrence is in the exposed group as compared with the unexposed. The odds ratio is another measure of association that is closely related to the relative risk. The ratio of the odds of disease in exposed individuals relative to the unexposed is called the *odds ratio*. The distinction between relative risk and odds ratio is now well known, although the terms were often used interchangeably in the early epidemiologic and statistical literature. The odds ratio is particularly important for two reasons. First, for rare diseases, it closely approximates the relative risk. Second, the odds ratio can be determined from either a cohort or a case-control study, whereas the relative risk can be exactly determined only from a cohort study, although it can be estimated from a case-control study by use of odds-ratio approximation.

2.4 Sources of Errors in Measurement Techniques

Exposure measurement has become more complex with the growth of the study of non-infectious diseases. Because there may be no single identified cause for the disease under study, because a single component may have small contribution, and because the interval from onset and cessation of exposure to appearance of disease is often measured in years, the agent of disease may leave no easily measurable indicator of past exposure. The range of agents of interest has increased substantially.

The objective of exposure measurement is to obtain measurements that are necessary to meet the research objectives. This will mean measurement of the variables defined by the study hypotheses, measurement of any known or suspected confounding variables, and measurements of variables that may be thought to modify the effects of the main causal variables. For each exposure variable, the objective of measurement is to obtain measurements that maximize validity or minimize error.

Error in measurement can be introduced during almost all phases of a study, with data collection being one of the most vulnerable phases. A method providing more satisfactory information is often a more elaborate, expensive or inconvenient one for practical purposes. But, the method chosen should be able to provide the maximal accuracy within the bounds of the investigator's resources and other practical limitations.

In epidemiology, past exposure is of prime importance, and there are usually no records that can provide the data required [2]. The person providing subjective data may either be the subject of the study or a proxy respondent. Subjective responses are prone to different sources of error including, among others

- lack of understanding of the tasks by the subject,
- failure in recall of the required data and influence of recent exposure on memory of past exposure,
- tendency of the subject to over-report socially desirable behaviours and under-report socially undesirable behaviours, and
- short term variability in biological characteristics.

These factors tend to lead to systematic errors, although lack of understanding would also introduce random error.

The use of proxy respondents, that is, people who provide information on exposure in place of the subjects themselves, is an important variation on the subjective methods of exposure measurement. Proxy respondents are used when the subject of study are for some reason (e.g., death, youth, lack of knowledge of exposure) unable to provide the data required. They are used most commonly in case-control studies of fatal diseases. The proxies may provide the data directly to the investigator, or records of information about the subject provided by a proxy may be used.

Data on exposure provided by proxies are prone to all the errors of data provided by the subjects themselves and perhaps some additional ones. The proxy may never have known the facts required. In addition, when death is the reason for the subject's unavailability at the interview, the fact of death may alter the proxy's recall of relevant facts. For some exposures, the proxy may give a more accurate account than the subject would have done.

The method of direct observation of subjects has a number of strengths and weaknesses. On the positive side, it can be more objective, can be used for low impact behaviours, and allows for a substantial amount of detail. Among its negative side, it requires extensive training of observers which may otherwise introduce observer error. The other important sources of

error include inadequate sampling of time-periods, biased sampling of time-periods, too many events to record accurately, observer fatigue with 'drift' in recording, and an effect of the observation on the behaviour being observed [2]. These latter effects tend to introduce systematic error.

Sometimes, records that have not been collected specifically for the purpose of measurement of exposure may be used in the study. The use of such records can be a valuable alternative to the collection of data directly from subjects, but they are themselves prone to errors. A record may be incomplete or in error, or perhaps not even made. Records may be lost or altered and there may have been systematic differences between multiple recorders in the items recorded and the way in which different items are defined. Moreover, in case of records of prescriptions of medications, intended exposures may be recorded but the subject may not have taken the stated dose. Both random and systematic errors are possible.

One source of differential measurement error is the recall bias when cases report exposures biased due to their knowledge or feelings about the disease. Other sources of differential measurement error include: the data collector's knowledge of the subject's disease status, biological effects of the disease or treatment, biological effects or symptoms of the prodromic phase of the disease, and the subject's awareness of his/her risk of acquiring the disease. As shown in Chapter 4, random measurement error leads to bias towards the null hypothesis.

Another cause of error in exposure measurement is faulty design of the measurement instrument. The error can vary not only between two instruments which measure the same exposure, but also for a single instrument when applied differently. Measurement error could also differ between the population of cases and population of controls in a case-control study. Although measurement and recording can be completely automated, some in-

man action may be involved, for example, reading a clear, stationary dial. The human action may involve complex subjective judgment to a greater or less degree. Several types of human action may enter. In many sample surveys it is recognized that error of measurement can arise from the person being interviewed, from the interviewers, from the supervisor or leader of a team of interviewers, and from the processor who prepares the information from the recorded interview for analysis.

During data entry and analysis, there is a significant chance of error. There can be data entry errors, errors in conversion tables used to convert subject responses, and programming errors in analysis [2].

Errors or omissions in the protocol for the use of the instrument can be the source of error in measurement of exposure. This is due to the failure to specify the protocol in sufficient detail, failure to specify a method to handle unanticipated situations consistently, or failure to include standardization of instrument periodically throughout data collection. Poor execution of the protocol during data collection may introduce error in exposure measurement. For example, failure of data collectors to follow protocol in same manner for all subjects, failure of subjects to read instructions in self-administered questionnaire, improper handling and/or analysis of biological specimens, and influence of the personality, sex, race, or age of interviewer on subject's responses, can all be causes of exposure measurement error.

The quantity being measured may be fixed and static over time. Alternatively, it may be fixed at a point in time, but vary with time. Sometimes we deliberately measure the wrong quantity, using a substitute measurement that is cheaper or more convenient [5]. When the quantity being measured varies with time, we may in effect be using the wrong measurement if we treat measurements made some months earlier as if they applied to the situation today. Sometimes the error of measurement is actually a sampling error.

2.5 Measures of Measurement Error

In order to visualize the measures of measurement error, consider a simple model of measurement error in a population given by

$$X = T + b + E.$$

Here the observed measure X differs from the true measure T by a systematic error or bias b and the subject error E . In this context, the subject error E varies with the subject. For a population of potential study subjects, X , T , and E are random variables with mean μ_X , μ_T , and μ_E , respectively, and variances σ_X^2 , σ_T^2 , and σ_E^2 , respectively. In this model, it is assumed that $\mu_E = 0$, and the correlation coefficient of T with E (ρ_{TE}) is zero.

Two indicators of measurement error are used to describe the validity of X , that is, the relationship of X to T in the population of interest, based on the model. They are: *bias* and *precision*. The bias b , or average measurement error in the population, is the difference between the population mean of X and the population mean of T : $b = \mu_X - \mu_T$.

The precision is a measure of the variation in the measurement error in the population. The precision is normally associated with the observed measure X . One measure of precision is the variance σ_E^2 of E . Often the correlation of T with X , ρ_{TX} , is used as a measure of precision and called the *validity coefficient of X*.

2.6 Impacts of Measurement Error

Both the mean and variance of the measured exposure will differ from the true exposure mean and variance because of measurement error. Measurement

errors have an effect on the observable mean and variance of an exposure variable within a population. Of greater concern is the effect of exposure measurement error on the measure of association between an exposure and an outcome in a study. A commonly used measure of association is the *odds ratio*, the odds of disease at one level of exposure relative to the odds of disease at another level of exposure. Measurement error that leads to bias in the odds ratio is called *misclassification bias* or *information bias*.

Differential measurement error can have an effect on correlation or regression coefficients. Differential measurement error occurs when exposure measurement error varies by outcome status (i.e., disease or non-diseased). It can cause the observed association between the measured exposure and the outcome to appear stronger or weaker than the true association. It can also lead to an association in the opposite direction, thus completely invalidating the results of a study.

Non-differential random exposure measurement error can lead to attenuation towards the null value of no association in the measure of association between the exposure and the outcome. An important observation on the effects of non-differential measurement error is that the magnitude of the bias in the odds ratio or the correlation coefficient does not depend on the sample size. Thus, increasing the sample size does not reduce the bias. However, increasing the sample size would increase the power to detect the attenuated association as significantly different from the null hypothesis.

The effect of measurement error upon estimated regression coefficients has long been recognized. In this context, consider the linear regression model with one independent variable defined as follows:

$$Y_i = \alpha + \beta x_i + e_i$$

($i = 1, 2, \dots, N$), where $(x_1, x_2, \dots, x_N)$ is fixed in repeated sampling and

the e_i are independent $N(0, \sigma_e^2)$ random variables. Following Fuller [11], the least squares estimator

$$\hat{\beta} = \frac{\sum_{i=1}^N (x_i - \bar{x})(Y_i - \bar{Y})}{\sum_{i=1}^N (x_i - \bar{x})^2}$$

is unbiased for β and has the smallest variance of unbiased linear estimators.

Let us consider regression models where one is unable to observe x_i directly. Instead of observing x_i , one observes $X_i = x_i + u_i$, where u_i is a $N(0, \sigma_u^2)$ random variable representing measurement error.

Let us investigate the effect of measurement error on the least squares coefficient in the above model under the assumption that the x_i are the random variables with variance $\sigma_x^2 > 0$. As in Fuller [11], we assume the vector $(x_i, e_i, u_i)^T$ to have the following distribution:

$$(x_i, e_i, u_i)^T \sim \text{NI}[(\mu_x, 0, 0)^T, \text{diag}(\sigma_x^2, \sigma_e^2, \sigma_u^2)],$$

where $\text{diag}(\sigma_x^2, \sigma_e^2, \sigma_u^2)$ is a diagonal matrix with the specified elements on the diagonal. According to Fuller [11], the vector $(Y_i, X_i)^T$ has a bivariate normal distribution with mean

$$E\{(Y, X)\} = (\mu_Y, \mu_X) = (\alpha + \beta\mu_x, \mu_x)$$

and covariance

$$\begin{bmatrix} \sigma_Y^2 & \sigma_{XY} \\ \sigma_{XY} & \sigma_X^2 \end{bmatrix} = \begin{bmatrix} \beta^2\sigma_x^2 + \sigma_e^2 & \beta\sigma_x^2 \\ \beta\sigma_x^2 & \sigma_x^2 + \sigma_u^2 \end{bmatrix}.$$

Let $\hat{\gamma}$ be the regression coefficient computed from the observed variable. It is given by the following expression:

$$\hat{\gamma} = \frac{\sum_{i=1}^N (X_i - \bar{X})(Y_i - \bar{Y})}{\sum_{i=1}^N (X_i - \bar{X})^2}$$

Thus,

$$E\{\hat{\gamma}\} = \frac{\sigma_{XY}}{\sigma_X^2} = \beta \frac{\sigma_x^2}{\sigma_x^2 + \sigma_u^2} = \gamma$$

From above, we can conclude that for the bivariate model with independent measurement error in X , the least squares regression coefficient is biased towards zero (under assumption that the measurement error in X , is independent of the true values, x_i , and the errors, e_i).

One way to describe the effect of measurement error is to say that the regression coefficient $\hat{\gamma}$ has been *attenuated* by the measurement error. The ratio $\kappa = \sigma_x^2 / \sigma_X^2$ defines the degree of attenuation, and is called the *reliability ratio* in the literature. When the controlled variables have measurement error, the regression coefficient is not always attenuated: the coefficient may even be inflated [21].

The impacts of measurement error on correlation and regression analyses have been studied in several areas of research. Many statistical papers have discussed the theoretical aspects of estimation of regression coefficients [13, 36]. Fleiss [10] discussed various issues related to designing studies involving unreliable measurements. In dietary studies, many researchers have examined the potential attenuation of simple correlation or regression coefficients caused by the large intraindividual variation of different dietary variable [21].

2.7 Reducing the Effects of Measurement Error

Several approaches to the reduction of measurement error and its effects are discussed in [2], including the use of multiple measures of exposure. The use of the average (or sum) of two or more measures of the exposure for each subject in an epidemiological study can be an effective method of decreasing the

measurement error, in comparison with the use of a single measurement. The measures may be based on repeated administration of the same instrument, or measurements from two different instruments.

In general, the use of multiple measures refers to repeated measurement of all subjects in an epidemiological study to reduce measurement error. It may be the case that the two or more measures to be averaged do not have equal variance. In this situation, averaging a precise measure with a less precise measure may result in a variable which is less valid than the better measure alone. Only the random error will be reduced by averaging. When the errors are not equal, or they are correlated, there may be little or no reduction in measurement error.

There is another approach to the use of multiple measures to improve the validity of the exposure measure. In this approach, when two or more measures are inconsistent beyond some tolerance level, further information (e.g. re-questioning the subjects) can be obtained to resolve the difference.

Very often adjustments to the study data are made to account for the impact of measurement error. By using estimates of the exposure measurement error from a validity study, it is possible to adjust the observed exposure-disease association from the epidemiological study to yield an estimate of the true effect. A great deal of work has been done on adjustment procedures which incorporate information from a validity or reliability study of the exposure in the statistical analysis of disease-exposure relationship ([1, 8, 11]). These methods may prove to be useful in accounting for measurement error.

Systematic quality control procedures before, during, and after data collection are necessary to identify and correct measurement errors. Careful design of the data collection forms, complete documentation of study procedures, and pre-testing of the data collection instrument will eliminate some

source of error. Review of the completed data forms and checks on the computerized data can uncover data items that need clarification or correction.

2.8 Chapter Summary

Measurement error is an important cause of bias in epidemiology. It is obvious that any deviation from the actual measurement can sometimes produce misleading results about the relationship between exposure and disease. Error in measurement can be introduced during almost all phases of an epidemiological study.

This chapter made an attempt to give an overview of measurement errors in epidemiology. Specifically, consideration was given to the sources of measurement error, the impacts of measurement error on mean and variance of the measured exposure and on the estimated regression coefficient, and means to reduce the effects of the measurement error.

Chapter 3

Adjustment of Exposure Measurement Error: A Review of Some Recent Methods

3.1 Introduction

Both natural and man-made alpha-emitting radionuclides in our environment can pose a risk to human health. However, natural sources currently make the largest contribution to human exposure. Among the natural sources, inhaled radon and radon decay products are the largest contributors to population exposure and might be responsible for a large number of lung-cancer deaths each year [28]. A committee on the Biological Effects of Ionizing Radiation (BEIR) has been setup to study health effects of radon and other internally disposed alpha emitters. The committee deals with health effects of exposure to radon and its progeny, primarily because of a need to characterize the lung-cancer risk associated with exposure to radon and its short-lived daughters in different environments.

In this chapter, we describe three recent methods that deal with the estimation of radiation dose exposure in epidemiological studies. The first

method, suggested by Mitchell *et al.* [25], estimates occupational radiation dose to individuals using weekly dosimetry data at Oak Ridge National Laboratory. The second method, suggested by Lubin [23], considers the effects of exposure measurement error in underground miner data on the estimation of excessive relative risk and the identification of age, time since exposure and the inverse dose rate effect. The third method, suggested by Thomas [38], characterizes the relevant features of the distribution of true radiation exposure for a miner given his/her measured dose.

3.2 Background

3.2.1 Radon and Lung Cancer

Several alpha-emitting radionuclides occur naturally in our environment; others are produced for industrial, military, and medical applications. Recent attention has focused on the alpha-emitting radioisotopes because of their presence in drinking water, in indoor air in buildings, and in mines. Of the several isotopes of radon, radon-222 has the most important impact on human health.

Research in the United States and other countries has provided data on concentrations of radon and radon progeny in homes. The studies have also described the sources of radon and determinants of its concentration. Epidemiological data are available on some alpha-emitting radionuclides, such as radon and its daughters, radium and thorium. Numerous studies of underground miners exposed to radon daughters in the air of mines have shown an increased risk of lung cancer in comparison with nonexposed populations.

3.2.2 Measuring Radon Concentration

The most common dosimeter used in epidemiological radon studies is the alpha-particle track detector. Radon concentration is determined by counting the number of etched tracks made on plastic film by alpha particles. Both the counting and measurement processes are subject to error, which has been estimated to be about 15-25% [22]. This level of error in the measurement process thus defines the lower bound for the accuracy of any assessment of exposure to radon progeny based on alpha-particle track devices.

By convention, the concentration of radon daughters is measured in working levels (WL), and cumulative exposures over time are measured in working-level months (WLM). The working level (WL) is defined as any combination of the short-lived radon daughters in 1 liter of air that results in the ultimate release of 1.3×10^5 MeV of potential alpha energy [28]. The cumulative exposure in WLM is the sum of the products of radon-progeny concentrations and the times of exposure. For historical reasons, time is quantified into blocks of 170 hrs when the concentration is expressed in WL. Because of differences in the circumstances of exposure, 1 WLM in a home and 1 WLM in a mine will not result in the same dose of radiation.

Indoor radon is measured in becquerels per cubic meter (Bq.m^{-3}), the number of atomic decays per liter of air. In U.S. homes, the average radon concentration is about 46 Bq.m^{-3} and median concentration is 25 Bq.m^{-3} . With 70% occupancy and standard housing conditions, 1 year of residence at 37 Bq.m^{-3} results in approximately 0.2 WLM [22].

3.2.3 BEIR Committee Report

A committee on the Biological Effects of Ionizing Radiation (BEIR) [28] was setup to study health effects of radon and other internally disposed alpha

emitters. The committee's report deals with health effects of exposure to radon and its progeny, and was introduced by a need to characterize the lung-cancer risk associated with exposure to radon and its short-lived daughters in indoor domestic environments.

For estimation of risks associated with exposure to the alpha-emitting radionuclides, the most important human populations examined are the underground miners who are exposed to widely different concentrations of radon-222 progeny [28].

Two approaches are being used to characterize the lung-cancer risks associated with radon daughter exposure: mathematical representations of the respiratory tract that model radiation doses to target cells and epidemiological investigation of exposed populations, mainly underground miners. The committee preferred a direct epidemiological approach, because the studies of radon-daughter-exposed miners provided a direct assessment of human health effects. In analyzing the data, the committee used a descriptive analytical approach, rather than statistical methods based on biologically based theoretical models of carcinogenesis.

The committee's general approach was to examine how the age specific relative risk depends on the variables of interest. This was done by making a cross-classification of numbers of lung-cancer deaths and person-years at risk, by categories of these variables, and then fitting models to the rates given by the ratio of deaths to person-years in such a tabular classification. The committee fitted regression models with Poisson probability model for the number of deaths in each cell of the table, where the expected value was taken as the product of the person-years at risk for the cell and a cancer rate given by a parametric model. The parametric models for this analysis were expressed in terms of the excess relative risk. Much of the committee's analysis was based on models for relative risk of the general mathematical

form

$$r(a) = r_0(a)[1 + \beta\gamma(\nu)W],$$

where $r(a)$ is the lung-cancer mortality rate for a given age and calendar period, $r_0(a)$ is the baseline risk of lung-cancer mortality in the population, W is the cumulative exposure in WLM before age a , β is the basic slope of the dose-response relation, and $\gamma(\nu)$ represents modifying effects of variables (ν) other than cumulative exposure.

Using statistical regression techniques appropriate for survival-time data, the committee found that the probability of dying of a lung cancer at age a was best described by the following equation:

$$r(a) = r_0(a)[1 + 0.025\gamma(a)(W_1 + 0.5W_2)].$$

Here $r(a)$ is the lung-cancer mortality rate at age a , $r_0(a)$ is the baseline lung-cancer mortality rate in the 1980-84 U.S. populations, $\gamma(a)$ is 1.2 for ages less than 55 years, 1.0 for ages 55-64 years, and 0.4 for age 65 or higher; W_1 is the cumulative radiation exposure from 5 to 15 years before age a ; and W_2 is the cumulative exposure 15 years or more before age a . In this model, the excess relative risk varies with time since exposure, and depends on the age of exposure.

Several epidemiological investigations of the lung-cancer risk associated with radon daughter exposure in homes have been carried out, but the study populations have been small and the results inconclusive [28]. The committee judged these exploratory studies to be inadequate for the purpose of risk estimation. Its risk projections for the general population are therefore based on the studies of miners. The committee concluded that estimates of lung-cancer risks based on studies on miners can be used to estimate the potential lung-cancer risks associated with increased concentrations of indoor radon; however, the estimates derived are imprecise.

3.3 Some Recent Methods for Adjusting Exposure Measurement Errors

We now describe three recent methods which adjust for measurement error in the estimation of radiation dose exposure. The first method, suggested by Mitchell *et al.* [25], estimates occupational radiation dose to individuals using weekly dosimetry data at Oak Ridge National Laboratory. The second method, suggested by Lubin [23], considers the effects of exposure measurement error in underground miner data on the estimation of excessive relative risk. The third method, suggested by Thomas [38], adjusted for measurement error in the original measurement data for the Colorado miners data.

The main idea behind all three methods is quite similar, although each dealt with different types of data. Each method involves prediction of the true exposure given the observed exposure taking into account the measurement error. By modelling the distribution of the true exposure X by $f(X)$, and the distribution of the observed exposure given true exposure, $f(Z|X)$, each model leads to an estimate of $E(X|Z)$.

3.3.1 Method 1

Mitchell *et al.* [25] proposed a method for adjusting for measurement error in occupational studies of radiation carcinogenesis. The method deals with the estimation of occupational radiation exposures to individuals using weekly dosimetry data at the Oak Ridge National Laboratory (ORNL). The authors proposed the use of a probability distribution to describe an individual's dose during a specified period of time.

Statistical analyses of data from epidemiological studies of workers exposed to radiations have been based on recorded annual radiation doses. It is usually assumed that the annual dose values are known exactly, although

it is generally recognized that the data contain uncertainty due to measurement error and certain biases. The method proposed here takes into account the measurement error produced by the dosimetry system, and the bias that was introduced by policies that led to right censoring of small doses as zero. The method is applied to a sample of dose histories obtained from dosimetry records at ORNL.

At ORNL, a film dosimeter provided the official dose of record, while the pocketmeter readings were maintained as a part of an individual's dose records. The lower limit of detection of most sensitive film used at ORNL was 0.10 to 0.30 mSv. A lower detection limit of 0.10 mSv was possible if an experienced technician evaluated the exposed films. When hundreds to thousands of films were read in large batches by technicians with varying experiences, the lower limit of detection was around 0.30 mSv. A film badge reading of zero means the radiation dose to the worker was less than 0.30 mSv unless a smaller value is given. Weekly film badge readings were typically added up to obtain the annual recorded dose which is then regarded as known. The lower limit of detection of film badge, together with measurement error in the dosimetry system, could lead to substantial uncertainty in the recorded annual dose.

The authors describe a method of accounting for uncertainty and bias in the measurements of an individual's occupational radiation dose with film badges. The true dose is taken to be the quantity of radiation encountered by film badges worn by the individual during the period in question. The basic quantities of interest are: for each week, the unobserved true dose (x) to the film badge and the recorded dose (z) to the film badge. The objective is to provide the methodology for determining the estimated dose (in terms of a probability distribution) of an individual during a year, given the recorded weekly exposure data for that individual in that year.

Method

There can be only one true value for x . In the absence of knowledge of what that value is, a prior probability $P(x)$ is attached to every possible value of x , where $\sum_x P(x) = 1$. The distribution $P(x)$ refers to the distribution of probabilities over all possible values of x , which concerns one individual and one exposure period. (It may be noted that $P(x)$ is not the marginal distribution of the true dose in the study cohort.)

As the observed quantity (z) provides information about the unobserved quantity (x), the assumed relationship between z and x takes the form of a conditional probability distribution $P(z|x)$. The likelihood function of x given z is defined as $L(x|z) = P(z|x)$. By Bayes theorem,

$$P(x|z) = c(z)P(x)L(x|z),$$

where $c(z)$ is a normalizing constant which ensures that $\sum_x P(x) = 1$. In implementing this approach, $P(z|x)$ is determined by careful consideration of the properties of the measuring device. The prior distribution $P(x)$, on the other hand, is more problematic.

Suggested Implementation Approach

Estimating the Weekly Dose

For $P(x)$, the prior distribution of x , the lognormal distribution is used. The lognormal distribution is chosen partly for convenience and partly it reflects the general belief that the larger doses are less likely than the smaller doses. The lognormal distribution $P(x)$ has parameters μ and σ which are the mean and standard deviation of $\log(x)$. These values were chosen so that the distribution agrees reasonably well with a small sample of film badge readings for a single representative individual. In order to choose a prior

with particular values for percentiles, the following property of lognormal distribution is used:

$$X_\alpha = \exp(\mu + U_\alpha \sigma)$$

where X_α is the α -th percentile of the lognormal distribution and U_α is the α -th percentile of the standard normal distribution.

In order to compute the likelihood function $L(x|z)$, $P(z|x)$ is determined. Suppose $\hat{z}$ is the expressed dose to the badge; that is, the reading that would be recorded if there were no rounding (the readings are given to the nearest multiple of 0.05 mSv) or censoring (recording as zero all readings that are below a certain threshold). It was assumed that $\hat{z}$ has a lognormal distribution such that $\log(\hat{z})$ has mean $\log(x)$ and standard deviation $\alpha(x)$. Thus,

$$P(\hat{z}|x) = \frac{1}{\sqrt{2\pi}\hat{z}\alpha(x)} \exp \left\{ -\frac{1}{2\alpha(x)^2} [\log(\hat{z}) - \log(x)]^2 \right\},$$

where [25]

$$\alpha(x) = \begin{cases} -0.0884874 - 0.2654017 * \log(x) & 0 < x \leq 0.30 \\ 0.04658731 - 0.1532109 * \log(x) & 0.30 \leq x \leq 1.00 \\ 0.04658731 - 0.00643505 * \log(x) & 1.00 \leq x \leq 10.00. \end{cases}$$

The probability density of the recorded dose z is obtained from $\hat{z}$ by rounding and censoring convention. For fixed z , $L(x|z) = P(z|x)$ is the likelihood function. For a particular value of z , $P(x|z)$ is obtained by multiplying $P(x)$ times the likelihood $L(x|z)$ and normalizing so that the sum of probabilities is one. For computational convenience, the prior distribution $P(x)$ is discretized so that all of the probability mass is concentrated on multiples of a dose of 0.01 mSv (i.e, 0.00, 0.01, 0.02, so on). The authors use 500 discrete points to represent the continuous distribution $P(x)$. Thus, $P(x)$ is the probability that the lognormal variable with parameters μ and σ lies within 0.005 mSv of x . The posterior distribution $P(x|z)$ has discrete support also.

Estimating the Yearly Dose

Next, a yearly dose based on a sequence of n film badge readings obtained weekly from a single individual is estimated. Let $x_T = \sum_{i=1}^n x_i$ where x_i is the true dose to the badge worn by the individual during the i -th week, and z_i is the corresponding recorded dose. Let the set of n true doses be denoted by $X = \{x_1, x_2, \dots, x_n\}$ and the set of recorded doses by $Z = \{z_1, z_2, \dots, z_n\}$. The posterior distribution $P(x_T|Z)$ is calculated to serve as an estimate of x_T . For this, each week is treated to be independent of the others, so that

$$P(X|Z) = \prod_{i=1}^n P(x_i|z_i).$$

Conditional on the set of recorded doses Z , the set of true doses can be treated as independent random variables, whose individual distributions are given by $P(x_i|z_i)$.

The distribution of the sum x_T is obtained numerically. The authors generate a large random sample from the distribution $P(x_i|z_i)$. To generate x_{Tm} , the m -th value of x_T in this sample, the set $\{x_{1m}, x_{2m}, \dots, x_{nm}\}$ is first generated by drawing x_{im} from $P(x_i|z_i)$ for each i . These values are then summed:

$$x_{Tm} = \sum_{i=1}^n x_{im}$$

This procedure is repeated until a large sample is generated. A histogram of this sample can be viewed as a good approximation to $P(x_T|Z)$.

Use of Other Data to Specify the Prior

The available weekly data also includes a pocket-meter dose corresponding to each recorded film-badge dose. This weekly pocket-meter dose was calculated as the sum of minimum daily readings of a pair of pocket-meters.

The parameters μ and σ of the prior distribution $P(x)$ were fixed before. To lessen the chance of being misled by poor specification of these parameters,

the pocket-meter data is used to specify μ and σ . In particular, the natural logarithm of the weekly pocket-meter dose is used as the mean μ and the parameter σ is set to a value that puts the 95th percentile of $P(x)$ at $\mu + 6.00$ mSv. This provides a large amount of prior uncertainty and allows the recorded film-badge dose to be the dominating factor that determines the posterior dose distribution.

When some weekly pocket-meter doses miss, the individual's weekly pocket-meter dose average over the week (which is not missing) is used. When all weekly pocket-meter doses are missing they are considered to be zero for the purpose of specifying prior. In order to apply the logarithmic transformation to all the data, a small positive value is used to replace any zeros.

3.3.2 Method 2

Lubin [23] considered the effects of exposure measurement error in the underground miner data on the estimation of the ERR/WLM (excess relative risk/Working Level Month) and the identification of age, time since exposure, and the inverse dose rate effect. There are two goals of this analysis: 1) a demonstration of the potential impact of errors in exposure on estimates of the exposure response relationship, and on the evaluation of the factors that modify the exposure response, especially the inverse exposure rate effect; and 2) an evaluation of the probable impact of errors. The impact of errors in exposure was assessed by means of a sensitivity analysis, using reasonable assumptions on the degree of error in exposure.

The authors assumed that work history information and the number of hours of the exposure per day were essentially known without error. This assumption implies that the source of exposure error was the measurement and the assignment of radon and/or WL levels, and the use of those values to represent radon progeny exposure for individual workers. There was an

additional assumption that radon progeny exposure was closely linked to the dose of radiation to the lung, which is the quantity of principal interest. The propagation of exposure errors were assumed to be without systematic bias.

This framework for exposure errors does not account for all sources of errors in the estimation of radon progeny exposure. It has been assumed that the only source of error arises from the measurement of WL and ascribing WL values to miners. There are likely many other sources of errors including previous mining experience, missing or inaccurate work history records, amount of vacation and sick leave, numbers of hours per day underground, and the number of hours actually exposed. The characteristics of individual miners, such as the use of protective equipments and choice of work locations, may still be a possible source of exposure error.

Method

The approach is viewed in the context of the creation of a multiway person-years table, in which for the i -th miner in the k -th cell (with categories defined by attained age, calendar year, cumulative WLM, time since exposure, or other factors), the exposure rate in units of WL is observed to be $S_{z,i,k}$. Here, $S_{z,i,k}$ is an incorrect exposure rate due to random errors. The observed cumulative exposure for the cell is $S_{z,i,k} \times t_{i,k}$, where $t_{i,k}$ is the time since exposure for i -th miner in the k -th cell.

Let $E[S_{x,i,k}|S_{z,i,k}]$ be the "adjusted" exposure rate and $E[S_{x,i,k}|S_{z,i,k}] \times t_{i,k}$ be the expected true cumulative exposure in the cell. The lung cancer disease rate (hazard), denoted by $r(a; W_z)$ at age a , given observed WLM exposure W_z , can be expressed as follows:

$$r(a; W_z) = \int r(a; W_x, W_z) f_{x|z}(W_x|W_z) dW_x = \int r(a; W_x) f_{x|z}(W_x|W_z) dW_x,$$

where $f_{x|z}$ is the probability density function for the true WLM exposure W_x given the observed WLM exposure W_z . The second equality results from the

assumption that knowing W_z provides no information on disease outcome once W_x is known. The distribution of the true exposures depends on the variety of factors, such as calendar year or mine location.

Because it is assumed that exposure rate is the only factor subject to measurement error, the assessment is simplified by focusing on models for WLM and duration of exposure. Lubin considers a model in which the relative risk is given by

$$RR = 1 + \beta W_j^* \phi_i \gamma_t,$$

where ϕ_i and γ_t are the parameters associated with predefined categories of attained age and duration of exposure, and W_j^* is the effective exposure with

$$W_j^* = W_{1,5-14} + \theta_2 W_{2,15-24} + \theta_3 W_{3,25+}$$

Here, $W_{i,j-1}$ denotes true exposure in age group between i and j , and the parameters $\{\theta\}$ allow the effect of exposures to depend on how long ago they occurred. For notational convenience, the symbol $*$ is dropped from the rest of the equations.

Assuming that the age-specific background lung cancer rates, $r_0(a)$, depending on attained age and other factors, are known without error, the regression model for the disease rate takes the form

$$\begin{aligned} r(a; W_z) &= \int r_0(a) \times \{1 + \beta W_x \phi_i \gamma_t\} f_{1|z}(W_x | W_z) dW_x \\ &= r_0(a) \times \{1 + \beta E[W_x | W_z] \phi_i \gamma_t\}. \end{aligned}$$

Suppose that the true WLM exposure (in a given category) is expressed as $W_x = S_x \times t$, where S_x and t are radon progeny rate (measured with error) and duration of the exposure (measured exactly) respectively. Then, for an observed duration of exposure t , we get

$$r(a; W_z) = r_0(a) \times \{1 + \beta E[S_x | S_z] \times t \times \phi_i \gamma_t\}.$$

Estimation of β , ϕ_i and γ_i based on the true exposure is accomplished by fitting models to a person-years table which is created using adjusted WL and WLM. For each worker and for each year of follow up, the observed increment in WLM ($= S_i \times t$) is replaced by adjusted WLM computed as the product of adjusted WL and the observed duration of the exposure, $E[S_i|S_i] \times t$. The effect of the choice of the error distribution and its parameters are evaluated through a sensitivity analysis.

3.3.3 Method 3

Thomas [38] presented an analysis using original measurement data for the Colorado Plateau Uranium miners to BEIR VI committee. The goal of the error analysis was to produce a "dose adjustment procedure" which may be applied to statistical models for lung cancer risks. Such an adjustment procedure was designed to characterize the relevant features of the distribution of true radiation exposure for a miner given his/her measured dose.

Method

The key aspects of this approach was to estimate the disease model parameter β by maximizing

$$f(Y|Z, \beta) = \int f(Y|X, \beta)f(Z|X, \sigma)f(X|\gamma)dX$$

where

- (i) $f(Y|X, \beta)$ is the disease model, and β represents parameters relating radiation exposure X to disease risk;
- (ii) $f(Z|X, \sigma)$ is the measurement error model, Z being the measured radiation exposure, and σ represents a parameterization of the error in measuring these doses; and

- (iii) $f(X|\gamma)$ is the model for true radiation exposure X , and γ represents a parameterization of the location and shape of this distribution.

The initial analysis of the uranium miner's cohort was a straightforward extension of the A-bomb survivor method (Pierce *et al.* [31]). It was assumed that true dose rates for an exposure miner over each of 6 five-year periods (1946-50), (1951-55), (1956-60), (1961-65), (1966-70), and (1971-75) could be regarded as an independent realization of a Weibull random variable. A lognormal measurement error model was assumed for $Z(t)$, given the true dose rates $X(t)$, with mean zero and standard deviation set to values in the range from 0.25-1.0 corresponding to models with a coefficient of variation of 25-100% for the true dose ($\sigma = 0.5$ or 1.0 before 1960; 0.25 or 0.5 after 1960). For each such model, the Weibull parameters in $f(X|\gamma)$ were estimated by deconvolution, and moments of $f(X(t)|Z(t))$ were estimated using numerical integration.

The moments of the distribution of $X(t)|Z(t)$ were used in place of $X(t)$ in fitting exposure-time response relations. In particular, the dose-error corrections were made based on estimates of the shape of dose-response function, latency effects and dose-rate effects. To study the effect of measurement error on curvilinearity, the model used is

$$RR = 1 + \beta X e^{-\alpha X}.$$

To study the effect of measurement error on latency, the model used is

$$RR = 1 + (\beta_1 X_{5-9} + \beta_2 X_{10-19} + \beta_3 X_{20+}).$$

In case of dose-rate effect, the following two models are used. The first one is

$$RR = 1 + \int_0^2 B[x(u)]x(u)du.$$

where $B[x(u)] = Ax(u)^{\gamma}$. The second dose-rate model is given by

$$RR = 1 + \beta \bar{X} e^{-\gamma \bar{X}},$$

where $\bar{X}$ is the average dose-rate.

This method needed improvement as there were major differences between the uranium miners data and A-bomb survivor data. The radiation dose for the A-bomb survivors was delivered within a few seconds, whereas exposure to radiation for the Colorado uranium miners extended over years or over decades. The dose for the A-bomb survivors consisted primarily of low-LET (linear energy transfer) gamma-rays (and lesser doses of neutrons), whereas the uranium miners were exposed to high-LET alpha-particles. Furthermore, the measurement error situation is considerably more complicated for the uranium miners than for the A-bomb survivors. In particular, repeated measurements of dose rates, rather than an estimate of instantaneous exposure, were taken. Random error in the A-bomb survivors dose estimates is independent from survivor to survivor, with the dose for each survivor was estimated based on the unique situation he/she was placed at the time of the bombings. For the uranium miners, measurements were made on a "whole mine" basis. Many uranium miners doses were imputed, rather than measured. Dose-rate estimates from neighboring mines were used if recordings were not available in the mine in which the miner worked. Recordings made in one year were used to estimate doses in the same or neighboring mines in different years if those were missing. Because of the above differences between uranium miners and A-bomb survivor data, modifications were made to deal with dose-rates $X(t)$ rather than instantaneous exposure X .

The true average dose-rate $X_{m,t}$ to all miners in mine m during year t is not known. It is either estimated by one or more repeated mine measurements in that year or is imputed by the use of neighboring values.

Three methods of imputation were used: interpolation or extrapolation, area estimation, and guestimation. The measurements were extrapolated up to two years, and gaps of less than five years were filled with mean of adjoining measurements. By the area estimation procedure, gaps were filled by mean of surrounding area in the same year (data on locality, district, and state were used as needed based on a minimum three mines and ten measurements). Guestimation was based on experience before 1950.

Other than using imputed values, $X_{m,t}$ was estimated by one or more repeated measurements in that year. Separate models were used for measured and imputed values. The constants in these models were estimated by the original authors.

Models for Measured Exposure Rate

The proposed model for measured exposure rate is:

$$\ln(z_{m,t}) = x_{m,t} + \epsilon_{m,t} / \sqrt{N_{m,t}},$$

where

- $z_{m,t}$ = measured mean exposure rate,
- $x_{m,t}$ = true log mean exposure rate,
- $\epsilon_{m,t}$ = measurement error,
- $N_{m,t}$ = number of measurements,
- m = mine,
- s = state, and
- t = year - base year (1959.5).

In case of the measured exposure rate, the model for the true dose rate is the following:

$$x_{m,t} \sim N(\mu_{m,t}, \sigma_{m,t}^2),$$

where

$$\begin{aligned}\mu_{m,t} &= \mu_{s_m} - 0.091\,t + 0.489\ln(N_{m,t}), \text{ and} \\ \sigma_{m,t}^2 &= \sigma_{s_m}^2 - 0.152\,t.\end{aligned}$$

The model used for measurement error, when exposure was measured, is the following

$$\epsilon_{m,t} \sim N(0, \tau_{m,t}^2),$$

where

$$\begin{aligned}\tau_{m,t}^2 &= \ln(1 + CV_{m,t}^2), \\ CV_{m,t} &= \exp(-0.0496 + 0.0079\,t), \text{ and} \\ var(CV_{m,t}) &= 0.178 - 0.013\ln(z_{m,t}).\end{aligned}$$

Models for Imputed Exposure Rate

The proposed model for the imputed exposure rate is:

$$\begin{aligned}\ln(\hat{x}_{m,t}) &= x_{m,t} + \delta_{m,t}, \text{ and} \\ \ln(z_{m,t}) &= x_{m,t} + \epsilon_{m,t}/\sqrt{N_{m,t}}.\end{aligned}$$

where

$$\begin{aligned}\hat{x}_{m,t} &= \text{imputed mean exposure rate,} \\ z_{m,t} &= \text{measured mean exposure rate,} \\ x_{m,t} &= \text{true log mean exposure rate,} \\ \delta_{m,t} &= \text{imputation error,} \\ m &= \text{mine,} \\ s &= \text{state, and} \\ t &= \text{year - base year (1959.5).}\end{aligned}$$

In case of imputed exposure rate, the model for true dose rate is the following:

$$\begin{aligned}x_{n,t} &\sim N(\mu_{n,t}, \sigma_{n,t}^2), \\ \mu_{n,t} &= \mu_{sm} - 0.121\ t, \text{ and} \\ \sigma_{n,t}^2 &= \sigma_{sm}^2 - 0.048\ t.\end{aligned}$$

The model used for measurement errors, when exposure was imputed, is given by:

$$\begin{aligned}\delta_{n,t} &\sim N(0, \tau_{n,t}^2), \\ \tau_{n,t}^2 &= \ln(1 + CV_{n,t}^2), \text{ and} \\ CV_{n,t} &= 1.37\end{aligned}$$

The coefficient of variation $CV_{n,t} = 1.37$ comes from Hornung [14] and varies from 1.21 to 1.86 for different methods of imputation.

3.4 Chapter Summary

Three recent methods that have dealt with the estimation of radiation dose exposure in epidemiological studies were described in this chapter. The first method, by Mitchell *et al.* [25], estimated occupational radiation dose to individuals using weekly dosimetry data at the Oak Ridge National Laboratory. The second method, by Lubin [23], considered the effects of exposure measurement error in the underground miner data and suggested an approach for adjusting measurement error in observed exposures. The third method, by Thomas [38], suggested a dose adjustment procedure which may be applied to statistical models for lung cancer risks.

All three methods described in this chapter predicted the true exposure given the observed exposure after accounting for the measurement error.

Each method was tailor-made to deal with a specific set of data. Mitchell *et al.* [25] dealt with weekly dosimetry data from ORNL where the measurements were right censored as zeroes for small doses. Both Lubin [23] and Thomas [38] used Colorado miners data where for each miner, attained age, calendar year, cumulative WLM, time since exposure, duration of exposure, mine location, and previous mining experience were available. To account for the absence of data, Thomas used different methods of imputations such as interpolation, extrapolation, area estimation and guesstimation.

All three methods assume the true exposure is lognormally distributed; however, the parameters (mean and standard deviation) of the distribution are estimated from the data differently in each case. Lubin used the mean of the logarithm of observed exposure as an estimate of the mean, whereas Mitchell *et al.* exploited the properties of the percentile of the lognormal distribution coupled with other data to estimate the parameters. Thomas estimated the parameters of the lognormal distribution differently for measured and imputed exposures.

In all three methods, the error was assumed to be lognormally distributed with different parameters. Lubin and Thomas assumed the mean to be zero whereas Mitchell *et al.* derived it from the available data. The standard deviation was estimated differently in each method.

The computational requirements of all three methods differ significantly. The method by Mitchell *et al.* is particularly computationally intensive. Among all three methods, Lubin's method appears to be the simplest to use. Thomas treats the measured exposure and imputed exposure differently. Therefore, in order to find the correct relationship for estimating model parameters, it would require a thorough regression analysis using different models for measured and imputed data.

Chapter 4

Analysis of Colorado Miners Data: Accounting for Measurement Errors

4.1 Introduction

In this chapter, we assess exposure measurement error in the Colorado miners data. In particular, we study the effect of errors on the estimation of the radiation dose-response relationship. For this purpose, a simulation study is carried out to study the properties of the distribution of the dose-response parameter in two cases: (1) when exposure error is not accounted for, and (2) when exposure rate is adjusted for measurement error. We use the approach recently suggested by Lubin [23] to account for measurement error in the original exposure measurements. We also analyze the robustness of the suggested approach for adjusting for measurement error.

4.2 Colorado Miners Database

The U.S. Public Health Service (USPHS) has assembled a database on underground uranium miners working in the Colorado Plateau (located within the states of Colorado, Utah, New Mexico and Arizona) between 1950 and 1964. Currently, this cohort consists of 3,347 male white miners. These data are available in machine readable form from the National Institute for Occupational Safety and Health (NIOSH).

Entry into the cohort was defined by race, sex, working at least one month in the underground uranium mines, volunteering for at least one medical survey between 1950 and 1960 and providing personal and occupational data of sufficient detail (Lundin *et al.* [24]). The mortality experience of the cohort was updated through December 31, 1984 (Roscoe *et al.* [34]). Lung cancer mortality was defined as anyone assigned an International Classification of Diseases (ICD) code of 162 or 163, using rules in effect at the time of death.

To estimate radiation exposure, the USPHS and state officials made nearly 43,000 radon daughter measurements on 2,500 mines during the period 1951 through 1968. When no radon daughter sample were recorded for a mine during a given year, a value was estimated from measurements for that mine during adjacent years or from the data from the nearby mines or regional averages. Nearly 50% of the annual estimates were obtained in this way [24]. Detailed mine employment and other histories were obtained from the initial medical examinations, from annual uranium miner censuses, and from mailed questionnaires. Cumulative radiation exposures were estimated in the units of WLM. Concentration of radon daughters in WL specific to each mine and calendar year were also noted.

The USPHS has summarized radiation exposure histories on a computer tape. For each miner, the dates of underground uranium mining employment

in each mine and the promotion of time employed underground are available. Exposure to radon daughters from uranium mining ceased for most of the cohort members during the late 1960s. Possible errors in work histories and in estimated mine WL both contribute to potentially large errors in cumulative exposure estimates.

4.3 Previous Analyses

This cohort has been instrumental in establishing that occupational exposure to radon in underground mines increases the risk of lung cancer [16]. In one of the first comprehensive analyses, Whittemore and McMillan [40] examined lung cancer mortality among a cohort of white underground uranium miners in the Colorado Plateau. The authors used a general relative risk regression model to analyze the data, allowing for a ten year lag between exposure and lung cancer indication.

Hornung and Meinhardt [15] analyzed the data updated through 1982. This represented 69 additional lung cancer deaths since the last published follow-up through to 1977. Relative risks were estimated through using the Cox proportional hazards model with an internal referent group. The results indicated that the exposure-response relationship was slightly convex, predicting an excess relative risk between 0.9 and 1.4 cases per 100 WLM in the lower cumulative exposure range.

Mortality among the subcohort of nonsmokers followed through December 31, 1984 was investigated by Roscoe *et al.* [34]. They found a standardized mortality ratio of 12.7 (with 95% confidence limits of 8.0 to 20.1), confirming that exposure to radon daughters in the absence of cigarettes smoking is a potent carcinogen.

Zielinski and Krewski [41] analyzed the data updated as of 1984 in the

context of two-stage clonal expansion model of carcinogenesis [26, 27]. They fitted the approximate version of the model, which is widely used in practice. The data suggests that both radon and tobacco smoke increase the first stage mutation rates as well as proliferation of initiated cells. Both carcinogens seem to have minimal effect on the second stage. Based on this model, the interaction between smoking and radon appears to adhere more closely to an additive multiplicative risk model.

Pierce *et al.* [31] have considered errors in exposure measurement and their effects on the estimation of the radiation-dose response relationship in the Japanese atomic bomb survivors. Their goal was to estimate an estimate of the true dose-response relationship accounting for errors in dosimetry. Some plausible models for the dose estimation errors were considered, which have typical errors in a range of 30-40% of the true values. It was found that for these error models, the resulting estimates of excess cancer risk based on linear models were about 6-17% greater than estimates that make no allowance for dose estimation errors.

More recently, Lubin [23] has suggested a method for dealing with the effects of exposure measurement error in the underground miner data in the estimation of the excessive relative risk. This method assumes that work history information and the number of hours of the exposure per day were known without error or with negligible amount of error. A simulation study of this method is presented in the next section.

4.4 Simulation Study

Lubin's approach [23] of adjusting for measurement errors (described in Chapter 3 in more detail) is as follows. He suggests that when exposure rates are log-normally distributed and errors are multiplicative with true ex-

posure rate $S_T \sim LN[\mu, \sigma^2]$, and exposure error $U \sim LN[0, \tau^2]$, the observed exposure rate is then $S_z = S_T \times U$, so that $S_z \sim LN[\mu, \sigma^2 + \tau^2]$.

Given an observed exposure rate, $S_z = s$, the true exposure rate is log-normally distributed: $S_T|S_z = s \sim LN[\nu(s), \omega^2]$, where $\nu(s) = \mu + \{\ln(s) - \mu\}/\{1 + \tau^2/\sigma^2\}$ and $\omega^2 = \sigma^2\tau^2/(\sigma^2 + \tau^2)$. The expected value is $E[S_T|S_z = s] = \exp[\nu(s) + 0.5\omega^2]$. Hence, the adjusted WL concentration can be rewritten as follows:

$$E[S_T|S_z = s] = s^{\sigma^2/(\sigma^2 + \tau^2)} E[S_T]^{1/(\sigma^2 + \tau^2)},$$

which is the (geometric) mean of the expected value of the (unconditional) true exposure rate and the observed exposure rate. The greater the error variance τ^2 , the more the observed values are pulled towards the expected value.

In case of a simple linear excess *RR* model for true exposure, the *RR* for the observed WLM, W_z , is

$$\begin{aligned} RR(W_z) &= 1 + \beta \times E[S_T|S_z = s] \times t \\ &= 1 + \beta \times s^{\sigma^2/(\sigma^2 + \tau^2)} E[S_T]^{1/(\sigma^2 + \tau^2)} \times t \\ &= 1 + \beta^*(s) \times s \times t \\ &= 1 + \beta^*(s) \times W_z, \end{aligned}$$

where the exposure-response "parameter" $\beta^*(s)$ is a function of the observed exposure rate s :

$$\beta^*(s) = \beta \times E[S_T/s]^{1/(\sigma^2 + \tau^2)}.$$

The expression for $RR(W_z)$ illustrates the attenuation of the observed exposure response when the exposure is subject to error. It shows that observed W_z values above the expected value of the true exposure suppress the observed exposure-response β^* , while observed exposures below the expected

value increase the observed exposure-response relationship. That is, the exposure response in the observed W_z is concave from below. In other words, for a given value of W_z , a high exposure rate (i.e., large value for s) results in a smaller value for the observed exposure response β^* compared to a low exposure rate (i.e., small value for s). (Note that this is the pattern which defines an inverse exposure rate or *protraction enhancement effect*.)

Using Lubin's approach for adjusting for measurement error, we conducted a simulation study to observe what is the effect on dose-response parameter β in the following two scenarios: 1) when exposures are not adjusted for measurement errors, and 2) when exposures are actually adjusted for measurement errors. In this simulation study, we also assess the robustness of Lubin's approach.

For the analysis, we use data on 3,132 underground miners from the Colorado plateau cohort. The data available on each worker are: whether or not the worker had lung cancer, the age at which the exposure began, the age at which the exposure ended, the date of last observation, and the exposure rate. The excess RR per unit exposure β , assuming no measurement error, was estimated to be 0.38 cases per 100 WLM. An error U was incorporated into the exposure measurement for each miner by taking a random sample of 500 from a log-normal distribution with mean 0 and a specified variance τ^2 . Considering the error to be multiplicative, 500 observed exposures were simulated (the true exposure followed $LN(\mu, \sigma^2)$ and observed exposure = true exposure $\times$ error) for each individual. This provides 500 different samples of exposure data for each worker.

The dose-response parameter β was estimated for each of the 500 cases, providing an estimate of the sampling distribution of the estimated β for the raw exposure data. Using Lubin's approach, the 500 raw exposures were adjusted for measurement error, and β estimated using the adjusted

exposures. For each of the 500 estimates of β (both raw and adjusted), the standard error of the estimate was calculated.

Using the available data on exposure rate, the geometric mean of the observed WL was calculated. Under the assumed error structure, the mean of the logarithm of observed exposure rate was taken to be an estimate of μ .

To determine the values of σ^2 , we used the information provided in the joint NIOSH-NIEHS monograph by Lundin *et al.* [24] and in the NIOSH criteria document "Radon progeny in the underground miners" (1987). This was also considered by Lubin in his analysis. Lundin *et al.* showed that in 1950s, WL measurement data within most mines had a coefficient of variation (CV) between 0.5 and 1.5. An analysis of data in the criteria document of WL indicated that the CV for mines with 5 or more measurements per year was 1.1. The estimate of $\sigma^2 (= 0.79)$ was obtained by solving the expression for the CV for a log-normal distribution: $CV = 1.1 = [\exp(\sigma^2) - 1]^{0.5}$. An alternative CV of 1.5 ($\sigma^2 = 1.18$) was also considered.

The error in exposure was specified by $\exp(\tau)$, the geometric standard deviation of the error distribution. The following three cases for $\exp(\tau)$ were considered: 1) $\exp(\tau) = 1.5$, 2) $\exp(\tau) = 2.0$, and 3) $\exp(\tau) = 3.0$. These cases were also considered by Lubin.

The following six error schemes used used in our analysis.

- 1) True WL based on $CV = 1.1$ ($\sigma^2 = 0.79$); error based on $\exp(\tau) = 1.5$.
- 2) True WL based on $CV = 1.1$ ($\sigma^2 = 0.79$); error based on $\exp(\tau) = 2.0$.
- 3) True WL based on $CV = 1.1$ ($\sigma^2 = 0.79$); error based on $\exp(\tau) = 3.0$.
- 4) True WL based on $CV = 1.5$ ($\sigma^2 = 1.18$); error based on $\exp(\tau) = 1.5$.
- 5) True WL based on $CV = 1.5$ ($\sigma^2 = 1.18$); error based on $\exp(\tau) = 2.0$.
- 6) True WL based on $CV = 1.5$ ($\sigma^2 = 1.18$); error based on $\exp(\tau) = 3.0$.

The 500 raw exposures generated earlier were then adjusted by the following formulae

$$E[S_i|S_o = s] = \exp[\nu(s) + 0.5\omega^2],$$

where S_i is the true exposure, S_o is the observed exposure, $\nu(s) = \mu + \{\ln(s) - \mu\}/\{1 + \tau^2/\sigma^2\}$, and $\omega^2 = \sigma^2\tau^2/(\sigma^2 + \tau^2)$.

An estimate of β was obtained for each of the 500 adjusted samples. For the estimation of β , a simple linear excess RR model $RR = 1 + \beta WLM$ was considered. In order to study how the introduction of error affects the estimated value of β , a box plot (see Figure 4.1) of estimates of β based on raw and adjusted exposures were obtained for each of the six error schemes considered.

In the above analysis, we had knowledge of the actual values the error parameters τ and σ^2 , and adjusted the raw exposure using this information. In order to study the robustness of the above approach, we now adjusted the raw exposures using incorrectly specified error parameters. For example, when the raw exposure is known to have a log-normal distribution $LN(0, \tau^2)$ with $\exp(\tau) = 1.5$, we adjusted the exposures assuming a log-normal distribution $LN(0, \tau^2)$ with $\exp(\tau) = 3.0$.

The effect on β due to adjusting the raw exposure with an incorrect error parameters can be seen in Figures 4.2-4.4. Figure 4.2 shows the effect of adjusting measurement error with different error schemes when the observed exposure is known to have log-normal error with $\exp(\tau) = 1.5$. Figure 4.3 shows the effect of adjusting measurement error with different error schemes when the observed exposure is known to have log-normal error with $\exp(\tau) = 2.0$. Figure 4.4 shows the effect of adjusting measurement error with different error schemes when the observed exposure is known to have log-normal error with $\exp(\tau) = 3.0$.

From the true exposure rate, the β was estimated to be 0.38 with a standard error 0.10. From the distribution of the estimates of β of raw exposures, the mean of the β s and the mean of the standard errors were calculated. Similarly, mean of the β s and the mean of standard errors from the adjusted exposure were also calculated. Tables 4.1 and 4.2 list these values.

Table 4.1: Estimates of β for Unadjusted and Adjusted Data
when CV = 1.1

<i>Parameter</i>	<i>Unadjusted</i>		<i>Adjusted #1</i>		<i>Adjusted #2</i>		<i>Adjusted #3</i>	
$\exp(\tau)$	β	SE	β	SE	β	SE	β	SE
1.5	0.23	0.05	0.37	0.10	0.60	0.22	0.78	0.34
2.0	0.11	0.02	0.19	0.05	0.37	0.11	0.61	0.24
3.0	0.03	0.006	0.06	0.01	0.16	0.03	0.38	0.12
#1: Adjustment based on error distribution with $\exp(\tau) = 1.5$								
#2: Adjustment based on error distribution with $\exp(\tau) = 2.0$								
#3: Adjustment based on error distribution with $\exp(\tau) = 3.0$								

Table 4.2: Estimates of β for Unadjusted and Adjusted Data
when CV = 1.5

<i>Parameter</i>	<i>Unadjusted</i>		<i>Adjusted #1</i>		<i>Adjusted #2</i>		<i>Adjusted #3</i>	
$\exp(\tau)$	β	SE	β	SE	β	SE	β	SE
1.5	0.23	0.05	0.32	0.08	0.47	0.15	0.66	0.27
2.0	0.11	0.02	0.16	0.03	0.27	0.07	0.47	0.16
3.0	0.03	0.006	0.05	0.01	0.10	0.02	0.24	0.06
#1: Adjustment based on error distribution with $\exp(\tau) = 1.5$								
#2: Adjustment based on error distribution with $\exp(\tau) = 2.0$								
#3: Adjustment based on error distribution with $\exp(\tau) = 3.0$								

Notice that in Figure 4.1, when we analyzed the data with error (i.e. without adjusting for measurement errors) there is bias towards the null value of $\beta = 0$, and the confidence intervals around the central value of the estimates are comparatively narrow. That is, the precision of the estimate is overstated. In fact, under the scenario considered in this study, biases were so large that the simulated 95% confidence limits did not include the true value of the parameter. As we can see from Table 4.1, the bias was 0.35 when $\exp(\tau)$ was 3.0 whereas it was 0.15 when $\exp(\tau)$ was 1.5. When $\exp(\tau)$ was 2.0 the bias was 0.27.

When we implemented exposure adjustment using the true parameters of underlying exposure errors, the adjusted estimates of β moved towards the true value of $\beta = 0.38$. Furthermore, the distribution of adjusted β 's is subject to greater dispersion than that in the case of unadjusted β 's (refer to Figure 4.1). In all the cases considered, the bias was reduced. When we assumed $CV = 1.1$ for the true exposure distribution, the 95% confidence interval of the mean of adjusted β always included true value of β . On the other hand, when $CV = 1.5$, we still observed some bias (ranging from 0.06 to 0.14), although this bias was substantially reduced.

In the second part of our analysis, we investigated the robustness of the procedure for adjusting measurement exposure error. When we adjusted for exposure measurement error understating the variability of exposure errors (for example, choosing $\exp(\tau) = 3.0$ when the actual error has $\exp(\tau) = 1.5$), we obtained a reduction in bias. However, overstating this dispersion of the error distribution (corresponding to larger values of τ used in generating error) may lead to positive bias. As this approach is not robust, there is a need for a realistic assessment of the magnitude and distribution of measurement errors to avoid over-adjustment. To model the measurement error, replicate measurements are required.

Figure 4.1: Box Plots of Estimates of β (number of lung cancer cases per 100 WLM) Based on Raw and Adjusted Exposure

Figure 4.2: Box Plots of Estimates of β (number of lung cancer cases per 100 WLM) when $\exp(\tau) = 1.5$

Figure 4.3: Box Plots of Estimates of β (number of lung cancer cases per 100 WLM) when $\exp(\tau) = 2.0$

Figure 4.4: Box Plots of Estimates of β (number of lung cancer cases per 100 WLM) when $\exp(\tau) = 3.0$

4.5 Chapter Summary

Based on Lubin's [23] approach of adjusting for measurement error, we conducted a simulation study on Colorado miners data to observe the effect on dose-response parameter β in two cases: 1) when exposures are not adjusted for measurement errors, and 2) when exposures are actually adjusted for measurement errors.

When we analyzed the data with error, we noticed a bias towards the null hypothesis, and the confidence intervals around the central value of the estimates are relatively narrow. In fact, under the scenario considered in this study, biases were so large that simulated 95% confidence limits did not include the true value of the estimate.

Also in this chapter, we assessed the robustness of the procedure for adjusting measurement exposure error. When we adjusted for exposure measurement error understating the variability of exposure errors, we obtained a reduction in bias. However, we discovered that overstating the dispersion of the error distribution may lead to positive bias. In fact, this points to the importance of a realistic assessment of the magnitude and distribution of measurement errors to avoid over-adjustment.

Chapter 5

Analysis of Indoor Radon Concentration: Accounting for Seasonal Correction Factors

5.1 Introduction

The fact that occupational exposure to radon, particularly in uranium mines, is known to increase lung cancer mortality rates has raised questions about the possible impact of environmental exposure to radon on lung cancer. To address this issue, a number of case-control studies of environmental radon and lung cancer have been initiated in recent years [3, 4, 18, 19, 20]. Among these is a relatively large-scale study of incident lung cancer cases in Winnipeg [17].

Radon levels in homes were monitored during two consecutive six-month periods to obtain integrated readings based on CR-39 alpha track detectors. Significant differences were noted among measurements taken during different seasons of the year. In order that the measurements be comparable and able to reflect average annual concentrations, some corrections are required. Pinel, Fearn, Darby & Miles [32] suggested correction factors that will sea-

seasonally adjust measurements taken over other periods in a similar survey done in United Kingdom. They estimated seasonal correction factors for measurements taken over any number of months starting in any month using only six months of observation. The structure of the data collected in Winnipeg, Canada allows verification of this model by splitting our database into two subsets: one consisting of radon measurements values for first six-month observation period, and the second consisting of the remaining six-month observation period. In this chapter, we estimate parameters of the model from each database and assess the accuracy of predictions of yearly radon concentration based on six months of data.

5.2 Data for Analysis

Study subjects included only histologically confirmed incident cases of lung cancer occurring in the Winnipeg metropolitan area between 1984 and 1990 in patients ranging from 35 to 75 years of age. For each case, a control matched on age (± 5 years) and sex was selected at random from the general population. This yielded the target sample size of 750 case-control pairs, or 1500 subjects in total. Each subject, or proxy, was interviewed to obtain information on exposure to a variety of potential risk factors for lung cancer. During the course of the interview, subjects were asked to identify all previous residences that they had occupied. The study protocol called for radon dosimeters to be placed in all current and previous residences within the Winnipeg metropolitan area.

In most dwellings, two dosimeters were placed in the bedroom and two in the basement. For apartments, only bedroom measurement was collected. The bedroom area was selected as an indicator of residential exposure to radon in the living room area in the home because of the amount of time

people spend sleeping. The dosimeters were left in the homes for six months and then replaced by another set of dosimeters for the next six month monitoring period to provide total of twelve consecutive months of monitoring.

The 1,500 participants in this study identified a total of 7,703 homes that they occupied. Of these, radon dosimeters have been placed in 4,508 homes. As of June 30, 1992, a total of 28,465 radon readings are obtained from 4142 homes. Integrated annual radon measurements in Winnipeg for the basement and living areas combined ranged from 0 to 2,375 Bq/m³, with a geometric mean of 110.6 Bq/m³ and geometric standard deviation of 2.3 Bq/m³. The arithmetic mean was 155.7 Bq/m³.

The data were divided into two groups: (i) measurements taken in the basement and (ii) measurements taken in the bedroom. Each group (basement, bedroom) was further divided into two datasets: one for measurements taken over first six-month period and the other for the next six-month period.

Though each house was supposed to be monitored for two six-month periods, the actual measurement periods varied, some monitored for less than six months and some for over six months. Dwellings which were monitored for more than seven months were excluded from the analysis. The starting dates for the measurements were distributed approximately evenly throughout the year.

5.3 Underlying Model for Indoor Radon

Let M_i denote the average indoor radon concentration in dwelling i over its measurement period, measured in Bq/m³. The assumption of a constant background of 4 Bq/m³ leads to a model for indoor radon concentration of

$$M_i = 4 + \frac{1}{t_i^{(2)} - t_i^{(1)}} \int_{t_i^{(1)}}^{t_i^{(2)}} f_i(t) dt$$

where $t_i^{(1)}$ and $t_i^{(2)}$ are the times at which measurement of dwelling i begins and ends respectively, and $f_i(t) > 0$ is a function representing the indoor radon concentration in dwelling i at time t , expressed as an excess over background.

A simple model for seasonal variation takes the form

$$f_i(t) = s(t)h_i, \quad (5.1)$$

where $s(t)$ is a periodic function with a period of twelve (months) reflecting the radon level in a typical dwelling at the time t , and h_i is a multiplicative factor reflecting the difference between the typical indoor radon concentration and the concentration characteristic of dwelling i . It is assumed that the pattern of seasonal variation is common to all dwellings. The model thus becomes

$$M_i = 4 + \frac{1}{t_i^{(2)} - t_i^{(1)}} \left(\int_{t_i^{(1)}}^{t_i^{(2)}} s(t) dt \right) h_i.$$

Taking natural logarithms, we have

$$\log(M_i - 4) = \log \left(\frac{1}{t_i^{(2)} - t_i^{(1)}} \int_{t_i^{(1)}}^{t_i^{(2)}} s(t) dt \right) + \log(h_i).$$

In practice, it is convenient to measure time in months. For $j = 1, 2, \dots, 12$, let m_j denote the integral over month j , where $j = 1$ is January. If dwelling i is measured for six months beginning at the start of month j ,

$$\log(M_i - 4) = \log \left(\frac{1}{6} \sum_{k=j}^{j+5} m_k \right) + \log h_i, \quad (5.2)$$

with the convention that $m_{12+k} = m_k$. As the observed quantities $\log(M_i - 4)$ follow a normal distribution, it is assumed that the quantities $\log h_i$ are

also normally distributed, and are mutually independent with mean 0. The quantity m_j may then be interpreted as the geometric mean background adjusted radon level in month j for the population of dwellings from which the sample was drawn.

5.4 Statistical Model for Seasonal Variation

Our objective is to use the data to estimate m_j ($j = 1, 2, \dots, 12$) and then use these estimates to derive seasonal correction factors. Equation (5.2) gives multiplicative log-normal errors h_i . The structure of individual $(M_i - 4)$ excludes the approximation of log-normal distribution by normal. In order to be able to have additive normal error and to apply the standard theory, the estimation is based on values of $\log(M_i - 4)$ averaged over a number of dwellings, as follows. The following twelve pairs of means and variances were calculated from the data:

$$x_j = \frac{1}{N_j} \sum_{i \in T_j} \log(M_i - 4),$$

($j = 1, 2, \dots, 12$) and

$$c_j = \frac{1}{N_j - 1} \sum_{i \in T_j} [\log(M_i - 4) - x_j]^2,$$

($j = 1, 2, \dots, 12$), where $i \in T_j$ if the middle day of the measurement period for dwelling i falls between the middle of month $j-1$ and the middle of month j , and N_j is the number measurements included in the j^{th} sum. The middle of the measurement period was used to account for the slightly variable periods in a symmetric manner. Thus, the appropriate model for the x_j is

$$x_j = \log \left(\frac{1}{6} \sum_{k=j-3}^{j+2} m_k \right) + \log \hat{h}_j, \quad (5.3)$$

where $\bar{h}_j$ is the geometric mean of N_j number of h_i s. Equation (5.3) is linearized to the following model for $d_j = \exp(x_j)$:

$$d_j = \left(\frac{1}{6} \sum_{k=j-3}^{j+2} m_k \right) + \epsilon_j, \quad (5.4)$$

($j = 1, 2, \dots, 12$), with ϵ_j approximately normally distributed with standard deviation

$$s_j \approx d_j \sqrt{\frac{c_j}{N_j}}.$$

(Pinel *et. al* [32]). Writing (5.4) in matrix form, one obtains

$$d = Xm + \epsilon \quad (5.5)$$

where

$$X = \frac{1}{6} \begin{bmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 \\ 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 1 & 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 & 1 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 1 \\ 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 \end{bmatrix}$$

where $d = (d_1, \dots, d_{12})^T$, $m = (m_1, \dots, m_{12})^T$ and $\epsilon = (\epsilon_1, \dots, \epsilon_{12})^T$.

5.5 Estimation of Model Parameters

Since the above model is not of full rank, it is not possible to estimate the 12 m_j s without imposing some constraints. Therefore, we express the m_j

as combinations of sines and cosines. Any set of twelve numbers m_j can be expressed as

$$m_j = \beta_0 + \sum_{r=1}^5 \left(\alpha_r \sin\left(\frac{\pi r j}{6}\right) + \beta_r \cos\left(\frac{\pi r j}{6}\right) \right) + \beta_6 \cos(\pi j). \quad (5.6)$$

Since (5.6) is linear in the coefficients α_r and β_r , the model in (5.5) can be written as

$$d = XF\theta + e, \quad (5.7)$$

where $\theta = (\beta_0, \alpha_1, \beta_1, \dots, \alpha_5, \beta_5, \beta_6)^T$ and F is a matrix of sine and cosine terms. Evaluation of the matrix XF shows that it has five columns that are full of zeros, and hence that (5.7) allows estimation of the seven coefficients $\beta_0, \alpha_1, \beta_1, \alpha_4, \beta_4, \alpha_5, \beta_5$ but not the remaining five which correspond to cyclic trends of period 6, 3 and 2 months.

The parameters $\alpha_2, \beta_2, \alpha_3, \beta_3$ and β_6 corresponding to cyclic trends of period 6, 3, 2 months are constrained to be zero, and the remaining seven parameters are estimated by least squares applied to (5.7). The corresponding estimates $\hat{m}_j$ of the m_j are then calculated as

$$\hat{m}_j = \hat{\beta}_0 + \sum_{r=1,3,5} \left(\hat{\alpha}_r \sin\left(\frac{\pi r j}{6}\right) + \hat{\beta}_r \cos\left(\frac{\pi r j}{6}\right) \right), \quad (5.8)$$

where $\hat{\alpha}_r$ and $\hat{\beta}_r$ are the least squares estimates of α_r and β_r respectively. Standard errors for $\hat{\alpha}_r$ and $\hat{\beta}_r$ and thence for $\hat{m}_j$ were calculated from the standard deviations s_e of the d_j .

A simpler model is obtained by setting the coefficient for $r = 3, 5$ to zero. This constrains the m_j to follow a pure sine wave of period 12 of the form:

$$\hat{m}_j = \hat{\beta}_0 + \left(\hat{\alpha}_1 \sin\left(\frac{\pi j}{6}\right) + \hat{\beta}_1 \cos\left(\frac{\pi j}{6}\right) \right). \quad (5.9)$$

5.6 Correcting Indoor Radon Measurements for Seasonal Variation

If a dwelling is measured for t months beginning on the first day of month j , the resulting measurement, according to the model above, will be

$$M = 4 + \left(\frac{1}{t} \sum_{k=j}^{j+t-1} m_k \right) h.$$

A full twelve months of measurements would have resulted in

$$M^{(12)} = 4 + \left(\frac{1}{12} \sum_{k=1}^{12} m_k \right) h.$$

Thus, the appropriate correction formula is

$$M^{(12)} = 4 + f_{j,t}(M - 4),$$

where the correction factor $f_{j,t}$ is given by

$$f_{j,t} = \frac{t \sum_{i=1}^{12} m_i}{12 \sum_{k=j}^{j+t-1} m_k}. \quad (5.10)$$

5.7 Analysis

The analysis was done separately for each of the four datasets discussed previously. The $\hat{m}_j$, $\hat{m}_t$ and their standard errors were calculated for each of these from datasets. The seasonal correction factors based on each six-months observations were also obtained. Tables 5.1-5.4 show the results obtained for each of the datasets.

The average yearly radon concentration for basement and bedroom were predicted by the given formula using seasonal correction factors. The observed yearly radon concentration was also calculated for each dwelling in both the basement and bedroom based on each of the two six-month periods for which data is available.

The following tables (Tables 5.1-5.4) give number of measurements (N_j), geometric mean radon gas concentration (d_j) for measurements with middle day falling between the middle of the month ($j - 1$) and the middle of month j , standard deviations (s_j) and estimates ($\hat{m}_j$) and ($\hat{m}_j$) of monthly geometric mean concentrations together with their standard errors in Bq/m³.

Table 5.1: Basement Radon Levels Period 1

j	Month	N_j	d_j	s_j	$(\hat{m}_j)$	(SE)	$(\hat{m}_j)$	(SE)
1	January	262	206.1	9.44	171.8	21.8	221.9	6.0
2	February	240	191.8	9.03	246.1	20.9	204.0	6.0
3	March	158	150.8	9.25	190.9	23.2	167.4	5.7
4	April	80	133.4	8.50	78.9	24.5	122.0	5.2
5	May	268	121.4	5.90	84.9	25.1	80.0	4.9
6	June	363	93.1	5.90	47.4	24.4	52.5	4.8
7	July	346	73.5	6.48	97.1	21.3	47.0	5.0
8	August	375	96.3	7.29	22.8	20.7	64.9	5.2
9	September	310	88.4	7.61	78.0	23.0	101.5	5.2
10	October	202	129.0	6.78	190.0	24.6	146.9	5.2
11	November	202	141.8	7.19	184.1	25.1	189.0	5.4
12	December	242	188.0	8.29	221.5	24.4	216.4	5.7

Table 5.2: Basement Radon Levels Period 2

j	Month	N_j	d_j	s_j	$(\hat{m}_j)$	(SE)	$(\hat{m}_j)$	(SE)
1	January	329	192.9	8.13	172.6	26.4	199.7	5.8
2	February	268	179.3	8.44	183.4	23.6	182.4	5.7
3	March	343	154.3	9.40	139.5	21.9	155.2	5.5
4	April	252	127.7	5.89	157.7	25.9	125.4	5.2
5	May	171	107.9	6.56	102.0	26.8	101.0	5.1
6	June	273	132.8	5.04	48.5	24.9	88.5	5.3
7	July	288	130.5	8.54	118.4	26.1	91.2	5.7
8	August	251	108.7	9.29	107.5	24.3	108.5	6.1
9	September	173	112.6	8.16	151.4	22.2	135.7	6.4
10	October	145	150.8	9.63	133.3	26.0	165.5	6.3
11	November	166	149.0	11.57	188.9	26.5	190.0	6.1
12	December	389	199.2	7.02	242.5	25.7	202.5	6.0

Table 5.3: Bedroom Radon Levels Period 1

j	Month	N_j	d_j	s_j	$(\hat{m}_j)$	(SE)	$(\hat{m}_j)$	(SE)
1	January	295	114.5	7.47	85.2	19.3	130.7	5.0
2	February	288	108.0	7.21	145.5	16.8	120.8	5.1
3	March	180	76.4	8.79	120.5	17.3	95.3	5.0
4	April	92	65.3	8.61	37.7	16.4	60.9	4.5
5	May	280	65.3	4.20	19.7	18.3	27.0	3.8
6	June	393	35.2	3.40	-6.7	20.9	2.5	3.1
7	July	387	14.4	1.91	39.6	18.7	-5.9	2.9
8	August	444	24.3	2.81	-20.7	16.3	4.0	3.2
9	September	356	21.2	2.82	4.3	17.3	29.5	3.8
10	October	222	56.1	6.10	87.1	16.5	63.9	4.2
11	November	240	71.4	5.53	105.1	18.0	97.8	4.1
12	December	276	96.6	7.77	131.5	21.3	122.3	4.7

Table 5.4: Bedroom Radon Levels Period 2

j	Month	N	d_j	s_j	$(\hat{m}_j)$	(SE)	$(\hat{m}_j)$	(SE)
1	January	368	119.8	6.68	113.6	17.5	130.6	4.3
2	February	313	99.4	7.00	136.0	16.8	117.0	4.0
3	March	403	89.5	5.48	65.9	16.4	92.6	3.7
4	April	279	76.9	4.16	78.0	17.4	64.2	3.4
5	May	196	56.8	3.66	52.7	16.9	39.2	3.3
6	June	319	53.3	4.24	0.5	16.1	24.4	3.3
7	July	337	58.4	4.37	40.9	17.1	23.8	3.5
8	August	288	37.4	4.53	18.4	17.2	37.4	3.8
9	September	193	43.8	5.36	88.5	16.3	61.8	4.1
10	October	160	82.4	6.38	76.4	17.4	90.2	4.3
11	November	176	86.6	7.77	101.7	17.3	115.2	4.1
12	December	421	122.2	5.97	153.9	16.5	130.0	4.4

In order to see how well the model suggested by Pinel *et al.* [32] fits, the predicted yearly radon concentration values were plotted against the observed yearly radon concentration values. Figure 5.1 shows plots of predicted vs. observed for all the four datasets.

A recovery factor was also calculated by taking the ratio of predicted and observed data. Any value close to 1 indicates a good approximation. The recovery factor was also plotted against the observed values. Figure 5.2 shows the plots of recovery factor vs. the observed data for the four datasets.

The above four datasets were subjected to further analysis using another model

$$\ln Y = \ln Y_1 + \sum_{j=1}^{12} \sum_{i=5}^7 I_{X_{(j,i)}}((j,i) \in X_{(j,i)}),$$

where $X_{(j,i)} = ((j,i)$: if starting month = j , period of observation = i), Y is the average yearly radon concentration, and Y_1 is the radon concentration observed in one six month period. The same analysis as for the model using seasonal correction factor was done for the above multiplicative model. Figure 5.3 shows the plots of predicted values obtained from the multiplicative model vs. the observed values for all the four datasets. Similarly, the recovery factor was calculated and plotted against the observed values. Figure 5.4 shows the plots of recovery factor vs. observed values.

Tables 5.5-5.8 give percentage of prediction (using seasonal correction factors) for two basement and bedroom periods. Tables 5.9-5.12 give percentage of prediction (using multiplicative model) for two basement and bedroom periods.

Table 5.5: Percent Error in Prediction Using Seasonal Correction Factors
(basement-period 1)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	748	24.5	748	24.5
20	628	20.6	1376	45.1
25	285	9.4	1661	54.5
30	247	8.1	1908	62.6
40	366	12.0	2274	74.6
50	224	7.3	2498	82.0
60	173	5.7	2671	87.6
70	112	3.7	2783	91.3
80	69	2.3	2852	93.6
90	77	2.5	2929	96.1
100	51	1.7	2980	97.8
110	68	2.2	3048	100.0

Table 5.6: Percent Error in Prediction Using Seasonal Correction Factors
(basement-period 2)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	962	31.6	962	31.6
20	787	25.8	1749	57.4
25	309	10.1	2058	67.5
30	230	7.5	2288	75.1
40	294	9.6	2582	84.7
50	223	7.3	2805	92.0
60	99	3.2	2904	95.3
70	57	1.9	2961	97.1
80	43	1.4	3004	98.6
90	15	0.5	3019	99.0
100	15	0.5	3034	99.5
110	14	0.5	3048	100.0

Figure 5.1: Observed vs. Predicted Values for All Four Datasets

Figure 5.2: Recovery Factor vs. Observed Data for All Four Datasets

Figure 5.3: Observed vs. Predicted Results for All Four Datasets Based on the Multiplicative Model

Figure 5.4: Recovery Factor vs. Observed Data for All Four Datasets Based on the Multiplicative Model

Table 5.7: Percent Error in Prediction Using Seasonal Correction Factors
(bedroom-period 1)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	505	14.6	505	14.6
20	481	13.9	986	28.6
25	217	6.3	1203	34.8
30	203	5.9	1406	40.7
40	371	10.7	1777	51.5
50	313	9.1	2090	60.5
60	219	6.3	2309	66.9
70	154	4.5	2463	71.3
80	132	3.8	2595	75.2
90	154	4.5	2749	79.6
100	144	4.2	2893	83.8
110	560	16.2	3453	100.0

Table 5.8: Percent Error in Prediction Using Seasonal Correction Factors
(bedroom-period 2)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	747	21.6	747	21.6
20	627	18.2	1374	39.8
25	291	8.4	1665	48.2
30	260	7.5	1925	55.7
40	383	11.1	2308	66.8
50	274	7.9	2582	74.8
60	187	5.4	2769	80.2
70	155	4.5	2924	84.7
80	113	3.3	3037	88.0
90	94	2.7	3131	90.7
100	74	2.1	3205	92.8
110	248	7.2	3453	100.0

Table 5.9: Percent Error in Prediction Using the Multiplicative Model
(basement-period 1)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	895	29.4	895	29.4
20	760	24.9	1655	54.3
20	760	24.9	1655	54.3
25	274	9.0	1929	63.3
30	251	8.2	2180	71.5
40	331	10.9	2511	82.4
50	221	7.3	2732	89.6
60	114	3.7	2846	93.4
70	83	2.7	2929	96.1
80	48	1.6	2977	97.7
90	26	0.9	3003	98.5
100	15	0.5	3018	99.0
110	30	1.0	3048	100.0

Table 5.10: Percent Error in Prediction Using the Multiplicative Model
(basement-period 2)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	1059	34.7	1059	34.7
20	819	26.9	1878	61.6
25	287	9.4	2165	71.0
30	203	6.7	2368	77.7
40	285	9.4	2653	87.0
50	161	5.3	2814	92.3
60	100	3.3	2914	95.6
70	56	1.8	2970	97.4
80	27	0.9	2997	98.3
90	19	0.6	3016	99.0
100	10	0.3	3026	99.3
110	22	0.7	3048	100.0

Table 5.11: Percent Error in Prediction Using the Multiplicative Model
(bedroom-period 1)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	745	21.6	745	21.6
20	664	19.2	1409	40.8
25	289	8.4	1698	49.2
30	265	7.7	1963	56.8
40	396	11.5	2359	68.3
50	265	7.7	2624	76.0
60	207	6.0	2831	82.0
70	169	4.9	3000	86.9
80	91	2.6	3091	89.5
90	56	1.6	3147	91.1
100	39	1.1	3186	92.3
110	267	7.7	3453	100.0

Table 5.12: Percent Error in Prediction Using the Multiplicative Model
(bedroom-period 2)

% Error in Prediction	Frequency	Percent	Cumulative Frequency	Cumulative Percent
10	790	22.9	790	22.9
20	690	20.0	1480	42.9
25	380	11.0	1860	53.9
30	266	7.7	2126	61.6
40	434	12.6	2560	74.1
50	261	7.6	2821	81.7
60	141	4.1	2962	85.8
70	107	3.1	3069	88.9
80	77	2.2	3146	91.1
90	63	1.8	3209	92.9
100	40	1.2	3249	94.1
110	204	5.9	3453	100.0

When we predict yearly observations using seasonal correction factors based on first six months of data in bedrooms, we capture 60.5% of the observations for the data on bedroom within a 50% error in prediction (see Table 5.7). However, when we use the multiplicative model for the same dataset, 76% of the observations fall within a 50% error in prediction (see Table 5.11). Consider now the second six months of bedroom data. In this case, the prediction of yearly observations using seasonal correction factors captured 74.8% of observations within a 50% error range (see Table 5.8). 81.7% of the observations were within the same range in case of the multiplicative model as shown in Table 5.12.

Although the prediction of yearly observations using basement data showed improvement in the case of multiplicative model over seasonal correction factors, the magnitude of improvement was not as substantial in the case of bedroom data. For example, 82% of observations fell within a 50% error in prediction for seasonal correction factors (see Table 5.5), whereas 89.6% were within the same range for first six month of data in the basement (see Table 5.9). Similarly, for the basement data from the second six months period, seasonal correction factors captured 92% of the observations within a 50% error range (see Table 5.6) and the multiplicative model captured 92.3% within the same range (see Table 5.10).

The above observations can also be seen in Figures 5.2 and 5.4. When one compares Table 5.5 with Table 5.9, Table 5.6 with Table 5.10, Table 5.7 with Table 5.11, and Table 5.8 with Table 5.12, one can observe that the prediction using the multiplicative model is always better than that using the seasonal correction factors.

5.8 Chapter Summary

Radon levels in homes were monitored using two six-month periods with integrated readings obtained using CR-39 alpha track detectors. Significant differences were noted among measurements taken during different seasons of the year. Pined *et al.* [32] suggested correction factors that will seasonally adjust measurements taken over other periods in a similar survey done in U.K. In this chapter, we used Pined's approach for radon levels monitored in Winnipeg to predict yearly observation using only measurements taken over any number of months starting in any month using only six months of observation. We considered two models (seasonal correction factor model and the multiplicative model) to predict yearly radon concentration using only six months period of observation. From the analysis, we observed that the multiplicative model outperforms the seasonal correction factor model.

Chapter 6

Summary and Conclusions

6.1 Summary of Main Contributions

The main contributions of the thesis were the following

1. Three recent methods dealing with measurement errors in the estimation of radiation dose exposure were reviewed. The first method, suggested by Mitchell *et al.* [25], estimated occupational radiation dose to individuals using weekly dosimetry data at Oak Ridge National Laboratory. The second method, suggested by Lubin [23], considered the effects of exposure measurement error in the underground miner data on the estimation of excessive relative risk and the identification of age, time since exposure and the inverse dose rate effect. The third method, suggested by Thomas [38], characterized the relevant features of the distribution of true radiation exposure for a miner given his/her measured dose.
2. The Colorado miners' data were analyzed to account for exposure measurement error. In particular, we studied the effect of errors on the estimation of the radiation dose-response relationship. A simulation study was carried out to observe the properties of the distribution of

the dose-response parameter in two cases: (1) when exposure error is not accounted for, and (2) when exposure rate is adjusted for measurement error. We used Lubin's approach [23] to account for measurement error in the original exposures. Furthermore, we also analyzed the robustness of the suggested approach of adjusting for measurement error

- 3 Residential radon concentration in homes in Winnipeg, Canada, were analyzed to account for seasonal variations. Radon levels in homes were monitored using integrated readings taken over two six-month periods. Significant differences were found among measurements taken during different seasons of the year. In order that the measurements can be comparable among each other and be able to reflect average annual concentrations, some corrections are required. Based on the work of Pinel, Fearn, Darby & Miles '32], we estimated correction factors that will seasonally adjust measurements taken over other periods for the Winnipeg data

6.2 Areas of Future Work

The results in this thesis does not deal with all issues in the assessment of exposure measurement error in epidemiological studies. There still remain many important practical issues that need to be considered to fully understand the actual behavior and effect of measurement error on true dose-response relationship.

In the analysis of Colorado miners data, we considered the effect of radon exposure in producing lung cancer. We did not take into account individual workers' habits like smoking, wearing protecting equipments, and choice of work locations. These factors should be taken into consideration for an analysis to produce more realistic results. In our analysis, we assumed that

the distributional properties of errors is known. In practice, this is not the case. In order to do a proper adjustment, the distribution of errors has to be carefully determined. Furthermore, we also assumed that errors are multiplicative. Should it not be the case, the claims made in the analysis would be somewhat inaccurate. An area of future work would be to address some of the issues raised here in revising the procedures for accounting for measurement errors.

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