Epidemiologic Studies of the Cancer near the Cotter Uranium Processing Facility

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1. Introduction

Epidemiology is the study of health and disease in populations. Its methods have been used to address a range of topics including evaluation of the health effects of exposure to ionizing radiation. This review begins with a brief discussion of the methods used by epidemiologists to study radiation health effects, followed by a discussion of the Life Span Study of atomic bomb survivors and some studies of the effects of environmental exposures to ionizing radiation. The latter part of this report provides a critical review of several epidemiological studies of cancer in Lincoln Park, Colorado and discusses the prospects for additional research in this community.

2. Epidemiologic Methods

All epidemiologic studies must address concerns about the accuracy of measurements of exposure and disease, and the appropriateness of comparisons between groups of people.

2.1 Measuring exposure

People have to be accurately classified with respect to their exposures if an association between radiation exposure and disease is to be accurately assessed. If people have not been accurately classified into exposure groups then evidence of any adverse effect of radiation exposure may be obscured.

It is often presumed that studies of occupational exposure to radiation may have advantages relative to studies of environmental radiation exposures, since the magnitude of occupational exposures is typically greater than the magnitude of environmental radiation exposures and a researcher may have better information about the doses received by workers in occupational settings than about the doses received by people in environmental settings. For example, workers at nuclear facilities have often been issued personal dosimeters to monitor penetrating radiation exposures, a seemingly ideal measurement situation. While records of individual dose estimates are clearly a valuable resource, changes over time in who was monitored, the sensitivity of dosimeters, and the frequency of reading dosimeters could affect the reliability of recorded doses. In addition, some workers might have removed their badges before performing tasks which entailed high exposures in order to ensure that their recorded external exposures were below standards which would otherwise require them to stop work.

In environmental and occupational settings, internal exposure to radionuclides typically is more difficult to assess than external radiation exposure. Ingested or inhaled alpha- and beta-emitting radionuclides have greater density of ionization than gamma or x-rays, but they have little penetration, so the relevant dose is delivered to a particular organ or cells within the organ. Knowledge about retention of radionuclides has been used to estimate exposures, and information from excreta samples (urine/fecal analysis) or field data (nose swipes, air samples, skin and clothing contamination estimates) are traditionally employed to estimate body burdens of workers. Estimates can also be made using whole-body counters that detect the penetrating radiation emitted by the internally deposited particles. However, most epidemiological studies have used crude indicators to identify those people likely to have been exposed to internal radionuclide contamination. In occupational settings, exposure categories might be based on job titles, area monitoring data, or history of monitoring for internal radionuclides, while in environmental settings, exposure categories might be determined by geographical location and patterns of environmental contamination.

2.1.1 Timing of exposures

The proper classification of people in a study by level of exposure requires not only good measurement of exposure, but also correct decisions about which periods of exposure are etiologically relevant. Sometimes only the doses received several years in the past are considered in forming exposure groups based on the assumption that cancers take time to develop and that recent exposures are not relevant to disease (so-called "lag" or "latency" analyses). Chronic exposures might have a greater opportunity to impact an organism during especially susceptible states; or it may be that only high dose rate exposures are relevant to the onset of later disease. So, a further difficulty in interpreting radiation-cancer associations, beyond the measurement process itself, is that mechanisms of radiocarcinogenesis are not sufficiently well understood to provide a sound theoretical basis for knowing in advance what should be measured.

2.2 Measuring disease

The ability to accurately quantify the effects of radiation exposures also depends on accurate measurement of the outcome. Long-term studies of cancer typically rely on cancer mortality, rather than cancer incidence. In the United States, death certificates are the only universally collected health data, consequently mortality is an endpoint that can be readily determined in nationwide follow-up studies. There are important limitations, however, to mortality studies. The sensitivity and specificity of cancer death certificate diagnoses is often not very good. Incident cancers that are in remission, unrelated to the primary cause of death, or undetected at the time of death from other causes, may not be counted. Furthermore, non-fatal health effects cannot be assessed in mortality studies. While studies of cancer incidence overcome these obstacles, for many US states comprehensive cancer registry data began to be collected relatively recently and there is no national registry that may be used to easily ascertain cases when people move across state boundaries.

2.3 Comparing Groups of People

Most epidemiological studies are observational. They attempt to imitate a controlled experiment by making exposed and unexposed groups as similar as possible in every way other than exposure itself. The method of the discipline is to observe whether disease occurs more or less commonly among individuals who received an exposure than among those who did not. Comparability of groups with different levels of exposure is important in order to be able to attribute differences or similarities in disease rates between groups to radiation *per se*. This is accomplished both through the design of the study and through statistical analysis of the data.

One widely-used method involves comparison of disease rates in the study population to that of the general population using Standardized Incidence Ratios or Standardized Mortality Ratios (SIRs or SMRs, respectively). This method of analysis is useful in settings in which there is little or no ability to accurately discriminate between people in a study population with respect to exposure level (either because exposure estimates are unreliable or because historical exposures were of similar magnitude for most people in the study). Such analyses permit an investigator to contrast cause-specific disease rates for the people in a study population, to age-, sex-, race-, and calendar-period appropriate rates for an external referent population. The study group and the referent group that are being compared are therefore balanced by means of adjustment for differences in age, sex, race, and birth cohort. However, these groups are not necessarily balanced with respect to other factors that may influence disease rates.

Interpretation of the SIR or SMR as an effect measure that represents the independent effect of exposures requires comparability (or 'exchangeability') of the study population and the external referent population. This condition may not be met if, for example, there are socioeconomic or other differences between people in the study group and the referent group that impact disease rates.(1-3)

As noted above, SMRs or SIRs are often calculated when an investigator has little or no ability to accurately classify people in a study population with respect to exposure. The contrast drawn (people in the study area to those in a referent area) implies that the data analyst is treating all people in the study population as though they have equal and identical exposures. If, in fact, the study population is composed of people some of whom received relatively high exposures (during an etiologically-relevant time period) and some of whom did not then collapsing these groups together for the purposes of calculating standardized rates will obscure important heterogeneity in disease rates.

2.4 Summary

Issues of exposure measurement, disease classification, and comparability of study subjects (between exposure groups and between the study population and the more general population) are issues for concern in reviewing the following studies.

The effects of measurement errors, selection bias, over-reliance on mortality data, and limited periods of follow-up tend to bias studies towards finding no radiation-cancer association. Given these impediments, it is very difficult to detect associations between low level ionizing radiation and cancer. Findings which have been reported may be expected to be biased downwards. It should also be noted that epidemiology is used for different purposes in different circumstances. Often, epidemiological studies are conducted in order to identify a potentially hazardous agent. Such studies may use relatively crude indicators of exposure, and yet evaluate whether an agent is associated with a disease.

3. *Radiation risk estimates*

The risk estimates used to inform assessments of environmental radiation exposures are derived primarily from studies of atomic bomb survivors.

3.1 Atomic bomb survivor studies

Recent reports of the US. National Academy of Sciences Committee on the Biological Effects of Ionizing Radiation, and the International Commission for Radiological Protection focus on the Life Span Study (LSS) of survivors of the atomic bombings of Hiroshima and Nagasaki as the primary source of information for understanding radiation health effects. These reports, subsequently, serve as a primary resource for a number of other recent reviews on radiation health effects. Most reports of results of LSS analyses concern radiation-related changes in cancer mortality rates among the survivors, often reported as the estimated excess relative risk of cancer mortality per Sievert (Sv) radiation dose (ERR_{1Sv}).

In the Life Span Study of atomic bomb survivors, estimation of the exposures received by thousands of survivors has occupied researchers for more than forty years. The level of radiation exposure received by an individual from the bombing was affected not only by where the person was situated geographically, but also their body position at the time of the explosion, whether they were shielded from the explosion, the type of shielding material, atmospheric humidity, patterns of movement and activities immediately after the explosion (due to concerns about residual radiation), ingestion of radioactive material, and bomb design. Exposure misclassification, which may result from incomplete information, and from inaccurate survey data elicited from a highly traumatized population, is likely to produce errors in dose estimates and in radiation dose-response estimates.

Overall, increases in solid cancers and leukemias have been observed with increasing doses; leukemia mortality has shown larger associations than solid cancers, with the largest excess risks among survivors who were under 20 years old ATB. The range of health effects from exposure to ionizing radiation may extend beyond cancer, to non-cancer diseases (recent evidence suggests that cardiovascular disease risk is associated with radiation dose in the LSS) and heritable genetic effects.

Summary

In section 2, we outlined some concerns that are common to all epidemiologic studies, which related to comparability of populations at risk and to exposure and disease measurement. Exposure measurement in studies of a-bomb survivors relied on questionnaire data collected over a period of many years after the bombing. Patterns of exposure were extremely complex due to shielding by buildings and terrain, and little attention has been given to the contribution of delayed, residual or induced radiation to the doses received by survivors presumed to have little or no radiation exposure. Evaluation of death certificate records also suggest problems of disease misclassification. It has been noted that the overall percentage agreement between death certificate and autopsy diagnoses in the LSS data was only 52.5%, with 25% of cancers diagnosed at autopsy missed on death certificates(4). These are issues which affect the internal validity of a study. Validity may also be evaluated with respect to the appropriateness of using results from one study population to make conclusions about people in other situations--this is called external validity. Some researchers have questioned whether it is appropriate to use results drawn from the LSS, a study population of five-year survivors of an atomic bomb detonation, to form conclusions about the effects of radiation in contemporary populations exposed to environmental exposures. One reason to question the validity of such conclusions relates to the difference in exposure patterns. The pattern of exposure from an atomic bomb blast is significantly different from exposure patterns in occupational and environmental settings. In contrast to studies of atomic bomb survivors, concerns about occupational and environmental exposures are related to the effects of long term exposure to low level radiation, at low dose rates. Others have raised concerns about selective survival of people after the atomic bombing. Premature deaths of people who were sensitive to the acute effects of radiation may have led to the selective removal of those who were more sensitive to the later effects of radiation as well. Consequently, when follow-up began five years after the bombing only a select population of less radiosensitive persons may have been left(5-7). A recent survey of mortality in Nagasaki during the period 1945-1950 has also suggested potential selective survival among A-bomb survivors(8). This situation raises questions about the applicability of estimates of radiation-cancer associations among A-bomb survivors to other populations.

One alternative source of quantitative radiation risk estimates come from large pooled analyses of workers in the nuclear industry. The largest study to-date is the International Collaborative Study of nuclear workers. While occupational cohort studies also suffer problems of exposure misclassification (e.g., problems of misclassification with respect to internal doses) and problems of outcome misclassification (due to reliance on death certificate data), as well as problems of bias due to confounding (i.e., non-comparability of workers in exposure groups with respect to unmeasured factors such as smoking), these studies provide a potentially important source of information on risks associated with protracted radiation exposures.

4. *Epidemiological Studies of Effects around Nuclear Facilities*

4.1 Introduction

While environmental releases of radiation are of wide concern, epidemiologic analyses of the effects of these releases suffer from lack of available data on magnitudes of exposure, pathways for exposure, and time-patterns of exposure. Furthermore, in a general population, complicated patterns of migration limit the ability to follow-up people to assess disease status. Environmental epidemiological studies generally rely on correlations between geographical patterns of exposure and disease incidence. A reasonable concern in such studies is the potential for confounding factors to lead to spurious observed associations (due to differences in the geographical distribution of other cancer risk factors); critics less often note that confounding, in addition to migration and errors in dose estimates, could lead to masking or underestimation of exposure effects.

Typically, these studies compare death or disease rates among populations presumed to have different levels of exposure. Environmental exposures are generally assumed to be low, consequently, differences in disease rates between populations are presumed to reflect very small differences in exposure magnitude. For example, excesses of childhood leukemia were reported in the area around Sellafield in the 1980s. An investigation of this cluster of leukemia was conducted by Gardner et al. Using a case-control study method, information was collected about all known cases of leukemia and lymphoma among children in the area health authority between 1950-1985 and compared to information about local controls selected from the birth registry. A number of potential risk factors were examined, and father's employment at the Sellafield nuclear facility was identified as an important risk factor (9-11). Furthermore, fathers of cases who had worked at Sellafield had larger cumulative preconception doses than fathers of controls who had worked at Sellafield. A subsequent study examined followup through 1991, attempting to avoid criticisms which were directed at previous analyses by specifying, a priori, the outcomes of interest and geographic areas defining the study population(12). Excess leukemia incidence was noted in the area, which the authors suggest might reflect occupational or environmental exposures.

In Scotland, excess childhood leukemia and non-Hodgkins lymphoma has been reported in the area around the Dounreay nuclear facility. The excess first reported in the 1980s has persisted with more recent follow-up through 1991 (13); a case-control study identified use of the local beaches as associated with childhood leukemia (14). An analysis of leukemia and lymphoma incidence around seven nuclear sites in Scotland found a significant excess only around Dounreay (15). Similarly, a case-control study of childhood leukemia near the La Hague plutonium reprocessing facility in France found evidence that environmental radiation exposure from recreational activities on beaches and from shellfish consumption could be associated with increased childhood leukemia among area residents (16, 17).

Cancer around the Rocky Flats nuclear weapons facility has been the subject of a more detailed investigation which used environmental exposure estimates. Johnson evaluated cancer incidence patterns for the period between 1969-1971 in areas with varied estimated levels of contamination from plutonium and other radionuclides emitted by the Rocky Flats plant near Denver, Colorado

(18). He compared the cancer incidence rates of four geographic regions around Rocky Flats that were determined using isopleths from an area-wide survey by the AEC in 1970. There was a 24 % higher cancer incidence in males in Area I (highest exposure) vs. Area IV (lowest exposure), and a 15 % higher cancer incidence in Area II vs. Area IV. For females, there was a 10 % increase in cancer incidence in Area I, and 10 % increase in Area II. Johnson concluded that exposure of general populations to Pu and other radionuclides may have an effect on cancer incidence rates and that further study is warranted to investigate the poorly understood dose response relationship between Pu exposure and cancer in populations living near nuclear facilities. In a re-analysis, Crump obtained similar results for 1969-71 and extended the analysis to 1979-81 (19, 20). Positive findings were diminished by adjustment for distance from the State Capitol. Crump argued that distance from the State Capitol was a measure of socioeconomic factors related to cancer incidence, however, he does not present findings for conventional measures of socioeconomic status, and provides no quantitative evidence for this assertion.

Reports of excess adult leukemia incidence around the Pilgrim power plant in Massachusetts led to an investigation of association between proximity to the facility during years of 'high emission' and leukemia incidence; a positive dose-response association was observed. In other analyses innovative applications of geographical information systems data were used in conjunction with cancer registry data to explore spatial and temporal distributions of cases.

An analysis of leukemia and lymphoma incidence was conducted in Northern Germany following reports of a cluster of childhood leukemia cases near a nuclear facility (21). A highly-detailed population-based case-control study of leukemia and lymphoma was subsequently conducted which assessed potential exposure to ionizing radiation from the routine operation of nuclear power reactors, as well as pesticide exposures, electromagnetic field exposures, illustrating an approach for a comprehensive assessment of known or suspected risk factors.

4.2 Conclusions

Epidemiological techniques are well suited to documenting strong risk factors that show little or minor variation in impact in various population subgroups, such as regular cigarette smoking or high dose ionizing radiation. However, due to the importance of environmental contamination and the potentially large population receiving exposure, radiation epidemiology must now focus on weaker relationships at lower exposure levels, where poor measurement and the presence of unmeasured differences between exposure groups become major potential problems. Relatively small differences in disease occurrence, such as those that are suspected in the case of many environmental radiation exposures, are difficult to detect. But small increments in disease incidence can have a great population impact when many people are exposed.

Environmental releases of radioactive material may be of particular concern because the effects of radionuclide exposures are believed to be modified by many substances. For example, gastric absorption of plutonium tends to be very low in occupational settings; however, in the presence of fluoride, chlorine, or carbonate ions, the gastric absorption of plutonium rises to near 100% absorption. Consequently, environmental releases of radionuclides that contaminate drinking water, which is often chlorinated and may contain fluoride and carbonate ions, may lead to high levels of internal contamination. Through the food chain, radionuclides may be incorporated and uptake increased as well.

The effect of low level radiation exposure on cancer incidence in populations is difficult to quantify with epidemiological methods. Epidemiological studies tend to suffer from poor measurement of exposures. Furthermore, movement of people across local and national borders makes long term follow-up (which must span decades to study cancer effects, or generations to study genetic effects) difficult and nearly always incomplete. These problems affect studies of atomic bomb survivors as much as studies of environmental contamination; and, the tendency of these problems is to bias studies towards an underestimate of the true consequences of radiation exposure (22). While radiation risk estimates from studies of atomic bomb survivors are often used, in conjunction with environmental exposure estimates, for the purposes of risk assessments it is important to note these common limitations of epidemiologic research.

5. *Critical Review of Epidemiological Studies of Cancer in Lincoln Park*

Several studies have been conducted of cancer among people living near the Lincoln Park Superfund site. The studies that have been conducted to-date involve comparisons of the observed numbers of cases of specific cancers to expectations based upon cancer rates in other parts of Colorado. In other words, these studies address the question "Are there more cancer cases in the Lincoln Park area than in other parts of Colorado?" It is reasonable to ask whether this is the question initially posed by the citizens of Lincoln Park. Suppose that the question of actual concern to members of the community is, "Have exposures to radiation or other hazards from the Superfund site increased my risk of developing cancer?" The comparisons of observed cancer cases in Lincoln Park to expectations based upon rates in other parts of Colorado do not necessarily have bearing on the latter question. The studies that have been done, therefore, may have given the right answer to the wrong question.

5.1 Limitations of study design

It is useful to consider some elements of study design that might be employed to provide a more direct investigation of whether exposures from the Lincoln Park Superfund site affected cancer rates of residents of Lincoln Park. To address such concerns one might enumerate a roster of people who have lived in the area during a specified period (e.g., anyone resident in the area during a period encompassing mill operations, 1958-1989). Those who lived in the area during the study period would then be followed up to determine their exposure status (e.g., based upon their residential and occupational history) and their disease status (e.g., based upon cancer diagnoses or causes of death). The relationship between estimated exposures from environmental contamination and subsequent disease could be assessed.

Such an approach differs in several important ways from the study design employed in the 1991, 1993, and 1998 analyses of cancer in this community. Rather than a fixed roster (i.e., cohort) followed over time, people entered and exited the study depending upon whether they moved into or out of the study area. As noted in section 2, follow-up of a roster of people in the US to determine cancer incidence is relatively difficult.

Also as noted in section 2, the adverse effect of an exposure may be obscured by misclassification of people with respect to exposure. If a person residing in the study area was diagnosed with cancer they were classified as an exposed case, regardless of how long they had lived in Lincoln Park. Similarly, if a person moved out of the area and was diagnosed with cancer they did not contribute to the case count for those residing in the exposed area, regardless of how long they had lived in Lincoln Park. Induction and latency periods were not considered. People were classified as exposed based upon residence at time of diagnosis; however, the exposure status of interest is presumably environmental exposures associated with residence years or decades prior to diagnosis. Temporal changes in the magnitude of exposure have not been considered in the design of the study or the interpretation of results. Concerns about environmental exposures from the uranium mill date back to 1968 and the mill stopped operations in the 1980s. As follow-up of this cohort continues, therefore, it may not be reasonable to expect that the exposure-related excess of disease will persist at the same magnitude indefinitely. The magnitude of the exposure may have changed; and, given that the magnitude of exposure does not remain constant, even if the rate of in-migration and out-migration is steady people will be increasingly misclassified with respect to exposure.

At the outset of a study it is useful to define outcomes of interest. The exposures of primary concern in Lincoln Park are uranium and its decay products. In this setting, lung cancer is one obvious outcome of concern. Ascertainment of lung cancer cases should be relatively complete and diagnoses should be relatively accurate, which supports consideration of this outcome.

5.2 Limitations in the interpretation of results

In addition to considerations of the determinants of validity of a study (e.g., exposure and outcome classification and appropriate comparisons) a critical review should consider the use of statistical methods and the interpretation of results derived from such methods.

Statistical modeling of epidemiological data is useful primarily as a means of data summarization and pattern detection. Statistical models should not be confused with biological or etiological models of disease processes. This seems to be a recurrent problem in the interpretation of evidence in the 1991, 1993 and 1998 reports. The proposition in these reports that chance is a causal explanation is wrong. Chance as a cause of health effects is only valid in scenarios where chance is introduced by the investigator (e.g., random assignment to exposure groups). In an observational setting, diseases are caused by biological and physical processes. We analyze these data using models in which we may choose to model observations as though they were random variables (e.g., conforming to Poisson or Bernoulli processes) however this is for purposes of data summarization and pattern recognition not biological inference. If more cases of disease occur in an area than expected then a scientist should not posit that this occurred because of chance. Reasonable explanations would be confounding, selection bias, or measurement error.

Similarly, interpretation of confidence intervals in these settings are only appropriate in quantifying what results might be observed if we assume that there is a super-population from which we could redraw observations, and we assume that the processes generating these data persistently conform to our statistical model, and we assume that there is no confounding, selection bias, or measurement error. Over a large number of replications, 95% of the confidence intervals constructed using this formula would include the true population parameter (in this case the ratio measure). However, this is a long list of assumptions. The point estimate of the standardized incidence ratio is the most likely value for the population parameter given the observed data at hand and the posited statistical model, values closer to the bounds of the confidence interval tend to be much less likely than the point estimate.

In the 1991, 1993, and 1998 reports, the authors give excessive attention to the lower bound of the 95% confidence interval while giving minimal attention to the point estimate which is the most likely estimate of the population parameter. During the period 1979-1990 the observed number of cases of lung cancer among men (41) is about forty percent greater than the expected number. With further follow-up through 1995 this has diminished to about 12% excess, although there is no reason to expect an excess to persist indefinitely nearly two decades after the facility has closed. Potential explanations for this observed excess relate to comparability of the study area and the referent area; perhaps the investigators made a poor choice of referent populations (i.e., confounding away from the null). On the other hand, possible explanations for attenuation include poor choice of referent (i.e., confounding toward the null) and also include exposure misclassification (e.g., due to migration patterns) and misspecification of the etiologically-relevant time window of exposure. In other words, there are plausible reasons to expect that the study design employed could have attenuated or obscured any true effect of exposure.

In contrast to statistical models are biological models of carcinogenesis. Cancer is typically viewed as a disease that does not have a single cause, even for a single person's case of cancer. Rather cancers are widely viewed as arising from a step-by-step process of induction that involves early and late stages of action, with agents that may act as initiators or promoters, including factors that spur clonal expansion or proliferation and factors that influence the environment of pre-malignant cells. Just as the statistical models employed for data summarization should be interpreted as such, this biological framework is important to keep in mind when reading assertions such as "smoking is generally believed to be the cause of 85% of lung cancers" and "90% of the Lincoln Park lung cancer cases for 1988-1999 had a history of smoking." Smoking is clearly a factor that influences the risk of lung cancer and plays a role in the multistage process leading to lung cancer. That does not imply, however, that radiation exposure has not also played a role in the induction of the very same cases of lung cancer. The fact that a lung cancer case has arisen among a smoker does not mean that this person would have developed cancer regardless of their radiation exposure (or, that the person's cancer would have developed at the same age).

6. Prospects for Further Epidemiological Studies of Cancer in Lincoln Park

The prospects for meaningful additional research addressing the health effects of exposures from the Lincoln Park Superfund site largely depend upon the ability to address the fundamental requirements for epidemiological research: exposures assessment, disease ascertainment, and valid contrasts between groups under study. The methods employed previously for analyses of standardized incidence ratios provide some useful information, although these methods clearly fall short on each of the requirements for valid inferences (i.e., exposure misclassification is substantial; disease ascertainment only occurs during the period when residents reside in the state; and contrasts adjust for basic demographic confounders but may well be unbalanced with respect to other risk factors of concern). While additional research could be done, if it fails to move beyond the limitations of the prior research then little will be added in terms of value in understanding these relationships.

That said, studies are done for a variety of reasons and in some circumstances the conduct of the study itself may be of benefit; for example, community-initiated research can serve as a catalyst for great democratic participation, self-organization, and community dialogue. However, in terms of etiological research, the fundamental elements of study design necessary for valid inferences must hold.

6.1 Case-control studies

As opposed to the idealized cohort study outlined in section 5.1, the case-control study design has been employed in a number of settings to investigate hypotheses about environmental factors influencing cancer risk. Some investigators have conducted studies that focus on identifying newly diagnosed cases in the community (for whom information might be obtained via interviews) while others have conducted studies that include retrospectively ascertained cases (many of whom will be deceased). Often more accurate and detailed information can be collected from living cases than from next-of-kin or acquaintances, although a larger number of cases might be identified retrospectively. If a study is focused on characterizing any exposure-induced excess risk of disease then retrospective ascertainment of cases may also be important if the magnitude of environmental exposures has tended to diminish in more recent years.

Dr. Jarvis has offered his assessment of the feasibility of a case-control study, with his first concern being limitations of statistical power. He noted that given: a study that included 55 lung cancer cases, standard assumptions about type I and II error, and a binary exposure that was of intermediate prevalence among the controls, the study would have power to detect an odds ratio of 3 (i.e., on average result in an effect estimate with 95% confidence intervals that excluded unity). On the one hand, such power estimates are unduly conservative as a guide for decision making for contemporary residents of Lincoln Park. In follow-up through 1995, 74 lung cancer cases had been ascertained (furthermore, there is no reason that citizens of Lincoln Park would be limited to conducting a case-control study only of lung cancer; cases could be enumerated for all cancers or even broader categories of disease). Also, assuming that a contemporary study could derive a categorical or continuous exposure classification, as opposed to the binary classification assumed by Dr. Jarvis, a statistical analysis based on trend tests would tend to have greater power than the test of a binary classification of subjects. While unstated, it appears that Dr. Jarvis' calculation assumes a 1:1 matched case-control design; such a design has approximately 50% of the statistical efficiency of a full cohort analysis. A more powerful case-control design would be obtained via a 4:1 or 5:1 control to case ratio; the latter would allow a study to have power to detect effects of smaller magnitude. Lastly, the presumption that power calculations should be premised on the construction of 95% confidence intervals (i.e., alpha=0.05 for type I error) is arbitrary and, in radiation epidemiology, often replaced by consideration of 90% intervals.

This is not to discount the fact that small magnitude effects associated with low level environmental exposures are very difficult to detect via epidemiological methods. However, the obstacles to such studies often follow more from measurement error problems than they do from the random (i.e., sampling) errors quantified by the statistical power calculations described above. I would argue that the fundamental question about the prospects for any epidemiological study in this community is "Is there a method for accurately estimating historical exposures among Lincoln Park residents?" As noted above, epidemiology is often a relatively crude tool well suited to detection of differences in disease rates between sizable groups of people who have markedly different exposure patterns (resulting in markedly different disease patterns). When the populations are small, the exposure patterns are poorly characterized, and/or the differences between groups in disease rates are not large, epidemiological methods may be inadequate to address community concerns.

Summary

Prior studies of cancer in Lincoln Park have suggested greater than expected numbers of lung cancer cases (as well as excesses of several other types of cancer). If there is no ability to accurately estimate historical exposures then there is very little basis for conduct of additional epidemiological research. If exposure estimates can be derived then one option is to use these in conjunction with previously reported radiation risk coefficients to derive estimates of the potential risks from these exposures. Alternatively, historical exposure estimates could be used with a cohort or case-control study design. Such studies often require substantial time and resources, and may suffer from low participation rates (in case-control studies), loss to follow-up, and measurement error. If the number of exposure-induced excess cases is small, it is easy for the adverse effects of exposure to be masked by the errors in the study data. Therefore, it is important to be circumspect about the potential of epidemiological research to detect the effects of environmental hazards, appreciate the limitations of such research, and recognize that when such studies are conducted the results seldom provide evidence that is unambiguous. In this context, I would view the limitations for studying the effects of environmental contamination in the Lincoln Park community not as primarily following from statistical power; rather the utility and validity of such a study will depend upon the accuracy and completeness of information on exposures, disease, and potential confounding factors that could be derived for the population and time period of concern.

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