Review of the Epidemiologic Literature on EMF and Health

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Exposures to extremely low-frequency electric and magnetic fields (EMF) emanating from the generation, transmission, and use of electricity are a ubiquitous part of modern life. Concern about potential adverse health effects was initially brought to prominence by an epidemiologic report two decades ago from Denver on childhood cancer. We reviewed the now voluminous epidemiologic literature on EMF and risks of chronic disease and conclude the following: *a*) The quality of epidemiologic studies on this topic has improved over time and several of the recent studies on childhood leukemia and on cancer associated with occupational exposure are close to the limit of what can realistically be achieved in terms of size of study and methodological rigor. *b*) Exposure assessment is a particular difficulty of EMF epidemiology, in several respects: *i*) The exposure is imperceptible, ubiquitous, has multiple sources, and can vary greatly over time and short distances. *ii*) The exposure period of relevance is before the date at which measurements can realistically be obtained and of unknown duration and induction period. *iii*) The appropriate exposure metric is not known and there are no biological data from which to impute it. *c*) In the absence of experimental evidence and given the methodological uncertainties in the epidemiologic literature, there is no chronic disease for which an etiological relation to EMF can be regarded as established. *d*) There has been a large body of high quality data for childhood cancer, and also for adult leukemia and brain tumor in relation to occupational exposure. Among all the outcomes evaluated in epidemiologic studies of EMF, childhood leukemia in relation to postnatal exposures above 0.4 µT is the one for which there is most evidence of an association. The relative risk has been estimated at 2.0 (95% confidence limit: 1.27–3.13) in a large pooled analysis. This is unlikely to be due to chance but, may be, in part, due to bias. This is difficult to interpret in the absence of a known mechanism or reproducible experimental support. In the large pooled analysis only 0.8% of all children were exposed above 0.4 µT. Further studies need to be designed to test specific hypotheses such as aspects of selection bias or exposure. On the basis of epidemiologic findings, evidence shows an association of amyotrophic lateral sclerosis with occupational EMF exposure although confounding is a potential explanation. Breast cancer, cardiovascular disease, and suicide and depression remain unresolved. *Key words:* cancer, chronic disease, epidemiology, extremely low-frequency EMF, review. — *Environ Health Perspect* 109(suppl 6):911–933 (2001).
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Man has evolved in an environment with extremely low exposure to time-varying extremely low-frequency electromagnetic fields (EMF) from natural sources, resulting from the activity of the sun, fields from the earth, and fields emitted by the human body. The advent of residential and industrial use of electricity for power, heating, and lighting, however, has brought about far greater and increasing exposures over the last 120 years, from the generation, transmission, and use of electricity (*1,2*). These exposures are now a ubiquitous part of modern life, and there has been concern in some quarters that they might have adverse health effects.

On initial consideration, it is not obvious that EMF would pose any hazard to human health. In particular, this radiation has insufficient energy to damage DNA directly, and therefore in principle should not be capable of initiating cancers. Concern about a possible danger has arisen in the last 20 years, however, and has initially been brought to prominence by a report in 1979 of an epidemiologic study in Denver by Wertheimer and Leeper (*3*). They found a relation between risk of childhood leukemia and a proxy measure of degree of exposure to EMF radiation from electricity transmission lines. Since that study, there has been a burgeoning of research in this area. The most intensive epidemiologic effort has concerned childhood malignancy, especially leukemia, but there has also been considerable research on possible occupational associations with cancer in adults, on cardiovascular and neurological/psychological diseases in adults, and on reproductive outcomes. This research has been accompanied by public apprehension about the possibility that exposures to EMF, particularly for children, might be a cause of malignancy.

Laboratory research has given no consistent evidence that EMF of the magnitude encountered in every day life for a substantial period can affect biological processes or that EMF affects the risk of cancer in animals. The epidemiologic literature is therefore particularly worth careful consideration because it is essentially on this evidence alone, at present, that suggestions about long-term effects on human health rest. In this review, therefore, we summarize and discuss critically the current state of epidemiologic knowledge and the strengths and weaknesses of the available evidence on the relation of EMF exposure in man to risk of cancer and other adverse outcomes. We have taken EMF to refer to time-varying electric and/or magnetic fields <300 Hz. Where studies have specifically measured electric and/or magnetic fields, we have indicated the type of field; where they have not, or where it is not clear from the report, we have referred to EMF generically. We have restricted our attention to epidemiology, not experimental human studies; and although we have referred to some research on physiological effects, these are not reviewed systematically, and the review is primarily concerned with pathological end points. Particular attention is paid to methodological issues and to exposure measures because these have been a contentious and difficult area of EMF research and are critical to appraisal of the existing literature. Finally, we comment on areas where further research is needed.

Exposure Assessment

Common Themes and Difficulties

The challenges in exposure assessment in EMF epidemiology have been discussed ever since the first paper was published by Wertheimer

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and Leeper (*3*). A criticism was that the wire-coding scheme Wertheimer and Leeper had used to classify the subjects' exposure would be much too crude to result in a meaningful categorization. All subsequent studies have, to some extent, been criticized for using a less than perfect exposure assessment, although the sources of these problems have been different across studies depending on their design.

With few exceptions the resulting exposure misclassification would be nondifferential and thus be most likely but not certain to result in a bias towards the null. In effect these problems in exposure assessment would not result in spurious associations between EMF and disease risk; if anything, they would mask real associations or lead to underestimation of their magnitude. Yet, if a study is positive despite a low correlation between a marker for EMF exposure and the true exposure, one could argue that the likelihood of alternative explanations, such as confounding, would be high. These were in essence the points made in relation to the wire codes used by Wertheimer and Leeper.

Consideration of the extent to which a particular study was successful in its attempts to assess EMF is essential when reviewing the literature. If it turns out that the validity of the EMF assessment correlates with the magnitude of the observed effect, it would be a key observation in that review.

Three major difficulties with respect to exposure assessment are repeatedly discussed in the EMF literature, namely, the lack of knowledge about a relevant metric and about the relevant induction period; the retrospective nature of the exposure assessments; and the incomplete characterization of exposure sources, and the inability to combine exposures from different sources into one metric.

Knowledge on relevant metric and relevant period of exposures. The exposure is complex and multifaceted because of the cyclical nature of exposures from power lines according to daily, seasonal, and secular patterns; the variation in exposure in a given residence from differences in power usage by persons residing in that home over the course of a day, a season, and over longer intervals; and the notable variation due to exposures from a wide range of different types of electrical appliances, with usage also varying over short- and longer term intervals. Thus, any effort, no matter how comprehensive, to capture retrospectively the variation by time of day, season, and longer periods will undoubtedly fall far short in capturing the complexity and multifaceted nature of the exposure. Regardless of the numbers, types, and repeated nature of any measurements of EMF, there will be incomplete characterization of exposures from all sources if the goal is to integrate exposure over long periods.

Because there is no known biological mechanism by which EMF can increase the risk of cancer or other diseases, the relevant exposure metric is unknown. Indeed, if such a metric were known, it would imply that important aspects of the mechanism were understood and that a health effect exists. Similarly, the induction period of any potential etiology is unknown, and therefore so is the period of exposure that should be examined as relevant to risk. The only known interaction between EMF and the human body is the induction of an electric current, which is proportional to the magnetic field (flux density). The magnetic field in its turn is proportional, among other things, to the electric current by which it is generated. The magnetic field is not easily shielded by vegetation or buildings. For these reasons the magnetic field rather than the electric field has been studied in most of EMF epidemiology.

A major issue has been how to handle the time variations in the magnetic field. In many study designs, the time-weighted average was used implicitly. This holds for all the studies based on a characterization of homes or jobs, such as wire-code and job-title studies. It has been argued that because the levels of currents encountered in the environment are orders of magnitude below the levels for which biological effects are seen, one should be looking at rapid changes in the fields or at short moments of highly elevated fields. Sufficiently rapid changes, called "transients," may indeed induce currents of a sufficient magnitude for biological effects to occur, although presumably not for a sufficiently long time for the cells to react; there are currently no epidemiologic data on this (*4*). Several of the studies that used sophisticated magnetic field meters, such as the EMDEX, have been able to look at various patterns of time changes, in addition to time-weighted averages (*5*).

Retrospective exposure assessments. All epidemiologic studies to date have been based on a retrospective assessment of the exposure; it is unlikely that prospective studies will ever be done, given the rarity of the outcomes of interest. In some studies the retrospective exposure assessment is explicit, such as when historical fields are calculated or when wire codes or job titles are determined for the etiologically relevant period. But studies that use actual measurements of the fields are also retrospective because it is often inferred that those fields would also apply retrospectively. Therefore, it has been a topic of discussion whether carefully assessed contemporaneous fields or more crudely assessed historical fields offer the best estimate of exposure during the relevant time period. To address this issue, several studies have examined the amount of change in the magnetic field from one period to another and to what extent a contemporaneous field can be used to predict the field at some historical point in time (discussed below).

Completeness of exposure characterization. The first epidemiologic study on EMF and chronic disease risk was based on a characterization of the homes of children with respect to potential magnetic field levels generated by nearby power lines (*3*). Obviously, this approach neglects magnetic field exposure encountered outside of the home and magnetic field exposure in the home from sources other than the power line. Similarly, the first study on occupational exposure, published a few years later, was based on job titles classified without the benefit of measurements and ignored all exposure outside of work (*6*). By taking measurements it is, in principle, possible to incorporate all in-home fields regardless of their source. A few studies have also combined exposure at work and exposure at home (*7*). Two studies have attempted to capture the complete exposure regardless of where it is experienced, by putting portable meters on children in case–control studies (*8,9*). However, this assumes that the behavior of the case children has not changed from that in the etiologically relevant period prior to diagnosis. Another attempt to capture the complete exposure would be to ask questions about use of appliances and other EMF sources, as was done in the U.S. National Cancer Institute (NCI) study (*10*). However, the questionnaire focused on selected appliances used by pregnant women, and on their offspring; and thus the results underascertained mothers' and subjects' exposures to magnetic fields from electric appliances. Furthermore, it is difficult to combine such answers into a single index that reflects the complete EMF exposure.

Residential

We describe here five types of measurements used in the majority of published epidemiologic studies of residential EMF exposure and focus on some of the difficulties associated with assessment of residential EMF exposures. Relatively few methodological studies have evaluated reproducibility of exposure measurements within residences, by data collector, and over time. In the absence of a clear "gold standard," only limited consideration has been given to the validity of the exposure assessment approaches undertaken to date. A further methodological issue complicating residential EMF (and other forms of residential) exposure assessment in children and adults is the problem of residential mobility. In the absence of data identifying the relevant timing for potentially carcinogenic or other exposures that may be etiologically related to occurrence of chronic disease outcomes, it is virtually impossible to pinpoint the timing of exposure that is to be retrospectively assessed; this issue is also discussed in more detail below.

Types of exposure measurement. WIRE CODES. Wire codes, a proxy measure of the potential for exposure to residential magnetic fields produced by electric current flow in nearby power lines, is a method for estimating magnetic field levels from visual inspection of the characteristic features (size of wires, closeness to the origin of electric current, etc.) and distance of power lines adjacent to residences. The first wire-coding classification, developed by Wertheimer and Leeper (*3*), categorized homes as having either high (HCC) or low-current configuration (LCC). Wertheimer and Leeper (*11*) subsequently expanded the wire-coding scheme to include four categories: very high current configuration (VHCC), ordinary high current configuration (OHCC), ordinary low current configuration (OLCC), and very low current configuration (VLCC). Savitz and colleagues (*12*) later added a category for homes with adjacent power lines buried underground (UG). If two or more power lines are adjacent to a residence, the Wertheimer–Leeper classification assigns a wire-code category to a residence on the basis of the shortest distance between a residence and the nearest transmission line, three-phase primary distribution line, first-span secondary distribution line, short first-span secondary distribution line, or second span secondary distribution line. The three-phase primary distribution lines are further classified as thick or thin according to the diameter of their conductors. Average measurements of residential magnetic fields have been shown to rise with increasing category of wire code in Seattle, Washington (*13*), Denver, Colorado (*14*), Los Angeles, California (*15*), nine Midwestern and mid-Atlantic states (*16*), and five Canadian provinces (*9*). Kheifets et al. (*17*) examined the distribution of wire-code categories according to spot magnetic field measurements using data from seven studies and found that the percent of homes included within the VHCC category varied from 3 to 12%, with the highest percentages observed for studies in Los Angeles. The distribution of spot-measured magnetic fields within each wire-code category was evaluated for four of the studies, with all showing a monotonic trend for increasing median field with increasing wire code in OLCC, OHCC, and VHCC categories, but the 10–90 percentile ranges in each category overlapped widely (*17*). Data from the 1,000-home study (*18*) and the nine-state NCI study (*16*) demonstrated a similar range in magnetic field levels within each wire-code category as was observed in Denver *(12)* but included markedly higher values than those seen in Los Angeles (*15,19*).

Practically, it can be difficult to visually distinguish between different types of secondary distribution lines or to estimate the conductor diameter, thus potentially leading to error. To minimize possible misclassification from such errors, a simplified wire-code scheme was developed by Kaune and Savitz (*20*). The modified wire-code classification includes three categories: high wire codes (HWC), medium wire codes (MWC), and low wire codes (LWC). The Kaune–Savitz classification was tested on data from the second case–control study in Denver (*12*) and the NCI study of nine Midwestern and mid-Atlantic states (*21*) and yielded similar but more precise risk estimates of the relation between residential wire-code level and childhood cancer (*16,22*). Data from the NCI study revealed that the difference in magnetic field measurements between extreme wire-code categories was greater for the Wertheimer–Leeper classification than for the Kaune–Savitz scheme, although cross-classification of residential magnetic field measurements by both wire-coding schemes demonstrated that the Kaune–Savitz modified code provided additional discrimination. In addition, the Kaune–Savitz code resulted in almost twice as many homes being assigned to the highest category compared with the Wertheimer–Leeper code, without an appreciable decrease in measured magnetic fields in homes in the highest category (*16*).

DISTANCE BETWEEN POWER LINES AND RESIDENCES. While early residential studies of EMF in the United States used the wire-code classification developed by Wertheimer and Leeper (*3,11*), some of the initial European investigations examined risk of cancer in relation to distance of subjects' residences from electric generating or transmission equipment, including high-voltage power lines, overhead power lines, substations, transformers, electric railroads, or subways (*23–25*). Subsequently, studies in the Nordic countries evaluated risk according to distance between residences and power lines (*26,27*) or between residences and overhead lines, underground cables or substations (*28*). In the NCI study, risk of childhood leukemia was evaluated according to distance of residences from transmission and three-phase, primary distribution power lines along with separate evaluation of other components of wire codes (*29*).

CALCULATED HISTORICAL MAGNETIC FIELD LEVELS. The availability of longstanding population registry databases (including computerized real estate data, population registry information, national cancer registry data and mortality registry data) in conjunction with assignment of a unique personal registration number to each individual at or close to birth has enabled unique types of population-based, linked registry cohort or nested case–control studies of cancer to be carried out within the Nordic countries (*30,31*). Detailed historical information from power companies on electric structures (including detailed maps and specifications of overhead high-voltage power lines, underground cables, towers, electric substations), distances (between towers, phases, etc.), the ordering of phases, and load on the power lines could be linked with population registry data to estimate residential magnetic field levels generated by power lines, using special computer programs. Variations of this type of approach, termed calculated historical magnetic fields, were used to estimate residential magnetic field levels in population-based epidemiologic studies carried out in Sweden (*32*), Denmark (*28*), Finland (*27*), and Norway (*26*). In effect, utilization of calculated historical magnetic field levels was closer in strategy to the exposure assessment approach used to assign wire codes to homes than to methods employing contemporaneous direct measurement of magnetic field levels in homes to estimate retrospectively past residential exposures.

RESIDENTIAL AREA MEASUREMENTS. In the absence of population registry data (which includes detailed information on the distance between transmission or distribution lines and residences) and historical information from power companies on structural and related characteristics of power lines and load data, the unique types of linked registry studies that are possible in Nordic countries are not feasible in most other countries. Elsewhere, direct contemporaneous magnetic (and sometimes electric field) measurements have been the most common approach used to estimate historical residential magnetic field levels. Initial studies characterized field levels using short-term, or "spot," measurements taken immediately outside (*23*) or within residences (*12*), the latter obtained in the child's and parents' bedrooms. Subsequently, 24-hr measurements were obtained in rooms in which subjects spent a substantial proportion of time, based on interview data (*9,15,19,21,33–37*). Such measurements are made after diagnosis, but unlike measurements based only on power lines, these in-home measurements reflect all sources of magnetic fields in the residence (*38*). Studies examining the relationship of children's personal magnetic field exposures with residential and school area measurements have demonstrated good correlation, particularly between 24-hr personal dosimetry and the 24-hr bedroom measurements of younger children in nine Midwestern and mid-Atlantic states in the United States (*39,40*). A study comparing personal and residential area measurements of children in the United Kingdom also demonstrated that a 90-min measurement within the child's home could classify children into the lowest 90% of exposure with acceptable sensitivity and specificity (*37,41*).

PERSONAL MAGNETIC FIELD MEASUREMENTS. Two Canadian case–control studies utilized personal exposure measurement (*8,9*). In each of these studies, children wore an EMF meter in a small backpack or waist pouch (the dosimeters were placed in close proximity to infants) for 48 hr; dosimeter measurements were evaluated in relation to information obtained from an activity diary (listing times and locations of the subject's activities) that parents were asked to complete. The rationale put forth by the investigators for using personal measurements was to ascertain children's EMF exposure from all sources, including residential, school, and other away-from-home exposures (*9*) and to provide more detailed information about characteristics of individual spatial and temporal variation in exposure (*8*). Experience is limited when this exposure assessment approach is used. The criticism is that any case–control differences observed might simply reflect changed activity patterns of cases following a diagnosis of leukemia. One of the two groups of Canadian investigators evaluated this issue and found that cases spent more time at home and less time at school than controls at the time of the personal measurement, but these differences accounted for only about 3% of the total time (*9*). These investigators also used alternative measures to model historical exposures (including 24-hr children's bedroom measurements, wire coding using the Wertheimer–Leeper and the Kaune–Savitz wire-coding schemes, and perimeter measurements of childrens' residences) and compared the risk estimates for leukemia associated with the modeled historical exposure estimates with the risk estimates for leukemia associated with those using personal dosimetry (*9*). (See below.)

Metrics evaluated. In most epidemiologic studies reported to date, residential magnetic field measurement data have been evaluated using spot measurements or time-weighted average levels or medians of longer-term measures (both of the latter representing measures of central tendency). Threshold levels, generally considered as exposures ≥0.2, 0.3, or 0.4 µT have been used (0.1 µT = 1 mG). Yet, other alternative metrics have been proposed (*42–44*), including other measures of central tendency (such as 30th, 40th, 60th, or 70th percentiles), peak exposures (defined as the highest measured values (e.g., 90th, 95th, or 100th percentiles), and measures of short-term variability, including the rate-of-change metric proposed by Wilson et al. (*45*), the modified rate-of-change metric proposed by Burch et al. (*46*), the number of consecutive values taken 30 sec apart that differ by a minimum absolute values of 0.03, 0.05, or 0.10 µT (*47*), and other measures of rapid change, such as transients (*5,48*). To date, only the data from the NCI study have been evaluated in an exploratory analysis of alternative metrics. The available measurements taken in the NCI study did not permit transients to be examined, but overall the measures that showed the strongest association with risk of leukemia were those of central tendency (*49*); the results of the exploratory analysis did not change the fundamental conclusion from the earlier report of the results of the nine-state U.S. study (*21*). A case–control study in Germany first described stronger associations of leukemia risk with night-time measurements (*33,34*); this finding was confirmed in the NCI study (*49*). Although some investigators have suggested the possibility of windows in the dose–response relation, for example, intervals of field strength that exclusively increase risk (*50*), data from the NCI study revealed no evidence for departure from linearity for any of the magnetic field strength indices (*49*).

Time period(s) evaluated. Some data suggest that one potentially important period of exposure for childhood cancer is during the prenatal period (*51,52*). However, etiologically relevant time windows for most cancers or other chronic diseases in adults are poorly understood. Even though other time periods (such as the preconception period, or perhaps an interval in early infancy) may also be etiologically important, there are only very limited data implicating any agents in these time periods in the etiology of childhood cancer or other childhood chronic diseases. The initial study assessing the relationship of EMF with childhood cancer estimated EMF in residences in which cases and controls resided at birth and death (*3*). Subsequently, investigators focused on homes in which cases resided: within a short interval prior to or at diagnosis (*12,37,53–55*); at birth (*25*); during pregnancy (*21,55*); at birth and/or diagnosis (*23*); closest to diagnosis or resided in longest (*15*); a varying length of time dependent upon the child's age at diagnosis (*8,9*); continuously during the 4-year interval prior to diagnosis (*56*); in the 5 years prior to diagnosis, regardless of number of homes (*21*); from conception to diagnosis (*19,28*); or during a particular year or period prior to diagnosis that a subject resided in a county with a high power line (*26,27,32*). For most residential studies of EMF in adults, the period evaluated generally included a specified interval (ranging from 4 to 15 years) prior to or at diagnosis (*11,57*) or during all the time a subject resided within a defined distance of a designated high-tension power line prior to diagnosis (*58,59*).

Retrospective exposure assessment limitations. Many assumptions must be considered in evaluating epidemiologic studies using retrospective exposure assessment. These assumptions have been described in many epidemiology texts and in previous reviews of the epidemiologic studies of EMF (*43,44*). In addition to other shortcomings described in more detail in other parts of this section on residential studies, one of the key issues is the extent to which contemporaneous area measurements (which include a comprehensive set of carefully performed measurements) provide an accurate estimate of past exposures. The literature on this topic is limited in the scope of the measurements, the number of residences evaluated, a relatively short interval between initial and subsequent measurements or other aspects (*41,60,61*). The results are discussed below.

Incomplete characterization of sources. With the exception of the two Canadian studies using personal dosimetry, none of the childhood or adult residential measurement studies attempted to include comprehensive assessment of all sources of exposure to individuals. The studies focusing exclusively on wire codes limited consideration of potential sources of exposure to residentially proximate power lines. Similarly, measurements focusing on the distance between a subject's residence and nearby power lines also restricted evaluation of EMF to nearby power lines. Those studies incorporating area measurements taken within residences would partially capture not only EMF exposures from nearby power lines to the specific site where the measurement was taken, but also the contribution of EMF exposures from nearby electric appliances. Yet, such area measurements were usually restricted to a limited number of places within a residence, thus capturing a limited number of sources of exposure within the residence. In addition, area measurements taken inside a home were often restricted to homes resided in at the time of measurement. Generally, most studies evaluated one residence per subject; sometimes studies focused only on residentially stable subjects or residentially stable controls in a case–control study. Subjects with substantial residential mobility were incompletely evaluated or sometimes excluded from studies focusing on area measurements. In general, historical calculated field measurements include not only a one-time estimate of an individual's exposure from nearby high power lines, but also a longer term temporal component of an individual's exposure. However, historical calculated fields do not include the contribution of EMF exposures from electric appliances or other sources. On the other hand, residentially mobile as well as residentially stable subjects are included in studies using this type of measurement if the residentially mobile subjects move to different homes within the corridor based on distance from specified power lines that define the target population.

Reliability and reproducibility of EMF exposure measurements. Given the problematic nature of retrospective exposure assessment and absence of knowledge about the relevant metric and biologically meaningful time period of exposure, a gold standard to compare with the extensive number of exposure assessment approaches used is not available. Although results of analytical epidemiologic studies are sometimes compared with large cross-sectional studies (*18*), the latter also include measurements obtained at a single point in time and employ different selection factors than those used in U.S. analytical epidemiologic studies. In addition, the U.S. power frequency characteristics as well as the transmission and distribution lines differ from those in many other countries. However, several studies described comparisons between two independent types of measurement. For example, the Swedish study of childhood cancer compared contemporaneous spot measurements within homes to the historical calculated fields for those homes (*32*), the five-province Canadian study compared a construct of area in-home measurements plus assigned wire-code levels to personal dosimetry (*9*), and several studies evaluated the distribution of one type of measurement stratified by a second type (*9,12,15,19,32,34,56*) or evaluated the correlation of different metrics for magnetic fields (MF) (*12,16,49*).

Few studies have examined reproducibility of assignment of wire codes to residences. In a study of 81 homes in Colorado, only 8 were assigned wire codes in 1990 that differed from the wire-code category determined in 1985 (*60*), and there was 92% agreement in wire-code assignments of 187 residences that were independently wire coded twice in the NCI study (*16*). For both studies, coding differences were due to differing distance measurements, differing characterization of primary distribution line-conductor sizes as “thick” or “thin,” and differing classification of secondary wires as “first-span” versus “second-span.”

The coefficients of correlation between residential area magnetic field spot measurements of 81 Colorado homes, despite differences in the time of day of the two measurements taken in the same home, ranged from 0.70 to 0.90, thus indicating good to very good correlation even though the two sets of measurements were taken 6 years apart (*60*). Repeat long-term measurements (e.g., 24 hr for all but one measurement, the latter taken over a 2-week period) taken every 2 months over a year in 51 homes in Detroit, Michigan, and Minneapolis–St. Paul, Minnesota showed good correlation of repeated measurements within a given residence over time, although a small but statistically significant seasonal effect was found (*61*). Nevertheless, considerable unexplained variability characterized measurements in about one third of the homes. The results support the need for at least one 24-hr measurement, but the likely improvement in exposure classification and decrease in misclassification that would result from such additional measurements must be balanced by the added intrusiveness and cost (*61*). Good correlation (correlation coefficient = 0.76) was seen for measurements taken less than 1 year apart in 607 residences in a nationwide study in the United Kingdom, whereas the correlation coefficient was 0.66 for the 182 repeated residential measurements taken 2 or more years apart (*41*). Only one investigation has reported the reproducibility of exposure measurement among data collectors assessing wire-code configurations, and the results showed good reproducibility (*16*). The results of the Swedish study, demonstrated a good correlation between contemporaneously calculated fields and spot measurements but a weaker correlation between historically calculated fields and spot measurements (*32*).

The validity of the residential area measurements (and school area measurements taken in the study in the United Kingdom) to capture childrens’ personal magnetic field exposures was evaluated in two substudies carried out for 24-hr each among 29 volunteers (*20*) and 64 control children (*40*) in the nine Midwestern and mid-Atlantic states in the United States, and during three separate weeks among 100 healthy children in the United Kingdom (*41*). Children under 9 years of age in the United States spent 40–44% of a typical 24-hr school day in their bedroom; at home, personal dosimetry levels were highly correlated with total 24-hr magnetic field exposure levels and with 24-hr area measurements taken in their bedrooms (*39,40*). Detailed results from the United Kingdom validation study will be published in the near future, but overall good correlation was seen between mean annual personal exposure and both the 90-min and 24-hr residential area measurements (*37*).

Occupational Exposure

Exposure assessment in studies of occupational EMF exposure and health outcomes has been a central concern since the earliest reports on neurobehavioral changes in high-voltage substation workers (*62*) and leukemia in electrical workers (*6*). Although one can readily determine an individual’s job title, or even the environment in which the worker spends time, determining the actual exposure to various forms of EMF is a major challenge. Before discussing the strategies used in past studies, the conceptual challenges to characterizing occupational EMF accurately should be noted.

Exposure metrics and period of relevance. As noted above, the specific exposure metric of interest is not known with certainty. The occupational environment has even more extreme variability than the residential environment, both temporally and spatially. In addition, exposure to electric fields, while mostly shielded in residential environments, might be important in occupational environments. Consider as an example the magnitude of exposure incurred by electric power company linemen in line work (often over 100 µT) compared with the exposure while in transit to the next work location (often close to zero). In the occupational environment, the selection of an index is likely to matter, and correlation across indices will not necessarily be high enough for alternatives to yield similar results (*63*).

Exposure assessment methods. Given the rarity of most of the diseases of interest, such as leukemia and brain cancer, it is impossible to measure directly the exposures of all the individuals of interest over the relevant etiologic period. For studying rare outcomes such as cancer, exposure of the thousands or myriad workers of interest is estimated on the basis of either a generic assignment of exposure or detailed assessment of a relatively small number of workers with extrapolation to the larger group of interest.

JOB TITLES. The earliest research concerning potential occupational health effects of EMF blurred the distinction between “exposed to EMF” and simply “working in an electrical occupation.” The modern era of research on occupational EMF exposure began with Milham (*6*), who compiled a list of jobs that were presumed, without empirical evidence, to incur elevated exposures to electric and/or magnetic fields, as they were thought to involve frequent or prolonged work in proximity to energized electric equipment. This list served as the basis for a multitude of epidemiologic studies that followed.

The notable advantage of reliance on job titles as the basis for assigning EMF exposure is the widespread accessibility of such information. Occupation at the level of a job title is readily available both in public records and in epidemiologic studies not focused on EMF. People can report their occupation directly, and even proxy respondents can do a respectable job reporting for their parent or spouse, as long as the expectation is at the level of a job title and does not require detailed information on work environment or work practices (*64*); cancer registration (*65*) allows the study of very large occupational cohorts. To address such rare diseases as leukemia and brain cancer, large populations are essential. Case–control studies that gather occupational histories can be evaluated for information on associations with work in electrical occupations (*66*).

Another important strength of examining job titles is the simplicity and ease of understanding how the exposure index was constructed. Evaluation of years of employment in a particular job is much more readily understood (and scrutinized) than complex indices integrating grouped jobs and imputed exposures, resulting in indices with such units as "microtesla-years." Job titles are uniquely transparent and direct in describing what was evaluated—everything that extends beyond the job title is an inference that is susceptible to error.

As an exposure marker, there is also a substantial disadvantage to job titles. The relation between the job title and actual workplace EMF exposure is not very strong or predictable (*67*). Some jobs that seem to involve EMF exposure may in fact not typically produce elevated exposure, and even those that do are tremendously heterogeneous across individuals and time (*68,69*). Special challenges arise in community-based studies, namely, those not limited to a specific company or industry, with attempts to assign exposure to very broad occupational groups (*70*) As the job title becomes more specific in its implications for work setting and activities (*71*), the value of job title as a marker of exposure is enhanced but still very poor with only 5% of variance explained (*67*).

Because job titles constitute nominal or at best ordinal indicators of exposure, there is no direct way to combine exposures over time without additional quantification and assumptions. Another major challenge in using job titles alone as a marker of EMF exposure is that the job simultaneously serves as a marker of many other exposures. Jobs constitute a package of exposures, and they cannot necessarily be isolated from one another unless there is an array of jobs with associated differing exposures. Even beyond correlated workplace exposures to chemicals or physical agents that might confound the association between EMF and disease, jobs are not chosen randomly, and socioeconomic, behavior, and other correlates of occupation could be pertinent to disease risk.

JOB EXPOSURE MATRICES. As the application of job titles to assignment of EMF exposure becomes more formal and sophisticated, it crosses the boundary into the realm of job–exposure matrices. A job–exposure matrix is most easily conceptualized as a table with jobs constituting the rows and assignment of exposure indices in the columns. In a sense, even an algorithm as simple as stating that workers in certain sectors (e.g., electric utility, electronic equipment repair) are exposed to EMF and others are not is already a crude job–exposure matrix, with 0's for the unexposed jobs and 1's for those thought to have exposure. The rows of that matrix corresponding to the level of detail in the jobs can be subdivided into increasingly specific administrative units and work locations. Similarly, the assignment of exposure scores can extend well beyond the dichotomy of exposed versus unexposed. There are a number of incentives to formalize the use of job titles in the form of such matrices.

The job–exposure matrix is a means of characterizing exposure for the many persons of interest whose occupational exposure cannot possibly be measured or even scrutinized in detail to assess potential exposure. Using jobs as the unit for aggregation, some but not all individuals holding that job can be evaluated through expert assessment or measurement and a score assigned to all those who hold or previously held the job.

The assignment of exposure can be based on informal assessment of the work location and activities. The next level of evaluation involves expert assessment through observation or background knowledge of the relevant industries. An expert panel, for example, might evaluate a list of jobs and determine whether there is likely to be elevated workplace EMF exposure associated with each. The most sophisticated approach requires a combination of expert evaluation and measurement for a sample of workers.

A number of studies have developed quantitative exposure matrices using this approach (*72–74*). The strategy starts with the selection of reasonably homogeneous job groups for assignment, sampling workers in those groups for direct measurement of workplace EMF exposure, using statistical approaches to assign exposure to the job group, and finally applying that information to all individuals in the study. The opportunity to develop a detailed, empirically driven job–exposure matrix is much greater within an industry than across many industries, in part because of the reduced diversity in types of jobs to evaluate but also because of ease of workplace access for measurement.

Providing quantitative exposure estimates for the jobs of interest offers the opportunity to quantify the variation in exposure within and between job groups (*67,72*). Moreover, when assigning exposures to time intervals that include multiple jobs, only quantitative indices can be integrated to produce a summary score. Quantification also allows for more direct comparisons across work settings (*67*) and helps to relate the literature on occupational EMF to studies of residential exposures and electric appliances.

The decision about the proper unit for analysis, namely, the rows of the matrix, is critical. Some argue, for example, that it is necessary to consider the specific power plant in making such assignments in the electric utility industry (*75*), not just the job title. The trade-off between the homogeneity of narrowly constituted groups and the limited number of measurements per group must be reconciled as well. Just as in the case of residential measurements, the incorporation of the many quirks of the specific person's activities on the particular day of measurement contributes to the exposure assignment. If the lineman's truck breaks down and he spends the day by the side of the road, that is part of what determines his exposure for the day. In principle, those events are part of the lineman experience, and with a large enough sample, those events should be part of what makes the sampled exposure representative of linemen.

Incompleteness of characterization of sources. Even at best, occupational EMF exposure characterization will be incomplete, given the failure to incorporate exposure encountered in the residence and through use of electric appliances. Also within the work environment, some incidental exposures such as those encountered by driving near overhead power lines or having an office located near electric conductors are nearly impossible to capture. Instead, occupational exposure assessment focuses on specific, observable sources of exposure that are distinctive to the job of interest.

Reliability and reproducibility. Although measurement of workplace exposure has been examined rather extensively to address day-to-day variability, the overall approach to assigning exposure in occupational studies has not been generally evaluated (*76*). That is, whether another set of investigators assigned the task of characterizing exposure would end up with the same scheme is open to question. For the simplest of job–exposure matrices, for example, dividing workers into operations versus office, the reliability would likely be quite good, whereas for the more detailed decisions on the job groups and the number and methods of measurement, reliability would likely be much lower.

Cancer

Childhood Cancer

Magnetic field exposures from power lines. OVERVIEW. Since Wertheimer and Leeper in 1979 (*3*) hypothesized that magnetic fields from residentially proximate high-tension power lines and electric power substations were associated with increased risks of childhood cancer, more than 18 additional epidemiologic studies in at least nine countries (Table 1) have used a spectrum of exposure

Table 1. Characteristics of studies and results on the relation between EMF exposure and childhood cancer.

Reference	Study population	Primary exposure metric(s)	Study design	Cancers (numbers cases/controls)	Wire codes RR (95% CI) (high category)	Magnetic field measurements RR (95% CI) (high category)
Wertheimer and Leeper, 1979 (*3*)	Denver residents born in Colorado. Cases: <19 yr, deaths (1950–1973). Controls: birth certificates	Wire code of diagnosis/death home	CC*	All cancers (328/328) Leukemia (155/155) Brain tumors (66/66)	2.25 (HCC) 2.98 (1.78–4.98) (HCC) 2.40 (1.03–5.41) (HCC)	— — —
Fulton et al., 1980 (*53*)	Rhode Island residents. Cases: <20 yr. Controls: birth certificates	Wire code. Cases: all lifetime homes. Controls: birth homes	CC	Leukemia (119/240)	1.00 (HCC)	—
Tomenius, 1986 (*23*)	Stockholm County, Sweden residents. Cases: <19 yr (1958–1973). Controls: birth certificates	Front door measurement birth and diagnosis residences	CC	All cancers (1,033/890) Leukemia (243/212) Brain tumors (294/253)	— — —	1.8 (≥0.3 μT) 0.3 (≥0.3 μT) 3.7 (≥0.3 μT)
Savitz et al., 1988 (*12*)	Denver residents. Cases: <15 yr (1976–1983). Controls: random digit dialing	Wire-code spot MF measurements child's bedroom, low power	CC	WC MF All cancers 320 128 Leukemia 97 36 Brain tumors 59 25 Controls 259 207	 2.20 (0.98–5.21) (VHCC) 2.75 (0.94–8.04) (VHCC) 1.94 (0.47–7.95) (VHCC)	 1.35 (0.63–2.90) (≥0.25 μT) 1.93 (0.67–5.56) (≥0.25 μT) 1.04 (0.22–4.82) (≥0.25 μT)
Myers et al., 1990 (*25*)	Yorkshire, England residents. Cases: <15 yr (1970–1979). Controls: birth register	Distance of home to nearest overhead line; estimated MF strength	CC	All cancers (374/588)	1.10 (0.47–2.57) (<25 m distance) 0.4 (0.04–4.33) (≥0.1 μT)	—
London et al., 1991 (*15*)	Los Angeles County residents. Case: <10 yr (1980–1987). Controls: friends and random digit dialing	Wire-code and 24-hr child's bedroom MF measurement in home lived in longest, low power	CC	WC MF Leukemia 211 162 Controls 205 143	 2.15 (1.08–4.26) (VHCC)	 1.22 (0.52–2.82) (≥0.125 μT)
Feychting and Ahlbom, 1993 (*32*)	Sweden residents within 300 m of 220 or 400 kV power line. Cases: <15 yr (1960–1985). Controls: selected at random from cohort to match cases	Historically calculated fields	Nested CC	All cancers (141) Leukemia (38) Brain tumors (33) Controls (554)	1.3 (0.6–2.7) (≥0.3 μT) 3.8 (1.4–9.3) (≥0.3 μT) 1.0 (0.2–3.9) (≥0.3 μT)	—
Olsen et al., 1993 (*28*)	Denmark residents. Cases: <15 yr (1960–1986). Controls: Central Population Registry	Historically calculated fields	CC	All cancers (1,707/4,788) Leukemia (833/1,666) Brain tumors (624/1,872)	5.6 (1.6–19) (≥0.4 μT) 6.0 (0.8–44) (≥0.4 μT) 6.0 (0.8–44) (≥0.4 μT)	—
Verkasalo et al., 1993 (*27*)	Finland residents within 500 m of 110–400 kV power line. Cases: <17 yr (1974–1990)	Historically calculated fields	Cohort	All cancers (140) Leukemia (35) Brain tumors (39)	1.5 (0.74–2.7) (≥0.2 μT) 1.6 (0.32–4.5) (≥0.2 μT) 2.3 (0.75–5.4) (≥0.2 μT)	—
Preston-Martin et al., 1996 (*19*)	Los Angeles County residents. Cases: <20 yr (1984–1991). Controls: random digit dialing	Wire code at diagnosis, first, and longest residence	CC	WC MF Brain tumors 281 106 Controls 250 99	 1.2 (0.6–2.2) (VHCC)	 1.7 (0.6–5.0) (≥0.3 μT)
Gurney et al., 1996 (*94*)	Seattle and surrounding western Washington State residents. Cases: <20 yr (1984–1990). Controls: random digit dialing	Wire code of diagnosis home	CC	Brain tumors (120/240)	0.5 (0.2–1.6) (VHCC)	—
Tynes and Haldorsen, 1997 (*26*)	Norway residents in census ward with high-voltage power lines. Cases: <15 yr (1965–1989). Controls: selected at random from cohort to match cases	Historically calculated fields	Nested CC	All cancers (532/2,112) Leukemia (139/546) Brain tumors (144/599)	0.9 (0.5–1.8) (≥0.14 μT) 0.3 (0.0–2.1) (≥0.14 μT) 0.7 (0.2–2.1) (≥0.14 μT)	— — —
Linet et al., 1997 (*21*)	U.S., residents of 9 mid-Atlantic and Midwestern States. Cases: <15 yr (1989–1993). Controls: random digit dialing	Wire-code residences >70% 5 yr before diagnosis; TWA MF measurements all residences combined >70% 5 yr before diagnosis	CC	WC MF Acute lymphoblastic leukemia 402 624 Controls 402 615	 0.88 (0.48–1.63) (VHCC)	 1.24 (0.86–1.79) (≥0.3 μT) 1.72 (1.03–2.86) (≥0.3 μT)
Michaelis et al., 1997 (*33*)	Northwest Germany (Lower Saxony) and Berlin residents. Cases: <15 yr (1991–1995). Controls: government office residents' registry	24-hr child's bedroom MF measurement	CC	Leukemia (176/414)	—	2.3 (0.8–6.7) (≥0.2 μT)
Dockerty et al., 1998 (*35*)	New Zealand residents. Cases: <15 yr (1990–1993). Controls: birth certificate	24-hr child's bedroom MF measurement	CC	Leukemia (115/117)	—	15.5 (0.3–7.6) (≥0.2 μT)

(Continued)

Table 1. Continued.

Reference	Study population	Primary exposure metric(s)	Study design	Cancers (numbers cases/controls)	Wire codes RR (95% CI) (high category)	Magnetic field measurements RR (95% CI) (high category)
McBride et al., 1999 (*9*)	Canada, residents of 5 provinces. Cases: <15 yr (1990–1994). Controls: province health insurance rolls	Wire code of home 2 yr before diagnosis	CC	Leukemia Wire code (303/309)	0.77 (0.37–1.60) (VHCC)	
		48-hr personal measurement		48-hr personal dosimetry monitoring (293/339)		1.04 (0.69–1.57) (≥0.2 μT)
		24-hr child's bedroom 2 yr before diagnosis		24-hr child's bedroom (272/304)		1.27 (0.69–2.33) (≥0.2 μT)
Green et al., 1999 (*8*)	Southern Ontario Canada residents. Cases: <15 yr (1985–1993). Controls: telephone marketing lists	Wire code spot MF measurements; 48-hr personal monitoring	CC	Leukemia Wire code (79/125)	1.5 (0.3–8.7) (OHCC + VHCC)	1.13 (0.31–4.06) (≥0.4 μT)
				Spot measurements (21/46)		
				48-hr personal monitoring (88/133)		4.5 (1.3–15.9) (≥0.14 μT)
UKCCS, 1999 (*37*)	England, Wales, Scotland residents. Cases: <15 yr (1992–1995). Controls: Family Health Services Authorities register	In-home MF measurements. Phase I: 90-min measurement in family room and spot measurements in child's bedroom. Phase II (highest 10%): 48-hr measurement in child's bedroom. School: spot measurements	CC	All cancers (2,265/2,270)	—	0.89 (0.34–2.32) (≥0.4 μT)
				Leukemia (1,094/1,096)	—	1.68 (0.40–7.10) (≥0.4 μT)
				Brain tumors (390/393)	—	0 cases/2 controls (≥0.4 μT)

Abbreviations: CC, case–control; TWA, time-weighted average; UKCCS, United Kingdom Childhood Cancer Study; WC, wire code; yr, years.

assessment methods to evaluate the relationship. Over time, the epidemiologic studies have also generally enrolled larger numbers of subjects; focused increasingly on childhood leukemia and, to a lesser extent, brain and nervous system tumors; addressed methodological shortcomings of earlier investigations; and increasingly collected data on a broad range of other suspected confounding factors. Descriptions of the epidemiologic studies of EMF and childhood cancer can be found in the original reports. A brief summary is presented in Table 1. The reader is also referred to comprehensive reviews and summaries of the literature by expert committees appointed by the National Radiological Protection Board in the United Kingdom (*77,78*), the National Research Council of the U.S. National Academy of Sciences (*43*), and the National Institute of the Environmental Health Sciences (part of the U.S. National Institutes of Health) (*44*). In this section of the review we provide a historical synthesis of the epidemiologic studies of childhood cancer risk in relation to magnetic field exposures from power lines and from electric appliances. Among the emphases are the evolution of the childhood cancer outcomes evaluated, the growing sophistication of the exposure assessment strategies used, and the increasing understanding of the methodological issues.

TOTAL CHILDHOOD CANCER. Wertheimer and Leeper (*3*) reported significantly elevated risks for total childhood cancer (relative risk [RR] = 2.25) in Denver due to excess risks for childhood leukemia (RR = 2.98), brain and nervous system tumors (RR = 2.40), and lymphomas among nonoverlapping cases and controls (RR = 2.08). Comparing subjects residing in homes with high current configurations to those living in homes with low current configuration, a subsequent study in Denver found similar, albeit slightly lower, risks for all cancers combined (*12*). Although risks for all childhood cancers combined were also evaluated in one U.K. (*25*), and five Nordic studies (*23,26–28,32*) (Table 1), the biological and etiological interpretation of results for a grouping of disparate childhood malignancies is unclear.

LYMPHOMAS. Subsequent to the two studies in Denver, which reported elevated risks of lymphoma on the basis of 18 cases residing in HCC homes (*3*) and 3 cases in VHCC homes (*12*), results of later investigations have not supported a link between children's estimated residential magnetic field exposures and childhood lymphomas (except for a 5-fold, nonsignificantly elevated risk reported by Olsen et al. (*28*) on the basis of a single case). The studies reveal little evidence of a relationship between childhood lymphoma and MF exposure from residentially proximate power lines, but the data include very small numbers of highly exposed cases (Table 1).

BRAIN AND NERVOUS SYSTEM TUMORS. Significantly increased relative risks of brain tumors were reported in the first (RR = 2.4) (*3*) and second (RR = 1.9) (*12*) Denver studies among children residing in homes characterized by HCC and VHCC, respectively. However, later studies in the United States (*19,55*) generally have not found excess risks of brain and nervous system tumors associated with high residential wire-code configurations. Direct spot measurements in Denver (*12*) and 24–48-hr residential magnetic field measurements were also not linked with increased risks in Los Angeles (*19*) or the United Kingdom (*37*). Calculated magnetic field levels were not linked with increased risks of childhood brain and nervous system tumors in Sweden (*32*) or Norway (*26*), whereas nonsignificantly increased risks in Denmark (*28*) and a smaller risk in Finland (*27*) were based on two and three cases of brain and nervous system tumors, respectively. The absence of a relationship between residential EMF exposures and childhood brain tumors in the large and methodologically rigorous Los Angeles study (*19*) and in the nationwide U.K. (*37*), Swedish (*32*), Danish (*28*), and Norwegian (*26*) studies focusing on childhood brain tumors do not show that childhood brain tumors are etiologically linked with exposure to residential sources of EMF (Table 1).

LEUKEMIA. Studies of EMF have increasingly focused on childhood leukemia. Increasingly sophisticated exposure assessment approaches have been used in more recent studies.

Wire-code classification. The evolution of the wire-code configuration classification scheme, originally created by Wertheimer and Leeper (*3*) and further refined by Wertheimer and Leeper (*11*), Savitz et al. (*12*), and Kaune and Savitz (*20*), is described above. All studies examining the relationship of wire-code configuration and risk of childhood leukemia employed the case–control design. The relation between wire-code configuration and measured magnetic field levels may be influenced by in-home electric wiring, grounding, electric appliances, and other nearby sources of EMF (*12*). Wire-code levels predict measured magnetic fields in all areas of the United States, although the correlation is not very strong (see above). The significantly elevated risks estimated for childhood leukemia in relation to high wire-code configurations in Denver (*3,12*) and Los Angeles (*15*), were not replicated in Rhode Island (*53*), in nine mid-Atlantic and Midwestern states (*21*) or in five provinces in Canada (*9*) (Table 1).

Distance between power lines and residences. Several investigations evaluated the relation between distance of residences from power lines or other sources of high magnetic fields and risk of childhood leukemia (*24,26,29,32*). One study used a measure of distance but reported results only as a measure of voltage (of the two closest transmission or distribution lines) divided by the distance in meters, the square of the distance or the cube of the distance (*56*), a type of measurement not used in other studies, and thus difficult to evaluate or compare with other studies. Elevated risks (OR = 1.45, 2.0, 1.3) of childhood leukemia were reported for the small fraction (0.6%) of children residing within 100 m or 50 m of an overhead power line or within 25 m of a substation, respectively, in southeast England (*24*). An excess risk of leukemia was observed among children residing 50 m or less from 220 or 400 kV power lines in Sweden (based on 6 cases) (*32*). However, risk of childhood leukemia was not increased among children residing less than 51 m from high-voltage lines in Norway (based on 9 cases) (*26*). Risk of acute lymphoblastic leukemia was not increased among children residing within 40 m of transmission lines (based on 10 cases) or three-phase primary distribution lines (based on 105 cases) in nine Midwestern and mid-Atlantic states in the United States, nor was risk increased according to the contribution of all transmission lines and three-phase primary distribution power lines near a child's residence (based on 108 cases) (Table 1) (*29*).

Calculated historical magnetic field levels. The novel exposure assessment approach used in the Nordic countries (see above) linked data from various registries with long-term power line load data and specifications for power lines and associated structures obtained from the utility industry (*32*). The Nordic studies, although varying somewhat in study design, were all population based. Two studies defined cohorts residing within a specified distance of high-tension power lines, then ascertained childhood cancer cases within the cohorts during specified periods (a nested case–control approach) (*26,32*). A third study used a similar cohort method, reporting results from a cohort analysis (*27*). The Danish study identified incident childhood cancer cases during a specified period and selected matched controls from the central population register; proximity to high-voltage facilities was assessed using maps of high-tension overhead lines or underground cables, and residential magnetic field levels estimated from the distance of the subject's residence from the line or cable, the characteristics of nearby power lines, and electricity load data (*28*). Among the leukemia cases with estimated residential magnetic field exposure levels ≥0.2 µT (7, 3, 3, and 2 in Sweden, Denmark, Finland, and Norway, respectively), a 3.8-fold increased risk of leukemia was reported in Sweden (*32*), a 6-fold increase in Denmark (*28*), a 1.6-fold increase in Finland (*27*), and no excess risk in Norway (Table 1) (*26*).

Residential measurements. In residential studies assessing exposure using spot and/or 24-hr or longer area magnetic field measurements, increases in leukemia, ranging from 1.3- to 1.5-fold elevated, were reported for children with average magnetic field exposures ≥0.2 µT in Denver (based on 3 cases) (*12*), Los Angeles (based on 20 cases with exposures ≥0.268 µT) (*15*), Lower Saxony and Berlin, Germany (based on 4 cases) (*33,34*), nine Midwestern and mid-Atlantic states in the United States (based on 58 cases) (*21*), five provinces in Canada (based on 54 cases) (*9*), and the United Kingdom (based on 21 cases) (including England, Wales, and Scotland) (*37*). A 3.3-fold increase (95% confidence interval [CI] = 0.5–23.7) of leukemia was linked with 24-hr children's bedroom time-weighted average measurements ≥0.2 µT in a study in New Zealand (based on 5 cases) (*34,79*), and an odds ratio of 1.1 (95% CI = 0.31–4.06) was linked with point-in-time measurements ≥0.13 µT taken in the child's bedroom in a study in southern Ontario, Canada (based on 21 cases) (Table 1) (*36*). The latest study is from Germany and showed a relative risk of 1.6 (0.7–3.7) for 0.2 µT and 3.2 (1.3–7.8) for nighttime exposure (*80*).

Personal magnetic field measurements. Two Canadian studies employed personal exposure measurements as the primary direct measure of children's exposure to magnetic field levels. Unfortunately, it is difficult to compare results between the two Canadian studies or between the southern Ontario study and those conducted elsewhere because results of the study by Green et al. (*8*) are not reported using the same categorical cut point of ≥0.2 µT provided in most reports, despite an adequate number of cases (*n* = 20, according to Table 1) with average magnetic field exposures ≥0.2 µT. McBride et al. (*9*) reported only a small difference between cases and controls in activity patterns, but the results from personal dosimetry measurements are difficult to interpret in the absence of more widespread use of this measurement approach.

Summary of results of individual studies, meta-analysis, and pooled analysis. Greatest weight should be given to results of the methodologically more rigorous studies with larger numbers of subjects with high MF exposure levels (*9,21*) and to population-based studies with few methodological shortcomings (*26–28,32,37*). Extensive efforts have been undertaken to summarize quantitatively the individual studies in meta-analyses (*43,44,77,78,81–84*) and pooled analyses (*85,86*). Pooled analysis offers the availability of raw data as a special advantage, but, similar to meta-analysis, requires great care in the methodological approach used and interpretation of results (*87–89*). Using data from studies in six European countries (*26–28, 32–34,37*), nine Midwestern and mid-Atlantic states in the United States (*21*), five provinces in Canada (*9*), and New Zealand (*35,79*). Ahlbom et al. (*85*) found risk to be near the no-effect level among the 3,203 children with leukemia and 10,338 control children with summary residential MF exposure levels <0.4 µT, whereas a 2-fold leukemia risk (RR = 2.0, 95% CI = 1.27–3.13) was observed among the 44 leukemia cases (of whom 24.2 represented the expected number and 19.8 the excess number) and 62 control children with estimated residential MF exposures ≥0.4 µT. Thus, fewer than 20 children among 3,203 with leukemia represent the excess over expected numbers among children residing in homes with magnetic field exposure levels >0.4 µT. Adjustment for potential confounding variables did not appreciably affect the results.

Magnetic field exposures from electric appliances. Five studies have evaluated risks of childhood leukemia (*15,35,90,91*) or brain and nervous system tumors (*19,35,90*) associated with use of electric appliances. All the studies employed interviews of subjects' mothers to help assess exposure information. Overall, the small number of studies and the absence of measurement data within the studies preclude straightforward interpretation of results. The results based on interview data are summarized briefly below.

LEUKEMIA. A few associations were observed in two or three studies. Two investigations (*12,91*) reported small increases in risk associated with prenatal use of electric blankets, but only one of these (*12*) found a dose–response effect. There was little evidence of elevated risk of leukemia in offspring associated with mothers' prenatal use of other types of electric appliances. Postnatal use of electric blankets (*12,35,91*) and hair dryers (*15,91*) was linked with modestly elevated risks in more than one study, but there was no evidence of dose–response relationships. Risk of leukemia was increased overall, but no dose–response effect was found, among children watching black-and-white television in Los Angeles (*15*), whereas leukemia rose with increasing number of hours children watched television (mostly color televisions, as few black and white televisions were used), regardless of the child's distance from the television set in the nine Midwestern and mid-Atlantic states (*91*). An MF measurement study of more than 70 televisions of volunteer families in the greater Washington, DC, area concluded that MF exposures were not substantially greater than ambient levels at typical distances that children sit while watching television or playing video games on television screens (*92*). Risks were increased for postnatal exposure to a few other appliances in a single study (*91*), but overall the findings were not consistent among the four studies, nor was there generally evidence of dose–response relationships.

BRAIN TUMORS. There was little consistency among the results of the three studies that have evaluated risk of childhood brain tumors associated with prenatal and postnatal exposures to electric appliances. The first study (*90*) reported a dose–response relation for increasing number of night-time hours of maternal use of electric blankets and risk of brain tumors in offspring. This finding was not replicated in the other studies. However, Preston-Martin and colleagues (*19*) described small increases in risk of brain tumors among the offspring of mothers who used waterbeds during pregnancy. Dockerty et al. (*35*) found no associations of childhood brain tumors with maternal prenatal use of electric appliances, but noted nonsignificantly elevated risk of childhood brain tumors linked with postnatal use of electric blankets, waterbeds, and curling irons.

Overall, only limited data are available on electric appliances and risk of childhood leukemia or brain tumors. There is little convincing evidence that EMF exposures from maternal prenatal or children's postnatal use of electric appliances is associated with increased risk of childhood leukemia or brain tumors.

Methodologic issues. SELECTION BIAS AND CONFOUNDING. Important methodological considerations in the design, conduct, and interpretation of every epidemiologic study include the potential for selection biases. Although the possible role and the effect of each of these biases have been discussed in most of the summaries of the relation of EMF and childhood cancer (*43,44,77*), relatively few studies have attempted to evaluate or quantify their relative importance.

Selection bias. Nonparticipants often differ from participants, and participation rates tend to be lower for controls than cases in case–control studies. The design and methods used in the Nordic studies do not require individual subjects to be approached, but rely on information available in various registries. Thus, selection bias is not an issue in the Nordic studies but is a concern in other studies. To evaluate the possible role of selection bias, Hatch et al. (*93*) compared the relation between childhood leukemia and wire codes and direct measurements of magnetic fields in homes of subjects who participated in all phases of the study with the relation in all subjects, including those who declined to allow access inside the home or on the property, in the U.S. study conducted in nine Midwestern and mid-Atlantic states. The results revealed somewhat higher odds ratios for childhood leukemia when partial participants were excluded. Similar but slightly smaller increases in the odds ratios were observed, compared to those based on all subjects, when subjects who allowed a measurement only outside the front door were excluded. Because partial participants tended to be characterized by lower socioeconomic status than subjects who participated fully, these findings suggested selection bias. Like almost all of the other case–control studies of childhood cancer and EMF, the case–control investigation in nine Midwestern and mid-Atlantic states was characterized by greater nonparticipation by controls than cases, and higher socioeconomic status among controls than cases. The investigators of the study in five provinces in Canada (*9*) and the nationwide study in the United Kingdom (*37*) also noted a somewhat higher socioeconomic status and lower participation among controls than cases in those studies. Selection bias due to nonparticipation or differential restrictions placed upon cases and controls may have affected the results. Differential residential stability requirements were placed on cases versus controls in Denver (*12*), and cases were more likely than controls to have resided in their home for their entire lifetime in Los Angeles (*15*). Subjects in the Los Angeles study who refused to participate at either the random digit dialing or interview stages did not have their homes wire coded (*15*). The case–control study in New Zealand also reported differential levels of participation between cases and controls and evidence of higher socioeconomic status among controls than cases (*35*). If residentially stable controls were also more likely to reside in neighborhoods with low residential EMF exposure or wire-code levels, a spurious relation may have resulted between residential EMF and childhood cancer. In contrast, selection bias (for wire codes but not for measurements) may have been reduced in the nine-state Midwestern and mid-Atlantic study compared to earlier studies in the United States. This was because wire codes were assessed for subjects who refused to participate in the second interview or to allow access to the home or property and magnetic field measurements were obtained immediately outside the front door for all residences eligible for measurement regardless of whether the data collector was permitted to take measurements inside the residences (*91*). Savitz et al. (*12*) also wire coded a higher proportion of subjects than the proportions included in the interview and in-home measurement components, because eligible homes were wire coded for subjects refusing to participate since access to the home or property was not needed for wire coding.

Confounding. An evaluation of the relation between a large number of potential confounding variables and wire-code levels and direct measurements in the nine state Midwestern and mid-Atlantic study (*22*) revealed that univariate adjustment for individual variables changed the odds ratios for acute lymphoblastic leukemia by less than 8% and simultaneous adjustment reduced the risk estimates by a maximum of 15% (*93*). Categories of potential confounding factors that were evaluated but found to demonstrate no effect or only a very small effect include socioeconomic factors (mother's and father's education and occupation, family income, racial/ethnic group, home ownership), residential features (urbanicity, primary source of heat, type of air conditioning), lifestyle factors (maternal or paternal smoking, breast feeding, maternal use of a sewing machine, time spent watching television), residential mobility, reproductive factors (mother's or father's age at first birth, total number of live births prior to the index diagnosis/reference date), and use of selected electric appliances (electric blankets, waterbeds, hair dryers, and others) (*93*). A comparison of the potential effects of confounding versus selection bias in the nine-state U.S. study suggested that confounding alone was unlikely to be an important source of bias. The conclusion that selection bias may be more of a concern than confounding in most studies of residential magnetic field exposures and childhood cancer risk (*93*) is further underscored by the inconsistency among studies in the relation between income and wire codes. Studies in Seattle (*94*) and Columbus, Ohio (*95*), reported inverse associations between income and wire-code levels, but no evidence of such a relationship was observed in the nine Midwestern and mid-Atlantic states study (*93*). In evaluation of risks associated with the use of electric appliances, the relevant exposure has been assumed to be magnetic fields. Yet, other features also characterize users of such electric appliances. For example, families in which children spend many hours watching television are likely to differ behaviorally and in other ways from families in which little television is watched. In the U.S. National Health Examination Survey, time spent watching television was reported to be a strong predictor of obesity during adolescence (*96*).

MEASUREMENT ERROR. As discussed in "Retrospective Exposure Assessment Limitations" a single, time-weighted average measurement taken after diagnosis may not represent typical levels or even the proper metric for the period or residential area that is relevant. Because elevated risk appears to be restricted to only a very small fraction of children who are highly exposed and because there is no basis for determining the pattern of measurement errors in each study, it is not possible to assess the extent of measurement error in a given study nor is it possible to correct for such unknown errors.

In the study by Savitz et al. (*12*) and the study by Feychting and Ahlbom (*32*) there was evidence of an association between traffic density and leukemia, but without adjustment for traffic density having an effect on the EMF and cancer relation (*97,98*).

REPORTING BIAS. Reports about one's own or one's child's typical behavior during years prior to an interview are prone to error, particularly because behavior patterns change rapidly with age. The respondent's report may reflect habits from another year or another child in the family. Nondifferential forms of error, for example, those affecting cases and controls equally, tend to reduce an apparent association between exposures and a disease (*99*) and may minimize true dose–response patterns. In case–control studies of childhood cancer, errors may be more likely to be differential, thus potentially exaggerating true case–control differences. Such differential errors can arise in several ways. When asked about prediagnosis behavior, mothers may actually report postdiagnosis behavior. Another type of problem that can result in differential misclassification is recall bias, in which the mother of a case may be more likely to recall minor exposures occurring several years previously, whereas a mother of a healthy child is more likely to forget such exposures. Another possibility is that mothers of cases may exaggerate the duration or frequency of earlier exposures, whereas mothers of controls may report such exposures more accurately. Exposures that have been linked repeatedly with increased cancer risk by the media may be more likely to be mentioned by mothers of cases than mothers of controls. It is possible that some of the associations reported for various electric appliances and childhood cancer may be due to recall bias, although attempts to evaluate this have not shown evidence of bias (*91,94*).

RANDOM VARIATION AND RANDOM ERROR. When several types of measurement or a battery of questions are applied to assess a single hypothesis, as in many of the studies of childhood cancer and EMF (including electric appliances), individual elements should not be overinterpreted. Random variation or random error increases the likelihood of a positive finding for at least one individual measurement or question within the group of measurements or battery of questions.

Summary. Following the original report by Wertheimer and Leeper (*3*) linking the three most common forms of childhood cancer with a proxy measure of residential EMF (wire codes), more than 18 studies in nine countries have shown no convincing evidence of a relationship of childhood brain tumors or lymphoma with residential exposure to EMF from nearby power lines. There is no clear evidence of a relationship between childhood leukemia and residential EMF exposures among children with estimated exposure levels under 0.4 µT. A 2-fold increase in relative risk of childhood leukemia, confined to a very tiny fraction of children (estimated as 0.8% in one large pooled analysis) with residential EMF exposures ≥0.4 µT, is difficult to interpret in the absence of a known biological mechanism or reproducible experimental support of carcinogenesis. There is also some evidence to suggest that selection bias may account for some of the increase in risk among the proportion of children with high residential EMF exposure. In the absence of new and convincing experimental evidence linking EMF with carcinogenesis, additional epidemiologic studies are unlikely to provide further clarification of the relationship unless large numbers of cases with exposures ≥0.4 µT can be accrued, and methodological shortcomings, particularly selection bias, can be minimized.

Adult Cancer

The literature on occupational EMF and cancer is voluminous, particularly for leukemia and brain cancer, whereas research on residential or appliance exposure in relation to those and other cancers in adults has been quite limited. The recent concern with possible effects of EMF on breast cancer, largely driven by the hypothesized effect on melatonin (*100,101*), has generated limited findings, which we discuss, but there are several major ongoing studies in the United States that have not yet been published. The bulk of epidemiologic evidence is on leukemia, brain cancer, and breast cancer.

Meta-analyses of the occupational EMF literature by Kheifets and co-workers (*81,100*) identified 38 pertinent studies of leukemia and 29 studies of brain cancer after truncating the list to those suitable for meta-analysis, and the literature has continued to grow. Because others have summarized the vast array of studies and because the more recent ones are so far superior to those that preceded them, the focus in this review is on the smaller number of studies with sophisticated approaches to exposure assessment. Those that rely solely on job titles will be summarized in the aggregate on the basis of previous reviews.

Leukemia. REVIEW OF OCCUPATIONAL STUDIES. The literature that began in the early 1980s consists of reports linking routinely collected information on job titles with cancer incidence or mortality in large populations. The exposure inferences were based solely on general knowledge of the exposures associated with those jobs, whether extrapolated from other studies or based on expert evaluation. In the aggregate (*81,102*), certain patterns emerge. There is a small increased risk of leukemia associated with work in electric occupations, with a relative risk the order of 1.2 across the many studies (*81*). Within the range of the 38 studies evaluated by Kheifets et al. (*81*), there was little difference in risk associated with various measures of study quality, but the range available for consideration was limited. Furthermore, there was no indication that jobs thought to have higher exposure (welders, electricians, linemen, and power plant operators) had higher risks than electric workers generally found to have lower exposures (installers, engineers, and television or radio repairmen). Across leukemia subtypes, where there have been striking differences in individual studies, in the aggregate, the differences are modest. Pooled relative risk estimates calculated by Kheifets et al. (*81*) ranged from 1.2 for chronic myeloid leukemia (CML) to 1.4 for chronic lymphocytic leukemia (CLL).

One other pooling effort is noted, namely the aggregation of the studies of electric utility cohort studies in the United States, Canada, and France (*104*). Previously published studies of roughly comparable design (*73,105,106*) were analyzed using common methods to juxtapose and ultimately pool the results. Despite what appeared to be rather impressive differences in leukemia results across studies, with no association found in southern California Edison workers (*105*) or in an aggregation of U.S. utility workers (*106*), and mixed but generally positive results for the Canada–France study (*73*), the results were broadly compatible within the range of random variation. That is, despite the large size of these studies, random error alone could well account for the spectrum of results that were obtained once a common set of statistical tools was applied. Beyond the application to these specific studies, this observation is an important reminder about the challenges of interpreting ostensibly contradictory findings where the results do not differ dramatically and precision of all the studies is limited. Including results from Ontario Hydro, the pooled relative risk estimate for leukemia was 1.09 per 10 μT-year (95% CI = 0.98–1.21).

The major studies of occupational electric or magnetic field exposure and leukemia that relied on measurement-based job-exposure matrices are summarized in Table 2. Where data were adequate, results for major leukemia subtypes are presented as well, but summaries of results were necessarily selective. Several studies are readily described as showing no indication of increased risk of leukemia in association with occupational magnetic field exposure based on the published analyses (*105–108*). In contrast, an equal number of studies did show indications of increased risk with greater estimated magnetic field exposure (*71,73,75,109,110*). In most of the supportive studies, the relative risk estimate in the uppermost category for total leukemia was between 1.5 and 2.0, but for some leukemia subtypes, the estimates were larger and less precise. Acute lymphocytic leukemia (AML) was more substantially elevated in two studies (*73,110*) and CLL in the study by Floderus et al. (*71*). Electric fields have received less attention, with one study suggesting a strong association (*75*), one an inverse association (*111*), and two no association (*107,112*).

Whether we examine a large number of studies on the basis of job title or a smaller number of studies using relatively advanced exposure assessment technology, the inferences tend to be similar. Some individual studies show notably positive associations between measures of EMF and leukemia, with dose–response gradients and reasonable precision, whereas other studies broadly similar in

Table 2. Summary of the principal studies of occupational EMF exposure and leukemia and brain cancer using measurement-based job–exposure matrices.

Reference	Setting, industry	Leukemia results, RR (95% CI)	Comments on leukemia results	Brain cancer results, RR (95% CI)	Comments on brain cancer results
Matanoski et al., 1993 (*109*)	U.S., telephone workers	>Median (mean): 2.5 (0.7–8.6)	Increases association with longer latency	Not available	—
Floderus et al., 1993 (*71*)	Sweden, general population	2nd quartile: 0.9 (0.6–1.4) 3rd quartile: 1.2 (0.8–1.9) 4th quartile: 1.6 (1.1–2.4) CLL/2nd quartile: 1.1 (0.5–2.3) CLL/3rd quartile: 2.2 (1.1–4.3) CLL/4th quartile: 3.0 (1.6–5.8)	Weaker association for median exposure; no association with AML	2nd quartile: 1.0 (0.7–1.6) 3rd quartile: 1.5 (1.0–2.2) 4th quartile: 1.4 (0.9–2.1)	Slightly stronger gradient for median fields, time above 0.2 μT
Sahl et al., 1993 (*105*)	California, electric utility	>Median: 1.0 (0.8–1.4) >99th percentile: 1.1 (0.8–1.4)	Slight association for fraction >5.0 μT	>Median: 1.0 (0.6–1.5) >99th percentile: 0.8 (0.5–1.3)	—
Theriault et al., 1994 (*73*)	Canada–France, electric utility	>Median: 1.5 (0.9–2.6) >90th percentile: 1.8 (0.8–4.0) CLL/> median: 1.5 (0.5–4.0) AML/> median: 3.2 (1.2–8.3)	Association primarily at Ontario Hydro	> Median: 1.5 (0.9–2.8) >90th percentile: 2.0 (0.8–5.0) Astrocytoma/> median: 1.5 (0.9–2.8) Glioblastoma/> median: 1.3 (0.5–3.8) Benign tumors/> median: 2.3 (0.8–6.7)	Association consistent across three companies
Tynes et al., 1994 (*107*)	Norway, railway	Low: 1.0 (0.4–2.2) High: 0.6 (0.2–1.3)	—	Low: 0.8 (0.3–2.0) High: 0.9 (0.4–2.3)	—
		Electric field—low: 0.4 (0.2–1.1) Electric field—high: 1.0 (0.5–2.2)		Electric field—low: 0.7 (0.3–1.7) Electric field—high: 1.2 (0.5–2.8)	
Savitz and Loomis, 1995 (*106*)	U.S., electric utility	30–<50th percentile: 1.0 (0.7–1.6) 50–<70th percentile: 1.1 (0.7–1.8) 70–<90th percentile: 1.0 (0.6–1.6) ≥90th percentile: 1.1 (0.6–2.1)	Association with work as electrician; little difference for AML, CLL	30–<50th percentile: 1.6 (1.0–2.6) 50–<70th percentile: 1.5 (0.8–2.6) 70–<90th percentile: 1.7 (0.9–3.0) ≥90th percentile: 2.3 (1.2–4.6)	Weaker association with work in individual electrical occupations
Guenel et al., 1996 (*111*)	France, electric utility	Electric fields >50–75th percentile: 1.0 (0.5–2.0) >75–90th percentile: 0.7 (0.3–1.9) >90th percentile: 0.4 (0.1–1.3)	No confounding by magnetic fields, SES. Similar for AML, non-AML	Electric fields >50–75th percentile: 2.5 (1.0–6.2) >75–90th percentile: 1.4 (0.5–4.5) >90th percentile: 3.1 (1.1–8.7)	No confounding by magnetic fields, SES
Miller et al., 1996 (*75*)	Ontario, Canada, electric utility	Electric: >33–67th percentile: 2.1 (0.6–7.2)	Stronger association for AML, weaker for CLL.	Not available	—
		Electric: >67th percentile: 4.5 (1.0–19.7) >33–67th percentile: 1.7 (0.6–4.8) >67th percentile: 1.6 (0.5–5.1)	Slightly stronger for AML		
Feychting et al., 1997 (*110*)	Sweden, general population	0.13–0.19 μT: 1.4 (1.0–2.2) ≤0.20 μT: 1.7 (1.1–2.7) AML/0.13–0.19 μT: 2.1 (0.9–5.0) AML/≤0.20 μT: 2.7 (0.9–7.9) CLL/0.13–0.19 μT: 1.4 (0.7–2.5) CLL/≤0.20 μT: 1.9 (1.0–3.8)	Strong interaction with residential magnetic field exposure	0.13–0.19 μT: 1.0 (0.7–1.6) ≤0.20 μT: 1.0 (0.6–1.7)	—
Harrington et al., 1997 (*74*)	England, electric utility	Not available	—	>33–67th percentile: 1.1 (0.6–2.0) >67th percentile: 1.0 (0.5–1.9)	No effect with latency, adjustment for confounders
Rodvall et al., 1998 (*119*)	Sweden, general population	Not available	—	Glioma/0.2–0.4 μT: 1.1 (0.4–2.7) Glioma/>0.4 μT: 1.9 (0.8–5.0)	Weaker association for median than mean
Johansen and Olsen, 1999 (*108*)	Denmark, electric utility	Background: 1.0, low: 1.0, medium: 0.9, high: 1.1	—	Background: 0.5, low: 0.9, medium: 0.7, high: 0.7	—

SES, socioecomonic status.

design and quality, do not. The comparative analysis by Kheifets (*76*) points out how susceptible study findings are to subtleties of statistical methods and to random error. Without a formal meta-analysis, the results in Table 2 are likely to be consistent with a small gradient of increasing risk with increasing exposure that varies largely by chance across studies. Although individual studies may suggest that a stronger effect is found for electric fields (*75*), for specific subtypes of leukemia (*71*), or in conjunction with residential exposures (*110*), replication is required to draw conclusions about such patterns.

REVIEW OF RESIDENTIAL STUDIES. The effect of exposure from transmission lines has been studied in four case–control studies (*57,59,113,114*). No information, however, was collected in those studies either on other sources of residential exposures [except by Severson et al. (*57*)], or on occupational exposures [except by Feychting et al. (*110*)]. This may have resulted in substantial exposure misclassification. A small increased risk for all leukemia was seen in only one (*113*) of the four studies, in association with calculated magnetic fields of more than 0.1 µT in the year preceding diagnosis. Results of analyses of specific subtypes of leukemia are inconsistent across studies and difficult to interpret because of small numbers of exposed cases. An increased risk was seen for AML and CML but not for CLL in the Swedish study (*59*). The odds ratio for AML was reduced, however, and the risk of CML disappeared when analyses were restricted to subjects with no or very little occupational exposure, whereas the odds ratio for subjects with both high occupational and residential exposures increased (6.3, 95% CI 1.5–27 for both AML and CML, based on only 3 exposed cases). In the Finnish study, a significant increase was seen for CLL only, for exposures over 10 years before diagnosis and for durations of exposures of 12 years or more, based on 3 exposed cases (*114*).

The risk of leukemia from the use of electric appliances was considered in two case–control studies (*57,115–117*). Neither of these studies provides information about such risk, however, because of limitations of study design and exposure assessment.

CONCLUSIONS. The research on the risk of adult leukemia in relation to occupational and residential magnetic field exposure includes a number of large studies of varying quality, with the most research by far addressing occupational exposures. Some of these studies are excellent (*7,71,73,106,110*); applying sophisticated epidemiologic methods to the evaluation of the role of magnetic fields, though a few studies have attempted to address electric fields as well. Results from these studies have ranged from null to rather strong positive associations, with relative risks in the upper exposure categories above 2.0. Unfortunately, there is not a clear pattern in which the better studies are more or less likely to produce positive associations. In the aggregate, assuming random error accounts for differences among studies, the results are most consistent with a weak positive association, with relative risks for the more highly exposed groups of the order of 1.1–1.3. Relative risks of this magnitude are below the level at which epidemiologic methods can effectively assess causal relations. Nevertheless, the evidence at present supporting a role for EMF in the etiology of adult leukemia is weak. The standards for future epidemiologic studies to make a notable difference in the totality of evidence are extremely high. An exceptional opportunity to study very large populations with well-characterized, relatively high exposure and detailed cancer incidence data would be required to provide a significant advancement in our knowledge on this topic.

Nervous system tumors. REVIEW OF OCCUPATIONAL STUDIES. Completely analogous to the literature on electric occupations and leukemia, there is a sizeable literature on electric occupations and brain cancer. Interest in brain cancer as a potential consequence of EMF exposure began slightly later than the interest in leukemia, with an influential paper by Lin et al. (*118*) linking electric occupations to brain cancer using death certificate data. At the time of the meta-analysis by Kheifets et al. (*102*), 29 relevant reports had been published, most of which assessed exposure on the basis of job title alone. Most studies tended to show a small increase in risk of brain cancer among electric workers, with a pooled relative risk estimate of 1.2. Some studies showed no association, and the risk estimates were highly imprecise in many studies, reflecting the rarity of brain cancer. The association was stronger for studies that presented results restricted to gliomas (RR = 1.4) and was stronger for electrical engineers (RR = 1.7) but similar across the other specific occupational categories. There was no tendency either for jobs thought to have higher exposure or for studies with more sophisticated exposure assessments to show stronger associations. The pooling effort described above in which results from utility worker studies in France, Canada, and the United States were combined yielded an estimated relative risk of 1.12 per 10 µT-years (95% CI = 0.98–1.28), virtually identical to that found for leukemia (*104*). Once again, what appeared to be heterogeneity across studies was compatible with random variation around a common small effect.

Ten studies that provided risk estimates for electric or magnetic fields using measurement-based job-exposure matrices and brain cancer are summarized in Table 2. Not surprisingly, the study findings are mixed, with suggestions of positive associations in five (*71,73,106,111,119*) and the remainder showing no indication of an association. Even among the studies designated as positive, there were rarely monotonic dose–response gradients and the largest relative risk estimates rarely exceeded 2.0. No pattern could be identified on the basis of the type of study population (electric utility, general population). Too few studies presented results for histologic subtypes of brain cancer to draw conclusions about heterogeneity of risk. The evidence at present for supporting a role for EMF in the etiology of brain cancer is weak. Results are most compatible with a small association, with some studies finding no association and some finding a stronger effect. There are insufficient data to identify particular exposure sources or patterns or disease subtypes associated with larger relative risks.

REVIEW OF RESIDENTIAL STUDIES. The studies of residential exposures, once again, provide little additional information. Four studies have considered the risk of brain and CNS tumors in relation to residential exposures from high voltage transmission lines (*58,59,113,120,121*). No clear association was seen in any of these studies. Occupational exposure was taken into account in one study (*110*) but did not affect the results. None of these studies collected information on other sources of residential exposure.

CONCLUSIONS. The conclusions provided for EMF and adult leukemia are essentially applicable to the brain cancer literature as well. A large number of studies, mostly addressing occupational exposure, have generated measures of association ranging from null to rather strongly positive, but in the aggregate, relative risk estimates would be in the range of 1.1–1.3, a level at which a meaningful discussion of causality is not possible.

Breast cancer. REVIEW OF OCCUPATIONAL STUDIES. An interest in breast cancer as a possible consequence of electric and magnetic field exposure arose largely from a hypothesized mechanism proposed by Stevens and coworkers (*100,101*). It was hypothesized that electric and magnetic fields suppress the production of nighttime melatonin, analogous to light exposure at night, and that reduction in melatonin increases the risk of developing breast cancer. Over the past decade a fairly sizable body of research has addressed the influence of EMF on melatonin production. The question of an effect of EMF on melatonin lends itself to both human experimental studies (*122*) and observational studies of humans outside the laboratory. The literature from human experimental studies is generally negative regarding an effect of nighttime EMF on melatonin production (*123–125*).

Several observational studies of environmental exposures to EMF and melatonin, in contrast, have suggested effects in humans, but the pattern of findings is not persuasive. In the study of electric blanket users (*126*), only 7 of the 28 volunteers were affected, and in the studies of electric utility workers, an alteration in melatonin metabolite was found only in association with a rather unusual magnetic field metric (standardized rate of change) (*46*) or only among workers with low occupational sunlight exposure (*127*). At present, the theory regarding a melatonin pathway gets weak support from the empirical data.

The initial epidemiologic reports concerned male breast cancer, starting with two letters to the editor at *The Lancet* (*128,129*) that reported increased risks associated with electric occupations and electromagnetic field exposure, respectively. A large population-based case–control study in the United States provided much stronger support for an association, with an odds ratio of 6.0 (95% CI = 1.7–21) among electricians, telephone linemen, and electric power workers (*130*). Another reasonably large study was reported and it did not support an association (OR = 0.7, 95% CI = 0.3–1.9) (*131*). Large studies of electric utility workers did not find increased risks of male breast cancer associated with magnetic field exposure (*73,106*), though statistical power was quite limited because of the rarity of male breast cancer.

Research on breast cancer among women, a much more common disease, has been inhibited by the rarity of electric occupations among women. Analyses of a large database on occupation and mortality in the United States yielded an indication of a modestly increased risk of breast cancer mortality among female electric workers (OR = 1.4, 95% CI = 1.0–1.8) (*132*). Reanalyses of the same data set using slightly different methods to classify exposure indicated an association only among black women, not among white women (*133*). The limitations of relying solely on job title and cause of death are substantial, including a complete lack of information on potentially critical confounding variables. The most detailed study to date concerning electromagnetic fields and female breast cancer utilized a multistate case–control study combined with a systematic effort to classify jobs by exposure potential (*134*). On the basis of an analysis of the 5,223 cases and 7,236 controls who had worked outside the home, an increased risk was found for the highest potential for occupational exposure to electromagnetic fields (OR = 1.4, 95% CI = 1.0–2.1). The association was somewhat stronger among premenopausal women than among women overall (OR = 2.0, 95% CI = 1.0–3.8). Both Forssén et al. (*7*) and Kliukiene et al. (*135*) find some support for an association between EMF and breast cancer risk in women below 50 years of age; in the Forssén study this is particularly true for estrogen-receptor–positive breast cancer. The Forssén study is particularly interesting because it includes information on residential and occupational exposure combined.

REVIEW OF RESIDENTIAL STUDIES. Because of the rarity of occupational exposures to ELF among women, population-based studies of residential exposures have the potential of providing valuable information on risk of breast cancer related to ELF. The evidence from such studies is limited, however. The risk of breast cancer in women in relation to residential exposures from transmission lines has been considered in three studies (*113,130,136*). No association was seen in two studies (*113,120*), but in the third (*136*) a nonsignificantly increased risk was seen for exposure in the 6 years preceding the diagnosis, as well as in young women (under 50 years of age) and in women whose breast cancers were estrogen-receptor positive. Among women with estrogen-receptor–positive breast cancers and less than 50 years of age, the odds ratio was 7.4 (1.0–178) on the basis of only 6 exposed cases. No information, however, was available on other sources of exposure to ELF or on some important risk factors for breast cancer (such as parity and age at first pregnancy), which could confound the association.

The effects of electric blanket use were considered in one case–control study each of postmenopausal (*137*) and premenopausal breast cancer (*138*). A small, nonsignificant increased risk was seen in both pre- and postmenopausal women for continuous use of electric blanket throughout the night compared to never use. The increase reached statistical significance (OR = 1.5, 95% CI = 1.1–1.9) when the results of both studies were combined, although there was no association with duration of use. The results of these studies are difficult to interpret because of very low response rates and lack of information on type and age of the electric blankets or on other sources of ELF exposures (*139–141*).

The risk of male breast cancer in relation to transmission lines was considered in only one study (*136*). Only 9 cases were included in the study. A 2-fold, nonsignificantly increased risk was seen.

CONCLUSIONS. The totality of evidence linking EMFs to breast cancer, in men or women, remains weak. Nevertheless, given how common female breast cancer is and the multitude of studies seeking information on risk factors, further evaluation of occupational EMF exposure is desirable and should be feasible (*142*). The major limitation is in exposure prevalence and the opportunity to assess female occupational exposure more carefully. As the findings of three major studies of residential exposure to magnetic fields and breast cancer have not yet been disseminated, future research plans should await that information before deciding on the need for and direction of any new initiatives.

Other cancers. Brief mention should be made of several other cancers that have been investigated in relation to occupational EMF exposure. A marked association between pulsed EMF exposure and lung cancer was found in the Canada–France electric utility worker study (*143*), with a monotonic dose–response gradient culminating in an odds ratio of 6.7 (95% CI = 2.7–16.6) in the highest exposure stratum. Unfortunately, lack of comparable data and uncertainty about the nature of the exposure inhibited attempts at replication. The one effort to readdress this association was in U.S. electric utility workers and within the limitations of extrapolating a job–exposure matrix from one study to another, the findings were not corroborated (*144*).

Limited attention has been focused on non-Hodgkin's lymphoma (*145,146*), with some support for a possible association. Colon cancer was associated with electric field exposure in a French utility worker study (*111*), illustrating a number of sporadic elevations in cancer risk found across the series of studies in which the design permitted examination of all cancer types (*73,75*).

A particularly intriguing line of research has been the possibility of a relation between childhood cancer and parental occupational EMF exposure. However, results have been inconsistent and unconvincing (*147–149*).

Other End Points

Neurodegenerative Disease

Concerns about possible psychiatric or psychological effects of EMF exposure were raised by investigators from the Soviet Union in the late 1960s and early 1970s on the basis of anecdotal reports of symptoms such as insomnia, memory loss, and headache (*150*). However, these and other early reports have basically remained unconfirmed (*151*). Relatively recently, however, hypotheses relating EMF to neurodegenerative disorders have attracted a new interest. For a number of methodological reasons, these diseases are more difficult to study than cancer. The most obvious difficulty is that they are not recorded in registries in the same way as cancers and that mortality registries are less reliable as sources of cases. These and other difficulties are reflected in the literature. Unfortunately, the studies that have best avoided these problems suffered instead from small numbers. The overwhelming focus has been on amyotrophic lateral sclerosis (ALS) and Alzheimer's disease (AD) and there are

Table 3. Certain characteristics and findings of studies on the relation between EMF exposure and ALS.

Reference	Study population and subject identification	Definition and estimation of exposure	Study design	Numbers	Result RR (95% CI)
Deapen and Hendersen, 1986 (*154*)	Study population: not specified. Cases: ALS Society, U.S. in 1979. Controls: friends	Questionnaire: electrical occupation 3 yr prior to diagnosis	CC	518 cases (19 electrical occupation) 518 controls (5 electrical occupation)	3.8 (1.4–13.0)
Gunnarsson et al., 1991 (*155*)	Male population of Sweden 1970–1983. Cases: deaths with ALS as underlying or contributing cause in mortality registry. Controls: random sample from population	Job title in census 1960: electrical worker	CC	1,067 cases (32 exposed) 1,005 controls	1.5 (0.9–2.6)
Gunnarsson et al., 1992 (*156*)	Male population of central and southern Sweden in 1990. Cases: patients with MND in neurologic departments. Controls: random sample from population	Questionnaire: electrical work and exposure to MF	CC	58 cases (4 MF exposure) 189 controls	0.6 (MF exp) (0.2–2.0)
Davanipour et al., 1997 (*157*)	Study base: not specified. Cases: ALS patients at outpatient clinic in southern California. Controls: relatives	Questionnaire about occupational history: EMF exposure assessed by hygienist. Cumulative (E1) and average (E2) exposure	CC	28 cases 32 controls cutoff: 75th percentile, of case distribution	2.3 (0.8–6.6) average (E2)
Savitz et al., 1998 (*158*)	Male population in 25 U.S. states, 1985–1991. Cases: deaths from ALS. Controls: deaths from other causes	Job title on death certificate: electrical occupation in aggregate and individual jobs	CC	114 cases in electrical occupation in aggregate	1.3 (1.1–1.6)
Savitz et al., 1998 (*159*)	Male employees at 5 U.S. utility companies, 1950–1988. Cases: deaths with ALS noted on death certificate, identified through multiple tracking sources	Measurements and employment records. Combination of duration and EMF index	Cohort	9 cases with >20 years in exposed occupations	2.4 (0.8–6.7)
Johansen and Olsen, 1998 (*160*)	Male employees in Danish utility companies, observed 1974–1993. Cases: deaths from ALS in mortality registry	Employment records and job–exposure matrix: estimated average exposure level	Cohort	21,236 males in cohort. 9 exposed cases	2.5 (1.1–4.8)

MND, motor neurone disease.

only some scattered data on other diagnoses within this group of diseases (*152,153*).

Amyotrophic lateral sclerosis. Seven studies on ALS have been published (*154–160*). Certain characteristics of these studies are displayed in Table 3. All the studies are based on occupational exposure to EMF. Some used job title on the death certificate or a census record as a proxy for exposure and others used job history accompanied with a job–exposure matrix or some other exposure index to assess EMF exposure. The methods for diagnosis and case ascertainment varied across studies. Some studies used death certificate information, whereas others used cases from specialized neurological clinics.

The seven studies may be divided into three groups according to design features (Table 3). One group consists of the three studies that did not use mortality registries to ascertain the cases but instead identified them from neurological clinics or, in one instance, from an ALS society. Two of the three studies are clinically based and lack specified population bases from which the cases were generated and they used friends and relatives as the sources for controls (*154,157*). Thus, these two studies are susceptible to selection bias, the direction or magnitude of which cannot be predicted with any certainty. Therefore, despite other assets, such as specific diagnoses and careful exposure assessment in one of them, the overall contribution is limited. The third study in this group has a clearly defined study population from which in principle all prevalent and diagnosed cases were identified and the controls constituted a random sample from that population (*156*). Exposure assessment in this study, however, was based on a questionnaire with rather crude questions regarding electricity work and occupational exposure to EMF and the results were somewhat inconsistent (Table 4).

The next group consists of two studies that are both based on death certificates for the identification of cases and on job titles for the assessment of exposure (*158,159*), in one case from death certificates (*158*) and in the other from a census (*159*) (Table 3). The strengths of these two studies include minimization of selection and recall bias as a consequence of the reliance upon registry information. Also, the large numbers of subjects, reflected by the narrow confidence intervals, are considerable assets. The major weakness is the crude information on which exposure assessment is based. It is based only on job title at one point in time without any measurement or other data to back it up (Table 4).

The third group comprises the two latest studies based on cohorts of utility workers, one in the United States and one in Denmark (*159,160*). Both studies are designed such that the risk of selection bias is small, because they each start with a well-defined cohort and because deaths are searched for in mortality registries. Both studies also have employed detailed procedures for exposure assessment that involved classification of jobs on the basis of measurements. The duration of each job was another strength. Despite the large nominal sizes of the cohorts, however, the effective numbers of exposed cases are modest. These two studies are by far those that carry the most weight in overall assessment. The designs of the two studies are relatively similar and so are the findings. The combined results from these two studies is a relative risk of 2.7 (1.4–5.0) (Table 4).

Table 4. Pooling across groups of studies on EMF exposure and ALS.

Pooled studies	Number of studies	RR	95% CI
All	7	1.5	1.2–1.7
Clinically and ALS society-based studies	3	3.3	1.7–6.7
Mortality registry and census-based studies	2	1.3	1.1–1.6
Utility cohort studies	2	2.7	1.4–5.0

The combined results from the two utility worker studies (*159,160*) show a clear increase in ALS mortality. The combined confidence interval suggests that the risk increase is unlikely to be due to chance. There is no obvious bias in design, such as exposure or diagnosis misclassification, that could explain the elevated risk. If anything, such a bias would have been expected to result in an attenuation of the relative risk.

Table 5. Certain characteristics and findings of studies on the relation between EMF exposure and Alzheimer's disease.

Reference	Study population and subject identification	Definition and estimation of exposure	Study design	Numbers	Resulting RR (95% CI)
Sobel et al., 1995 (*161*)	Study population: not specified. Cases: three sets of AD patients examined, 77–93 years of age, at one neurologic clinic in the U.S. and two in Finland. Controls: three sets—vascular dementia patients, patients without neurologic disease, and neighborhood controls.	Interview data on primary occupation. Classification into high/medium vs low EMF exposure	CC	386 cases (36 exposed) 475 controls (16 exposed)	3.0 (1.6–5.4)
Sobel et al., 1996 (*168*)	Study population not specified. Cases: patients with probable or definite AD treated at AD medical center in California, USA. Controls: patients who were cognitively impaired or demented	Statewide data form information on primary occupation. Classification into high/medium vs low EMF exposure	CC	326 cases 152 controls	3.9 (1.5–10.6)
Feychting et al., 1998 (*163*)	Study population: subsample of the Swedish Twin Registry. Cases: identified through a screening and evaluation procedure. Controls: intact twins with one twin in each of two control groups when two twins were eligible	Interviews. Primary and last occupation. Classification into three levels, based on JEM, highest >0.2 µT	CC	55 cases 228 and 238 controls	0.9 (primary) (0.3–2.8) (similar with other control group)
Savitz et al., 1998 (*158*)	Male population in 25 U.S. states, 1985–1991. Cases: deaths from AD. Controls: deaths from other causes	Job title on death certificate: electrical occupation in aggregate and individual jobs	CC	256 cases in electrical occupations, in aggregate	1.2 (1.0–1.4)
Savitz et al., 1998 (*159*)	Male employees at five U.S. utility companies, 1950–1988. Cases: deaths with AD mentioned on death certificate identified from multiple tracking sources	Measurements and employment records. Combination of duration and EMF index	Cohort	16 cases with >20 years in exposed occupations	1.4 (0.7–3.1)

Abbreviations: JEM, job exposure matrix.

Thus, the two utility worker studies combined provide relatively strong evidence that work with EMF exposure in the utility industry is indeed related to increased ALS mortality (Table 4). This result is reinforced by the results of the other studies on ALS discussed above, even though the five other studies have to be given less weight.

Alzheimer's disease. Five studies on AD were found (*158,159,161–163*) (Table 5).

The first two studies shown in Table 5 were clinic-based, case–control studies. The first combined three series of AD patients, one from the United States and two from Finland (*161*). These series came from neurological centers that specialized in diagnosis and treatment of AD and can therefore be assumed to be based on high-quality diagnoses. For one series of AD patients vascular dementia patients were used as controls; for the second series, controls were other patients without neurological disease, and for the third, neighborhood controls. The second study comes partly from the same group of investigators and was an attempt to confirm the findings from their first publication (*162*). It was also based on patients from a specialized clinic in the United States and used another group of patients as controls. Both studies based exposure classification on jobs as reported by the patient or a relative. The major weakness is the lack of a specified study population and thus the potential for selection bias.

Of the three remaining AD studies, one was based on the Swedish Twin Registry. The investigators evaluated twins included in the registry, which was set up for the purpose of conducting genetic studies of dementia in twins (*163*). Exposure to EMF was assessed through interviews that included job history. Diagnostic quality in the study was good, as was the detail in which EMF exposure was assessed. Another strength was the defined population base for the study. The main problem with this study was its small size, as reflected by the relatively wide confidence intervals. It also had a contradiction in its findings depending on whether primary or last occupation was used as the basis for analysis.

The last two studies were discussed in the ALS section above, because they provide data on both diseases (Table 5). These are the death certificate study and the utility worker study, both in the United States (*158,159*). As discussed in the ALS section, these are both reliable studies, but the death certificate study used a crude measure for the EMF exposure assessment. The utility worker study is less suited for AD because of the limited usefulness of death certificate as a source of disease classifications. However, the investigators report results both for underlying causes of mortality and for contributing causes, and there is a difference between those results. When contributing causes are used, there is little support for an association between EMF and AD, while the use of underlying cause gives some support for such an association. Because of the nature of this disease, it seems more logical to look at contributing causes.

Interpretation. Even if the studies on ALS consistently suggest an increased risk in EMF-exposed subjects, one would like confirmatory results from additional studies, in studies specifically designed for the purpose. Assuming that the observed risk elevation is accurate, it still remains to be explained. Aside from the hypothesis that EMF exposure increases ALS risk, one must consider alternative explanations. One such alternative would be confounding from electric shock exposure. It is conceivable that exposure to electric shocks increases ALS risk and, also, that work in the utility industry carries a risk of experiencing electric shocks. Some of the reviewed studies did report analyses that indeed linked electric shocks to ALS (*154,156,160*), but none of the studies provided an analysis in which the relation between EMF and ALS was studied with control for electric shocks. A crude calculation can be made from data provided by Deapen and Hendersen (*154*), and this seems to indicate that the EMF association holds up even after control for electric shock experience.

As for AD, when evaluated across all the studies, there appears to be an association between estimated EMF exposure and disease risk (Table 6). However, this result is mainly confined to the first two studies in the United States, and it is not clearly confirmed by the later studies (*153,154,158,161,162*). The two studies that show excess (*161,162*) may have been affected by selection bias. Because the study populations are undefined, there is no way to determine the extent to which the controls are representative with respect to exposure of the population from which the cases originated.

Conclusion. For reasons discussed in the preceding sections, the ALS results are intriguing and point toward a possible risk increase in subjects with EMF exposure. However, confirmatory studies are needed, as is an appropriate consideration of confounding, for example, from electric shocks, as a conceivable explanation. As for AD, it appears that the excess risk is constrained to studies with weaker designs; thus support for the hypothesis of a link between EMF and AD is weak.

Suicide and Depression

Psychiatric disorders were discussed early in the literature about possible chronic health effects of EMF exposure, but research stopped, perhaps because the original findings were not replicated. However, more recently this research area has been revived, at least partly as a consequence of the hypothesis that EMF may affect melatonin levels.

Suicide. The studies on EMF and suicide are summarized in Table 7. The first of these was published in 1979 and was followed by five more studies, the latest published in 2000. The first study, in England and based on 589 suicide cases and controls, was carried out in two steps. In the first, EMF levels were estimated based on nearby power lines. In the second, measurements were taken in the homes of the study subjects (*164,165*). The study found higher fields at case homes than in control homes. However, the study is methodologically limited and has been criticized both for the ways subjects were selected and for the statistical analyses. The subsequent studies have used a range of different approaches to assess exposure varying from crude techniques based on distance between home and power lines, or on job titles, to more sophisticated approaches based on detailed information about cohorts of utility workers (*160,166–170*). Only the most recent study provides some support for the original findings.

Depressive symptoms. The next set of studies addresses depressive symptoms directly (Table 8). The first two are difficult to interpret because of methodological limitations related to the procedures for selection of study subjects because they did not use validated scales for identification of depressive symptoms (*171,172*). In addition, the study by Perry et al. (*172*) also reported unusually high average EMF levels that remain unexplained. The remaining studies used validated depression scales. One of these studies showed a clear association between proximity to power line and depression (*173*), whereas the other three provided little evidence for such an association (*174–176*). The study by Poole et al. (*173*) is well designed; it compares subjects on properties abutting a power line right-of-way to subjects further away, and the results appear internally consistent. The investigators report a relative risk of 2.8 (95% CI = 1.6–5.1). McMahan et al. (*175*) employed a similar design and measurements to confirm that the homes close to the line have considerably higher EMF levels than homes further away. This study also appears valid but yields a relative risk of 0.9 (0.5–1.9). McMahan et al. offer a number of possible explanations for the lack of consistency between these two studies but none of the explanations is convincing.

Interpretation and conclusion. When assessing the overall literature on EMF and suicide, it is necessary to consider the relative weights of the available studies together with their results. In doing so the original study must be given a relatively light weight in relation to the later studies because of methodological limitations. Nevertheless, the latest study also suggests that an excess risk may indeed exist.

The literature on depressive symptoms and EMF is difficult to interpret because the findings are not consistent. This complexity cannot easily be resolved by suggesting that one type of result can be confined to a group of studies with methodological problems or some other limitation.

Cardiovascular Diseases

Concerns about cardiovascular changes resulting from exposure to EMFs originated from the same sources as concerns about neurological effects, namely, descriptions in the 1960s and early 1970s of the symptoms among Russian high-voltage switchyard operators and workers (*62,150*). Although these reports remain unconfirmed (*177*), more recent investigations suggest that there may be some direct cardiac effects of EMF exposure, mostly related to heart rate. These effects, however, appear to occur only under certain conditions (*178*). No known substantive changes occur in other parameters of cardiac function, such as the shape of electrocardiogram or blood pressure, in relation to EMF exposure (*179*).

Several recent occupational cohort studies have examined mortality from cardiovascular disease (CVD) among electric utility workers. The first study (*168*) was carried out on a cohort of over 20,000 workers employed in an electric company in Quebec. Exposure to 60-Hz electric and magnetic fields was assessed principally through a job-exposure matrix. Among those exposed (who were all blue-collar workers), mortality rates were generally lower than those in the unexposed groups, including overall cardiovascular mortality. No analyses of mortality by CVD subtype were reported. In contrast, Savitz et al. (*180*) investigated risk for each subgroup of fatal cardiovascular disease in a cohort of

Table 6. Pooling across groups of studies on EMF exposure and Alzheimer's disease.

Pooled studies	Number of studies	RR	95% CI
All	5	2.2	1.5–3.2
Clinical-based studies	2	3.2	1.9–5.4
Population-based studies	3	1.2	0.7–2.3

Table 7. Certain characteristics and findings of studies on the relation between EMF exposure and suicide.

Reference	Study population and subject identification	Definition and estimation of exposure	Study design	Numbers	Result RR (95% CI)
Reichmanis et al., 1979 (*161*); Perry et al., 1981 (*165*)	Suicide cases and controls in England	Estimates of residential exposure from power lines. Measurements at subjects' homes	CC	589 suicide cases	Higher estimated and measured fields at case homes
McDowall, 1986 (*166*)	Persons residing in the vicinity of transmission facilities in specified areas in the U.K. at the time of 1971 census	Home within 50 m of substation or 30 m of overhead line	SMR	8 cases	0.75 (nonsignificant)
Baris and Armstrong, 1990 (*167*)	Deaths in England and Wales, 1970–1972 and 1979–1983	Job titles on death certificates. Electrical workers in aggregate and specific jobs	PMR	495 suicide cases in electrical occupations	No increase for electrical workers
Baris et al., 1996 (*168*)	Male utility workers, Quebec, Canada, 1970–1988. Cases: deaths from suicide, noted in mortality registry. Controls: 1% random sample from the cohort	Job exposure matrix based on positron measurements. E- and B- and pulsed fields from average and geometric means and from cumulative and current exposure	CC	49 cases of suicide 215 controls	No evidence for magnetic fields. Some support for some electric field indices.
Johansen and Olsen, 1998 (*108*)	Male employees in Danish utility companies observed 1974–1993. Cases: deaths from suicide, noted in mortality registry	Employment records and JEM: estimated average exposure level. Medium and high exposure	SMR	21,236 males in cohort-exposed cases	1.4 (nonsignificant)

Abbreviations: PMR, proportional mortality ratio; SMR, standardized mortality ration.

Table 8. Certain characteristics and findings of studies on the relation between EMF exposure and depression.

Reference	Study base and subject identification	Definition and estimation of exposure	Study design	Numbers	Result RR (95% CI)
Dowson et al., 1988 (*171*)	Persons in England who lived near 132-kV power line and persons who lived 3 miles away. Questionnaire asking about depression.	Distance between home and overhead power line.	Cross-sectional	132 near power line, 9 with depression; 94 away from power line,1 with depression	Strong association between depression and proximity to overhead power line
Perry et al., 1989 (*172*)	Persons with depression discharged from hospital in England; controls from electoral list.	Measurements at front doors. Average for case and control groups compared.	CC	359 patients discharged with diagnosed depressive illnesses	Average measurement: Cases: 2.3 mG Controls: 2.1 mG
Poole et al., 1993 (*173*)	Residents in 8 towns along a transmission line right-of-way in the U.S., 1987. A sample was interviewed. Depressive symptoms were identified by CES-D. Cutoff for depression was median of score.	Distance from power line: near vs far. Near: properties abutting right-of-way or visible towers.	Cross-sectional	382 persons interviewed	2.8 (1.6–5.1)
Savitz et al., 1994 (*174*)	Male veterans who served in the U.S. Army for the first time, 1965–1971. Two diagnostic inventories were used: the Diagnostic Interview Schedule and the Minnesota Personality Inventory. Lifetime depression used for report here.	Present job identified in interview together with duration. Electrical worker.	Cross-sectional	183 electrical workers, 13 with lifetime depression; 3,861 nonelectrical workers	1.0 (0.5–1.7)
McMahan et al., 1994 (*175*)	Population of neighborhood near a transmission line in Orange County, California, USA, 1992. Sample of homes near and one block away from power line. Depressive symptoms identified through questionnaire and CES-D scale.	Average EMDEX measurements at the front door: Homes on easement: 4.86 mG One block away: 0.68 mG	Cross-sectional	Total of 152 women	0.9 (0.5–1.9)
Verkasalo et al., 1997 (*176*)	Finnish twins who answered the BDI in 1990.	Residential magnetic field estimated from power lines near the homes.	Cross-sectional	12,063 persons	BDI scores not related to exposure

Abbreviations: BDI, Beck Depression Inventory; CES-D scale, Center for Epidemiologic Studies–Depression scale.

approximately 139,000 male utility workers (*180*). In this study it was hypothesised a priori that long-term exposure to magnetic fields leads to an increased risk of death due to cardiac arrhythmias and acute myocardial infarction. Primary cause of death was taken from the death certificate; exposure was assessed according to the duration of employment in occupations with high exposure to magnetic fields, and by cumulative exposure, building in various lag periods. Although overall cardiovascular disease and ischemic mortalities were lower in the study cohort than in the U.S. population, deaths from arrhythmia-related conditions and acute myocardial infarction were related to increasing exposure 5–20 years before death, using both indices. The specificity of the study hypothesis, which was crucial to the findings, arose out of evidence (although inconsistent) from human laboratory studies that a pattern of reduced heart rate variability occurred immediately after exposure to power-frequency magnetic fields (*181*). Reduction in heart rate variability is reported to be predictive of cardiovascular disease and death in adults in population-based studies (*182–184*). Changed heart rate variability reflects changed cardiac autonomic control (*185,186*), suggesting that this is a possible mechanism of action of EMF exposure on the heart. The limitations of speculating about causal mechanisms of types of CVD as coded on death certificates of uncertain validity and reliability have been pointed out (*187*). Also there are difficulties in explaining how the mechanism underlying the transient changes in heart rate variability seen in healthy young men after EMF exposure in controlled settings (*181,188*) can also explain deaths from arrhythmia and infarction many years after long-term occupational exposure to ELF EMFs. Indeed, a recent large study conducted in Sweden has shown no effect of EMF exposure on myocardial infarction (*189*).

Interpretation and conclusion. In summary, evidence of cardiovascular effects due to elevated exposure to magnetic fields is weak, and whether a specific association exists between exposure and altered autonomic control of the heart remains speculative until corroborating evidence from further large epidemiologic studies becomes available.

Reproductive Effects

In the 1980s, laboratory findings were reported showing that weak (approximately 1 μT) magnetic fields may adversely affect chick embryogenesis (*190,191*). In addition, clusters of adverse pregnancy outcomes were reported among users of video display terminals (VDTs) (*192*), and epidemiologic data were published suggesting that maternal use of electric blankets and water beds may influence fetal development (*193*). Subsequently, several studies of the effects of EMF exposure on reproductive health have been conducted (*194*).

Residential exposure. Studies investigating the reproductive effects of residential exposure to ELF magnetic fields have evaluated either exposures to general residential magnetic fields or to specific sources, namely heated waterbeds, electric blankets, and ceiling heating coils.

Several studies have been conducted of various reproductive end points in relation to general residential exposure. With regard to spontaneous abortion, high-intensity magnetic fields measured at the front doors of homes of volunteers' homes in a "work and fertility" cohort study in Finland, were associated with a marginally significant, 5-fold increased risk (based on fewer than 10 cases and adjusted only for smoking status) (*195*). Two later studies, Savitz and Anath (*196*) and Belanger et al. (*197*), found no increase in risk of spontaneous abortion however. An investigation arising out of a case–control study of childhood cancer, found pregnancies in homes with a magnetic field intensity >0.2 μT were no more likely than others to end in spontaneous abortion (*196*) (again small numbers of cases and design limitations weakened the results). Similarly in a prospective study of nearly 3,000 women in New Haven, Connecticut, intrauterine growth rate (IUGR) and spontaneous abortion were unrelated to wire code of maternal residence (classified as having HCC or LCC) (*197*). The second study also found no increased risk of low birth weight or premature delivery in relation to high residential EMF exposure (*196*). Meanwhile, birth defects were the outcome of interest in a study conducted in southwestern France to explore whether women living within 100 m of high-voltage power lines at the time of birth had children at increased risk of congenital anomalies (*198*). There was no such increase, though too few patients lived within 25 m of the power lines (i.e., actually experienced increased EMF exposure) to test the association properly.

Wertheimer and Leeper (*193*) first raised the possibility of a more specific association between maternal use of electrically heated beds and adverse pregnancy outcome. These investigators examined seasonal patterns of fetal growth and abortion among users of heated beds in Denver and reported that more abortions and more babies of low birth weight were conceived in winter than in summer months. The effects of heat could not be disentangled from those of EMFs however. Subsequently they showed a similar correlation between seasonality of spontaneous abortions occurring within a year prior to conception of a liveborn infant and exposure to ceiling cable heat (*199*). The data have been criticized because of biased ascertainment of births and abortions and because the rate of congenital malformations in the unexposed group was abnormally low (*200*).

Subsequently, four case–control studies examining the effects of electrically heated beds have been reported. No association was seen between recalled periconceptual electric blanket or heated waterbed use and neural tube and oral cleft defects identified in the New York State Congenital Malformations Registry (*201*). In a study of similar design, cases of congenital urinary tract anomalies without chromosomal abnormalities were identified through the Washington Birth Defects Registry and risk was calculated in relation to prenatal use of electric blankets and heated waterbeds. No increase in risk was seen among all cases and controls, but an increase was seen in the subgroup of women with infertility. Low response rates among cases and controls and the small number of exposed cases (five) in a subgroup analysis, detract from the reliability of these data (*202*). More recently, two case–control data sets have been analyzed to assess risk of neural tube defects and orofacial clefts in relation to periconceptual use of electric blankets, bed warmers, and heated waterbeds (*203*). A study based on medical records including autopsy and ultrasonography reports in clinics in various California urban areas found no clear evidence of increased risk of defects in relation to high frequency or duration of use of electrically heated beds.

Two prospective studies have also been conducted. In one the use of electrically heated beds by nearly 3,000 women receiving care at centers in the New Haven area was monitored. Time-weighted EMF exposure from beds was calculated based on bed-type–specific measurements multiplied by nightly hours of use reported at prenatal interview. No association was found between low birth weight or intrauterine growth rate and electrically heated bed use (*204*). Although electric blanket use at conception was weakly associated with spontaneous abortion, corresponding use of heated waterbeds was not. No measures of dose–response were associated with increased risk of abortion. The other study, of over 5,000 pregnant women, found that users of electric bed heaters had lower rates of spontaneous abortion than nonusers, and no increase in risk with increasing intensity of use was seen (*205*).

Occupational exposure. Studies of reproductive outcomes in relation to maternal occupational exposure to magnetic fields have mostly investigated pregnant women working with VDTs. Magnetic fields experienced by operators of most VDTs (and certainly modern VDTs are not materially higher than those experienced in the general environment (*207–210*), however. Thus the hypothesis that increased risk of reproductive outcomes is related to increased EMF exposure logically cannot be tested in studies where VDTs are the sources of EMF exposure. Moreover, in studies to date, possible confounding factors such as stress and other work-related factors have largely gone unaddressed (*192,208*). These problems notwithstanding, magnetic field exposure of VDT operators has largely been estimated by assessing time spent working at the terminal (*208*), and more than a dozen studies have addressed the question of the possible harm to pregnant women from VDT use (*192,194,207,208,211,212*), with no consistent evidence of an effect. Of these a minority of studies have measured magnetic fields emitted by VDTs directly, such as two large studies conducted in the United States and Finland, respectively (*206,210*). In the first (*206,213*), telephone operators who used VDTs in the first trimester of pregnancy had no excess risks of spontaneous abortions (*206*), low birth weight, or premature delivery (*213*). In the second, women employed as clerks in Finland in the period 1975–1985 who were selected from a national pregnancy database showed no overall increase in spontaneous abortions in relation to use of VDTs, though in a very highly exposed subgroup (20 exposed cases), a 3-fold increase in risk was seen after adjusting for ergonomic factors and mental stress. The possibility of recall bias, both of VDT use and mental stress, exists in this study; and response rate among cases and controls was relatively poor. Further, only 5–10% of VDT users in this study and no users in the previous study (*206*) were in the highest exposure category.

A few studies have investigated the reproductive health of groups besides VDT operators who have been occupationally exposed to EMFs. The increase in congenital malformations observed in the offspring of some 370 married men employed by a Swedish power company (*214*), was not observed in more recent studies (*215*), suggesting that the former may have been a chance result. Moreover, no plausible biological explanation for paternal transmission of risk is known (*192,216*). Similarly, little support has been found for the theories that either fertility of exposed workers (*208,217*) or the sex ratio of their offspring (*192,218*) are perturbed by exposure to low-level ELF magnetic fields.

Conclusion. Until the recent cohort studies of pregnancy outcome following residential and electric blanket EMF exposure (*197,204,205*), little evidence has been available on the effect of EMF exposure on overall reproductive health (*204,219*). Investigations addressing the diversity of reproductive outcomes are notoriously difficult, with assessment of spontaneous abortions being particularly so (*216*). Not only has the accuracy of pregnancy outcome assessment been questionable in many studies, but also exposure measurement has been of variable value and this is especially true of the vast majority of studies addressing reproductive health in relation to VDT use, which offer little information on EMF exposure.

Although there may be some relations among reproductive outcomes either through shared determinants or because one event precludes the occurrence of another (e.g., infertility and spontaneous abortion), the most realistic and promising strategy is to focus on specific, narrowly defined reproductive outcomes. When relevant studies are subdivided in that way, only spontaneous abortion has been examined in several studies of reasonable quality, and the evidence from those studies cumulatively suggests no association with EMF exposure is present.

Thus fundamental methodologic limitations preclude firm conclusions about reproductive outcomes. Studies with refined measurements of exposure and outcome could yield different results than those reported to date. However, on the basis of theoretical considerations and both experimental and epidemiologic studies (*43,103*), there is very little encouragement for pursuing research on EMF and reproductive health. Existing evidence does not support the hypothesis that maternal exposure to

EMF through residential, including heated bed, exposure or through the workplace is associated with adverse pregnancy outcomes.

Discussion

Epidemiologic investigation of possible associations of EMF exposure with risk of chronic disease is an unusually difficult enterprise. Certain conclusions can be drawn however:

a) The epidemiologic studies conducted on possible health effects of EMF have improved over time in sophistication of exposure assessment and in methodology. Several of the recent studies on childhood leukemia and on occupational exposures in relation to adult cancer are close to the limit of what can realistically be achieved by epidemiology, in terms of size of study and methodological rigor, using presently available measurement methods.

b) Exposure measurement is a particular difficulty of EMF epidemiology, in several respects:

- The exposure of interest is imperceptible, ubiquitous, originates from multiple sources, and can vary greatly over time and over relatively short distances.
- The relevant exposure period, for cancers at least, is before the date at which measurements can realistically be obtained and is of unknown duration and induction period.
- The appropriate exposure metric is unknown, and there is no substantiated biological mechanism or animal model from which to impute it.

c) In the absence of evidence from cellular or animal studies, and given the methodological uncertainties and in many cases inconsistencies of the existing epidemiologic literature, there is no chronic disease outcome for which an etiological relation to EMF exposure can be regarded as established.

d) A large body of high-quality data exists, with measurements of exposure, strong methodology, and large study sizes, for childhood leukemia and brain tumors and for occupational exposure in relation to adult leukemia and brain tumors. Among all the outcomes evaluated in epidemiologic studies of EMF, childhood leukemia in relation to postnatal exposures above 0.4 µT is the one for which there is most evidence of an association. The relative risk has been estimated at 2.0 (95% confidence limits (CL) = 1.27–3.13) in a large pooled analysis. This is unlikely to be due to chance but may be partly due to bias. This is difficult to interpret in the absence of a known mechanism or reproducible experimental support. In the large pooled analysis, only 0.8% of all children were exposed above 0.4 µT. Further studies need to be designed to test specific hypotheses such as aspects of selection bias or exposure. On the basis of epidemiologic findings, there is evidence for an association of ALS with occupational EMF exposure although confounding is a potential explanation. Whether there are associations with breast cancer, cardiovascular disease, and suicide and depression remains unresolved.

Overall, despite 20 years of extensive epidemiologic investigation of the relation of EMF to risk of chronic disease, there are still epidemiologic questions that need to be resolved. To be of value, however, future studies of these questions must be of high methodological quality, of sufficient size and with sufficient numbers of highly exposed subjects, and must include appropriate exposure groups and sophisticated exposure assessment. Especially for childhood leukemia, little is to be gained from further repetition of investigation of risks at moderate and low exposure levels, unless such studies can be designed to test specific hypotheses, such as selection bias or aspects of exposure not previously captured. In addition there is a need for studies in humans of possible physiological effects of EMF that might relate to risks of chronic disease.

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