APPENDIX E CURRENT STATUS OF RESEARCH ON EXTREMELY LOW FREQUENCY ELECTRIC AND MAGNETIC FIELDS AND HEALTH (June 3, 2022)

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Health Sciences Practice

Exponent®

Current Status of Research on Extremely Low Frequency Electric and Magnetic Fields and Health, 2018 through 2021

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Acronyms and Abbreviations

μT	Microtesla
AC	Alternating current
ADHD	Attention-deficit/hyperactivity disorder
ALL	Acute lymphoblastic leukemia
ALS	Amyotrophic lateral sclerosis
AMI	Acute myocardial infarction
B-ALL	B-lineage acute lymphoblastic leukemia
CgA	Chromogranin
CHD	Congenital heart disease
CI	Confidence interval
CNS	Central nervous system
DMBA	7,12-dimethylbenz[a]anthracene
DNA	Deoxyribonucleic acid
DOX	Doxorubicin
EFSB	Energy Facilities Siting Board
EHC	Environmental Health Criteria
ELF	Extremely low frequency
EMF	Electric and magnetic fields
Exponent	Exponent, Inc.
FITR	Fourier transform infrared
G	Gauss
GSH	Glutathione
Hz	Hertz
IARC	International Agency for Research on Cancer
ICES	International Committee on Electromagnetic Safety
ICNIRP	International Commission on Non-Ionizing Radiation Protection
JEM	Job exposure matrix
kV	Kilovolt
kV/m	Kilovolts per meter
MDA	Malondialdehyde

mG	Milligauss
mg	Milligram
ml	milliliter
MND	Motor neuron disease
NTP	National Toxicology Program
OR	Odds ratio
RR	Relative risk
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SOD	Superoxide dismutase
TBARS	Thiobarbituric acid reactive substances
TUNEL	Terminal deoxynucleotidyl transferase (TdT) dUTP Nick-End Labeling
TWA	Time weighted average
V/m	Volts per meter
WHO	World Health Organization

Limitations

At the request of the Narragansett Electric Company, Exponent, Inc., prepared this summary report on the status of research related to extremely low frequency electric- and magnetic-field exposure and health. The findings presented herein are made to a reasonable degree of scientific certainty. Exponent reserves the right to supplement this report and to expand or modify opinions based on review of additional material as it becomes available, through any additional work, or review of additional work performed by others.

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Executive Summary

This report was prepared to address the topic of extremely low frequency (ELF) electric and magnetic fields (EMF) and health at the request of the Narragansett Electric Company.

Section 1 of this report discusses the nature, sources, and typical environmental exposure levels of ELF EMF. ELF EMF are invisible fields surrounding all objects that generate, use, or transmit electricity. There are also natural sources of ELF EMF, including the electric fields associated with the normal functioning of our circulatory and nervous systems. People living in developed countries are constantly exposed to ELF EMF in their environments since electricity is a fundamental part of technologically-advanced societies. Sources of man-made ELF EMF include appliances, wiring, and motors, as well as distribution and transmission lines.

Research on ELF EMF and health began with the goal of finding therapeutic applications and understanding biological electricity (i.e., the role of electrical potentials across cell membranes and current flows between cells in our bodies). Over the past 50 years, researchers have examined whether ELF EMF from man-made sources can cause short- or long-term health effects in humans using a variety of study designs and techniques. This research considered many aspects of physiology and diseases, including cancers in children and adults, neurodegenerative diseases, reproductive effects, and cardiovascular disease.

Scientists use systematic methods to conduct and evaluate scientific research and assess the potential impact of a specific agent on human health; these methods are discussed in Section 2. Guidance on the possible health risks of all types of exposures comes from health risk assessments or systematic weight-of-evidence evaluations of the cumulative literature on a particular topic conducted by expert panels organized by scientific and government organizations. Policy makers and the public should look to the conclusions of these reviews, since they are conducted using established scientific standards by scientists representing the various disciplines required to assess the topic at hand. In a health risk assessment of any exposure, it is essential that scientists evaluate the type and strength of relevant research studies available. Human health studies vary in methodological rigor; therefore they vary in their capacity to extrapolate findings to the population at large. Furthermore, three types of studies—

epidemiology, *in vivo*, and *in vitro*—relevant to the particular research topic must be evaluated concurrently to understand possible health risks.

The World Health Organization (WHO) published a health risk assessment of ELF EMF in 2007 that critically reviewed the cumulative epidemiologic and laboratory research to date, which accounted for the strength and quality of the individual research studies they evaluated. Section 3 provides a summary of the WHO's conclusions with regard to the major outcomes they evaluated. The WHO report provided the following overall conclusions:

> New human, animal, and *in vitro* studies published since the 2002 IARC Monograph, 2002 [*sic*] do not change the overall classification of ELF as a possible human carcinogen (WHO, 2007, p. 347).
>
> Acute biological effects [i.e., short-term, transient health effects such as a small shock] have been established for exposure to ELF electric and magnetic fields in the frequency range up to 100 kHz that may have adverse consequences on health. Therefore, exposure limits are needed. International guidelines exist that have addressed this issue. Compliance with these guidelines provides adequate protection. Consistent epidemiological evidence suggests that chronic low-intensity ELF magnetic field exposure is associated with an increased risk of childhood leukaemia. However, the evidence for a causal relationship is limited, therefore exposure limits based upon epidemiological evidence are not recommended, but some precautionary measures are warranted (WHO, 2007, p. 355).

Section 4 of this report provides a systematic literature review and a critical evaluation of relevant epidemiologic and *in vivo* studies published from December 2018 through December 2021. These recent studies did not provide sufficient evidence to alter the basic conclusion of the WHO—the research does not confirm that electric fields or magnetic fields are a cause of cancer or any other disease at the levels we encounter in our everyday environment. The current guidance from the WHO on its website states that "… the WHO concluded that current evidence does not confirm the existence of any health consequences from exposure to low level electromagnetic fields."[1]

A number of national and international scientific organizations have published reports or scientific statements with regard to the possible health effects of ELF EMF since January 2006, which are listed in Section 5. The conclusions of these documents are generally consistent with the WHO review published in 2007 and with the scientific consensus articulated in Section 4.

There are no national recommendations, guidelines, or standards in the United States to regulate ELF EMF or to reduce public exposures, although the WHO recommends adherence to the exposure limits established by the International Commission on Non-Ionizing Radiation Protection or the International Committee for Electromagnetic Safety for the prevention of acute health effects at high exposure levels, which are summarized in Section 6. In light of their assessments of the scientific research, some scientific organizations recommend low-cost interventions to reduce ELF EMF exposure. While the large body of existing research does not confirm any likely harm associated with ELF EMF exposure at low levels, research on this topic will continue to reduce remaining uncertainty.

Section 7 of this report provides an overall summary of the epidemiologic and *in vivo* research published since the WHO 2007 report was released. When these recent studies are considered in the context of previous research, they do not provide evidence to alter the conclusion that ELF EMF exposure at the levels we encounter in our everyday environment is not a cause of cancer or any other disease process.

Note that this Executive Summary provides only an outline of the material discussed in this report. Exponent's technical evaluations, analyses, conclusions, and recommendations are included in the main body of this report, which at all times is the controlling document.

[1] https://www.who.int/news-room/questions-and-answers/item/radiation-electromagnetic-fields. Accessed March 24, 2022.

1 Introduction

Questions about electric and magnetic fields (EMF) and health are commonly raised during the permitting of transmission lines. Numerous national and international scientific and health agencies have reviewed the research and evaluated potential health risks of exposure to extremely low frequency (ELF) EMF. The most comprehensive review of ELF EMF research was published by the World Health Organization (WHO) in 2007. The WHO's Task Group critically reviewed the cumulative epidemiologic and laboratory research through 2005, which accounted for the strength and quality of the individual research studies they evaluated.

The Narragansett Electric Company, formerly a subsidiary of National Grid, requested that Exponent, Inc. (Exponent) provide an easily-referenced document that updates a report previously prepared for the Rhode Island Energy Facility Siting Board as part of its Applications for the 2019 Rhode Island Transmission Projects (Exponent, 2019). Exponent (2019) systematically evaluated peer-reviewed research and reviews by scientific panels published through December 2018. This current report updates this earlier report with a systematic evaluation of peer-reviewed research and reviews by scientific panels published from December 2018 through December 2021, and describes if and how these recent results affect conclusions reached by the WHO in 2007.

Nature of extremely low frequency electric and magnetic fields

Electricity is transmitted as current from generating sources to high-voltage transmission lines, substations, distribution lines, and then finally to our homes and workplaces for consumption. The vast majority of electricity in North America is transmitted as alternating current (AC), which changes direction 60 times per second (i.e., a frequency of 60 Hertz [Hz]).

Everything that is connected to our electrical system (i.e., power lines, wiring, appliances, and electronics) produces ELF EMF (*see* Figure 1). Both electric fields and magnetic fields are properties of the space near these electrical sources. Forces are experienced by objects capable of interacting with these fields; electric charges are subject to a force in an electric field, and moving charges experience a force in a magnetic field.

- **Electric fields** are the result of voltage applied to electrical conductors and equipment. The electric field is expressed in measurement units of volts per meter (V/m) or kilovolts per meter (kV/m); 1 kV/m is equal to 1,000 V/m. Conducting objects including fences, buildings, and our own skin and muscle easily block electric fields. Therefore, certain appliances within homes and workplaces are the major source of electric fields indoors, while transmission and distribution lines are the major source of electric fields outdoors.

- **Magnetic fields** are produced by the flow of electric currents; however, unlike electric fields, most materials do not readily block magnetic fields. The strength of a magnetic field is expressed as magnetic flux density in units of gauss (G) or milligauss (mG), where 1 G=1,000 mG.[2] The strength of the magnetic field at any point depends on characteristics of the source. In the case of power lines, magnetic-field strength is dependent on the arrangement of conductors, the amount of current flow, and distance from the conductors.

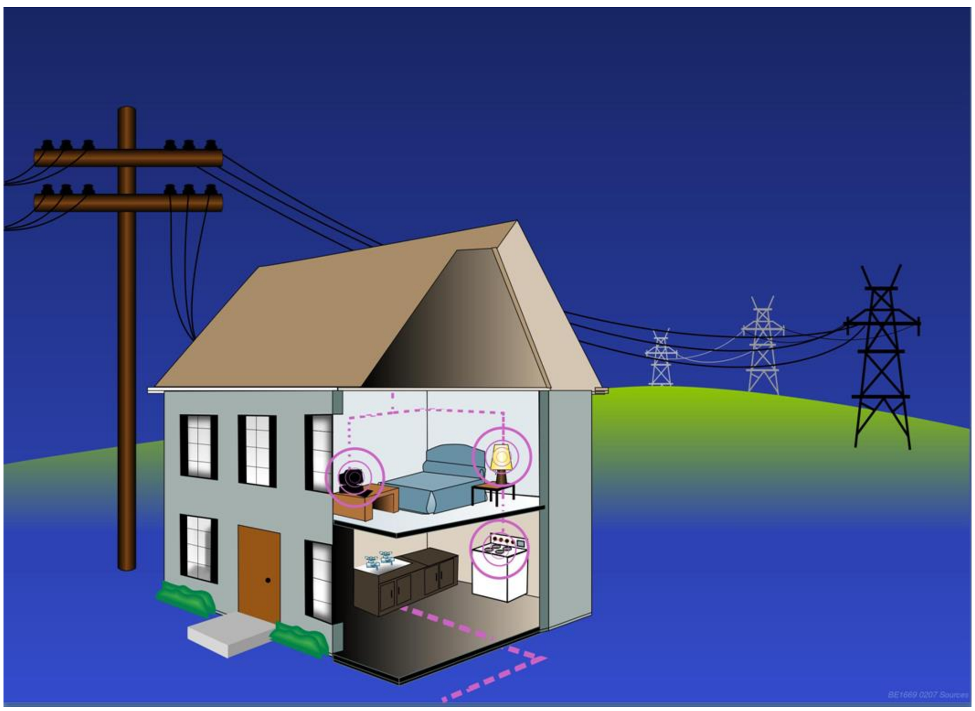

Figure 1. Numerous sources of ELF EMF in our homes (appliances, wiring, currents running on water pipes, and nearby distribution and transmission lines).

[2] Scientists also refer to magnetic flux density at these levels in units of microtesla. Magnetic flux density in units of mG can be converted to microtesla by dividing by 10 (i.e., 1 mG = 0.1 microtesla).

Sources and exposure

The intensity of both electric fields and magnetic fields diminishes with increasing distance from the source. Electric fields and magnetic fields from transmission lines generally decrease with distance from the conductors in proportion to the square of the distance, described as creating a bell-shaped curve of field strength around the lines.

Since electricity is such an integral part of our infrastructure and everyday life (e.g., in transportation systems and in homes and businesses), people living in modern communities are surrounded by these fields. Figure 2 describes typical EMF levels measured in residential and occupational environments, compared to levels measured on or at the edge of transmission-line rights-of-way. While EMF levels decrease with distance from the source, any home, school, or office tends to have a background EMF level as a result of the combined effect of the numerous EMF sources. In general, the background magnetic-field level in a house away from appliances is typically less than 20 mG, while levels can be hundreds of mG in close proximity to appliances. Background levels of electric fields range from 10 V/m to 20 V/m, while appliances produce levels up to several tens of V/m (WHO, 2007).

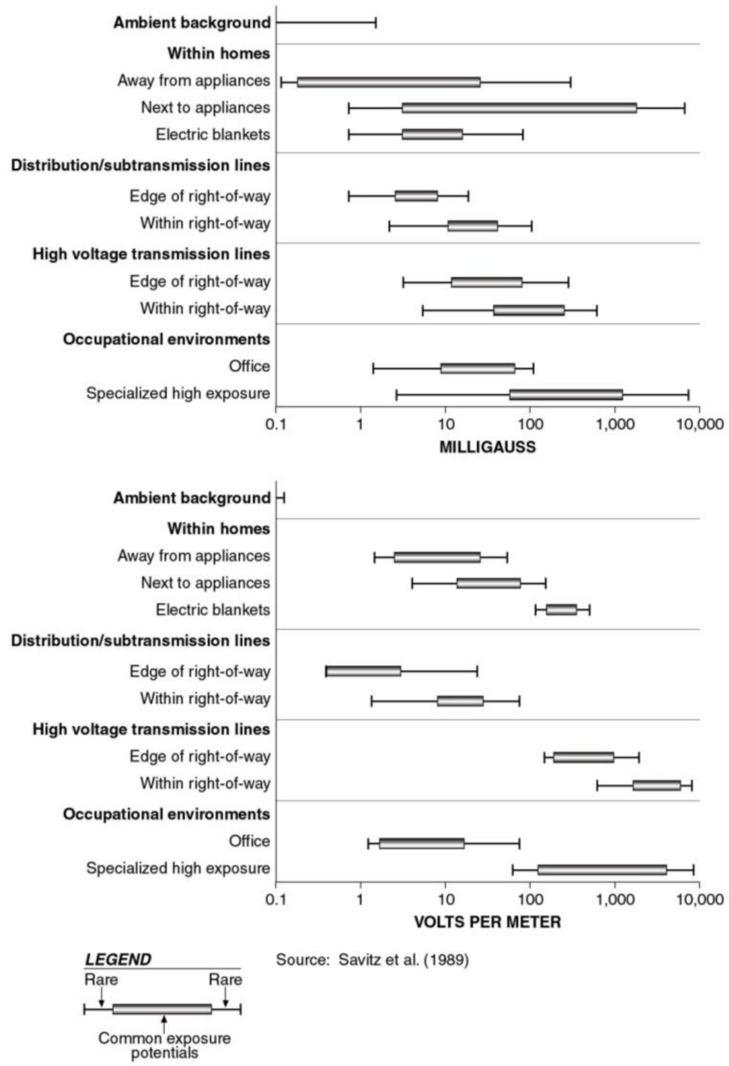

Figure 2. Electric- and magnetic-field strengths in the environment.

Experiments have yet to show which aspect of ELF EMF exposure, if any, may be relevant to biological systems. The current standard to evaluate EMF exposure for health research is long-term, average personal exposure, which is the average of all exposures to the varied electrical sources encountered in the many places we live, work, eat, and shop. As expected, this exposure is difficult to approximate, and exposure assessment is a major source of uncertainty in studies of ELF EMF and health (WHO, 2007).

Little research has been done to characterize the general public's exposure to magnetic fields, although some basic conclusions are available from the literature:

- *Personal magnetic-field exposure:*
  - The vast majority of persons in the United States have a time-weighted average (TWA) exposure to magnetic fields less than 2 mG (Zaffanella and Kalton, 1998).[3]
  - In general, personal magnetic-field exposure is greatest at work and during travel (Zaffanella and Kalton, 1998).
- *Residential magnetic-field exposure:*
  - The highest magnetic-field levels are typically found directly next to appliances (Zaffanella, 1993). For example, Gauger (1985) reported the maximum AC magnetic field at 3 centimeters from a sampling of appliances as 3,000 mG (can opener); 2,000 mG (hair dryer); 5 mG (electric oven); and 0.7 mG (refrigerator).
  - Several parameters affect the distribution of personal magnetic-field exposures at home: residence type, residence size, type of water line, and proximity to overhead power lines. Persons living in small homes, apartments, homes with metal piping, and homes close to three-phase electric power distribution and transmission lines tend to have higher at-home magnetic-field levels (Zaffanella and Kalton, 1998).
  - Residential magnetic-field levels are caused by currents from nearby transmission and distribution systems, pipes or other conductive paths, and electrical appliances (Zaffanella, 1993).
- *Workplace magnetic-field exposure*
  - Some occupations (e.g., electric utility workers, sewing machine operators, telecommunications workers) have higher exposures due to work near equipment with high magnetic-field levels (NIEHS, 2002).

[3] TWA is the average exposure to a chemical or physical agent over a given specified period (i.e., an 8-hour workday or 24 hours). The average is determined by sampling the exposure of interest throughout the selected period.

- *Power line magnetic-field exposure*
    - The magnetic-field levels associated with transmission and distribution lines vary substantially depending on their configuration, amount of current flow (load), and distance from conductors, among other parameters. At distances of approximately 300 feet from overhead transmission lines and during average electricity demand, the magnetic-field levels from many transmission lines are often similar to the background levels found in most homes, as illustrated in Figure 2 above, and as discussed in a National Institute of Environmental Health Sciences booklet on EMF (NIEHS, 2002).

Known effects

Similar to virtually any exposure, adverse effects can be expected from exposure to very high levels of ELF EMF. If the current density or electric field induced by an extremely strong magnetic field exceeds a certain threshold, excitation of muscles and nerves is possible (ICNIRP, 2010). Also, strong electric fields can induce charges on the surface of the body that can lead to small shocks (i.e., micro shocks). These acute, shock-like effects cause no long-term damage or health consequences. Limits for the general public and workplace have been set to prevent these effects, but there are no real-life situations where these levels are exceeded on a regular basis. Standards and guidelines are discussed in more detail in Section 6.

2 Methods for Evaluating Scientific Research

Science is more than a collection of facts. It is a method of obtaining information and of reasoning to ensure that the information and conclusions are accurate and correctly describe physical and biological phenomena. Many misconceptions in human reasoning occur when people casually interpret their observations and experience. Therefore, scientists use systematic methods to conduct and evaluate scientific research and assess the potential impact of a specific agent on human health. This process is designed to ensure that more weight is given to those studies of better quality, and to ensure that studies with a given result are not selectively chosen from available studies to advocate or suppress a preconceived idea of an adverse effect. Scientists and scientific agencies and organizations use these standard methods to draw conclusions about the many exposures in our environment.

Weight-of-evidence reviews

The scientific process entails looking at *all* the evidence on a particular issue in a systematic and thorough manner to evaluate if the overall data present a logically coherent and consistent picture. This is often referred to as a weight-of-evidence review in which all studies are considered together, giving more weight to studies of higher quality, and using an established analytic framework to arrive at a conclusion about a possible causal relationship. Weight-of-evidence reviews typically are conducted within the larger framework of health risk assessments or evaluations of particular exposures or exposure circumstances that qualitatively and quantitatively define health risks. Several agencies have described weight-of-evidence and health risk assessment methods, including the International Agency for Research on Cancer (IARC), which routinely evaluates substances such as drugs, chemicals, and physical agents for their ability to cause cancer; the WHO International Programme for Chemical Safety; the U.S. Environmental Protection Agency (US EPA), which sets guidance for public exposures; the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) for the European Union; and the U.S. National Toxicology Program (NTP) (USEPA, 1993, 1996; WHO, 1994; SCENIHR, 2012; NTP, 2015). Two steps precede a weight-of-evidence evaluation: 1) a systematic review to identify the relevant literature, and 2) an evaluation of each relevant study to determine its strengths and weaknesses.

The following sections discuss important considerations in the evaluation of human health studies of ELF EMF in a weight-of-evidence review, including exposure considerations, study design, and methods for estimating risk, bias, and the process of causal inference. The purpose of discussing these considerations here is to provide context for the later weight-of-evidence evaluations.

Exposure considerations

Methods to evaluate exposure range widely in studies of ELF EMF include:

- Classifying residences based on the relative capacity of nearby power lines to produce magnetic fields (i.e., wire code categories).
- Assessing exposure based on occupational titles.
- Calculating magnetic-field levels based on job histories (i.e., a job-exposure matrix [JEM]).
- Determining residential distance from nearby power lines.
- Taking spot measurements of magnetic-field levels inside or outside residences.
- Taking 24-hour and 48-hour measurements of magnetic fields in a particular location in a house (e.g., a child's bedroom).
- Calculating magnetic-field levels based on the characteristics of nearby power installations.
- Taking personal measurements of magnetic fields for a 24-hour or 48-hour period using a dosimeter.

Each of these methods has strengths and limitations (Kheifets and Oksuzyan, 2008). Magnetic-field exposure is ubiquitous, but it varies for each individual over a lifetime because the locations one frequents change and the ELF EMF sources in those locations also change. This lack of consistency makes valid estimates of personal magnetic-field exposure challenging. Furthermore, without a biological basis to define a relevant exposure metric (average exposure or peak exposure) and a defined critical period for exposure (e.g., *in utero*, shortly before diagnosis), relevant and valid assessments of exposure are problematic. Exposure misclassification is one of the most significant concerns in studies of ELF EMF.

In general, long-term, personal measurements are the metrics selected by epidemiologists. Other methods are generally weaker because they may not be strong predictors of long-term exposure and do not account for all magnetic-field sources. ELF EMF can be estimated indirectly by assigning an estimated amount of exposure to an individual based on calculations considering nearby power installations or a person's job title (e.g., using a JEM). For instance, a relative estimate of exposure could be assigned to all machine operators based on historical information on the magnitude of the magnetic field produced by the machine. Indirect measurements are not as accurate as direct measurements because they do not contain information specific to that person or the exposure situation. In the example of machine operators, the indirect measurement may not account for how much time any one individual spends working at that machine, any differences in the job tasks performed by each machine operator, or any potential variability in magnetic fields produced by the machines over time (Kheifets et al., 2009;[4] Gobba et al., 2011). In addition, such occupational measurements do not account for the worker's residential magnetic-field exposures.

Types of health research studies

Research studies can be broadly classified into three groups: 1) epidemiologic observations of people, 2) experimental laboratory studies of humans and animals (*in vivo*), and 3) experimental laboratory studies of cells and tissues (*in vitro*). Epidemiologic studies investigate how disease is distributed in populations and what factors influence or determine this disease distribution (Gordis, 2000), and attempt to identify potential causes for disease while observing people as they go about their daily lives. Such studies are designed to quantify and evaluate the associations between disease and reported exposures to environmental factors.

The most common types of epidemiologic studies in the ELF EMF literature are case-control and cohort studies. In case-control studies, people with and without the disease of interest are identified and the exposures of interest are evaluated. Often, people are interviewed or their personal records (e.g., medical records or employment records) are reviewed in order to establish the exposure history for each individual. The exposure histories are then compared between the diseased and non-diseased populations to determine whether any statistically significant

[4] Kheifets et al. (2009) reports on the conclusions of an independent panel organized by the Energy Networks Association in the United Kingdom in 2006 to review the current status of the science on occupational EMF exposure and identify the highest priority research needs.

differences in exposure histories exist. In cohort studies, on the other hand, individuals within a defined cohort of people (e.g., all persons working at a utility company) are classified as exposed or non-exposed and followed over time for the incidence of disease. Researchers then compare disease incidence in the exposed and non-exposed groups.

Experimental studies are designed to test specific hypotheses under controlled conditions and are vital to assess cause-and-effect relationships. An example of a human experimental studies relevant to this area of research would be ones that measure the impact of magnetic-field exposure on acute biological responses in humans, such as hormone levels. These studies are conducted in laboratories under controlled conditions. *In vivo* studies of animals and *in vitro* experimental studies also are conducted under controlled conditions in laboratories. *In vivo* studies expose laboratory animals to very high levels of a chemical or physical agent to determine whether exposed animals develop cancer or other effects at higher rates than unexposed animals, while attempting to control other factors that could possibly affect disease rates (e.g., diet, genetics). *In vitro* studies of isolated cells and tissues are important because they can help scientists understand biological mechanisms that relate to the same exposure in whole body humans and animals. The responses of cells and tissues outside the body, however, may not reflect the response of those same cells if maintained in a living system, so their relevance cannot be assumed. Therefore, it is both necessary and desirable to assess whether a particular agent could cause adverse health effects using both epidemiologic and experimental studies, and both approaches have been used to evaluate whether exposure to ELF EMF has any adverse effects on human health. Epidemiologic studies are valuable because they are conducted in human populations, but they are limited by their non-experimental design and typical retrospective nature. In epidemiologic studies of magnetic fields, for example, researchers cannot control the amount of individual exposure, how exposure occurs over time, the contribution of different sources, or individual behavior other than exposure that may affect disease risk, such as diet. In valid risk assessments of ELF EMF, epidemiologic studies are considered alongside experimental studies of laboratory animals, while studies of isolated cells and tissues are generally considered supplementary.

Estimating risk

Epidemiologists measure the statistical association between exposures and disease in order to estimate risk. This brief summary is included to provide a foundation for understanding and interpreting statistical associations in epidemiologic studies as risk estimates.

Two common types of risk estimates are absolute risk and relative risk (RR). Absolute risk, also known as incidence, is the amount of new disease that occurs in a given period. For example, the absolute risk of invasive childhood cancer in children 0 to 19 years of age for 2004 was 14.8 per 100,000 children (Ries et al., 2007). An RR evaluates whether a particular exposure or inherent quality (e.g., EMF, diet, genetics, race) is associated with a disease outcome and is calculated by looking at the absolute risk in one group relative to a comparison group. For example, white children 0 to 19 years of age had an estimated absolute risk of childhood cancer of 15.4 per 100,000 in 2004, and African American children in the same age range had an estimated absolute risk of 13.3 per 100,000 in the same year. By dividing the absolute risk of white children by the absolute risk of African American children, we obtain an RR of 1.16. This RR estimate can be interpreted to mean that white children have a risk of childhood cancer that is 16% greater than the risk of African American children. Additional statistical analysis is needed to evaluate whether this association is statistically significant, as defined in the following sub-section.

It is important to understand that risk is estimated differently in cohort and case-control studies because of the way the studies are designed. Traditional cohort studies provide a direct estimate of RR, while case-control studies only provide indirect estimates of RR, called odds ratios (OR). For this reason, among others, cohort studies usually provide more reliable estimates of the risk associated with a particular exposure. Case-control studies are more common than cohort studies, however, because they are less costly and more time efficient.

Thus, the association between a particular disease and exposure is measured quantitatively in an epidemiologic study as either the RR (cohort studies) or OR (case-control studies) estimate. The general interpretation of a risk estimate equal to 1.0 is that the exposure is not associated with an increased incidence of the disease. If the risk estimate is greater than 1.0, the inference is that the exposure is associated with an increased incidence of the disease. On the other hand, if the risk estimate is less than 1.0, the inference is that the exposure is associated with a reduced incidence of the disease. The magnitude of the risk estimate is often referred to as its strength (i.e., strong versus weak). Stronger associations are given more weight because they are less susceptible to the effects of bias.

Statistical significance

Statistical significance testing provides an idea of whether or not a statistical association is a chance occurrence or whether the association is likely to be observed upon repeated testing. The terms statistically significant or statistically significant association are used in epidemiologic studies to describe the tendency of the level of exposure and the occurrence of disease to be linked, with chance as an unlikely explanation. Statistically significant associations, however, are not necessarily an indication of cause-and-effect because the interpretation of statistically significant associations depends on many other factors associated with the design and conduct of the study, including how the data were collected and the number of study participants.

Confidence intervals (CI), reported along with RR and OR values, indicate a range of values for an estimate of effect that has a specified probability (e.g., 95%) of including the true estimate of effect. CIs evaluate statistical significance, but do not address the role of bias, as described further below. A 95% CI indicates that if the study was conducted a very large number of times, 95% of the measured estimates would be within the upper and lower confidence limits.

The CI range is also important for interpreting estimated associations, including the precision and statistical significance of the association. A very wide CI indicates great uncertainty in the value of the true risk estimate. This is usually due to a small number of observations. A narrow CI provides more certainty about the true RR estimate. If the 95% CI does not include 1.0, the probability that an association is due to chance alone is 5% or lower, and the result is considered statistically significant, as discussed above.

Meta-analysis and pooled analysis

In scientific research, the results of smaller studies may be difficult to distinguish from normal, random variation. This is also the case for sub-group analyses where few cases are estimated to have high exposure levels (e.g., in case-control studies of childhood leukemia and TWA magnetic-field exposure greater than 3 to 4 mG). Meta-analysis is an analytic technique that combines the published results from a group of studies into one summary result. A pooled analysis, on the other hand, combines the raw, individual-level data from the original studies and analyzes the data from the studies altogether. These methods are valuable because they increase the number of individuals in the analysis, which allows for a more robust and stable estimate of association. Meta- and pooled analyses are important tools for qualitatively synthesizing the results of a large group of studies.

The disadvantage of meta- and pooled analyses is that they can convey a false sense of consistency across studies if *only* the combined estimate of effect is considered (Rothman and Greenland, 1998). These analyses typically combine data from studies with different study populations, methods for measuring and defining exposure, and disease definitions. This is particularly true for analyses that combine data from case-control studies, which often use very different methods for the selection of cases and controls and exposure assessment (Linet, 2003). Therefore, meta- and pooled analyses are used not only to synthesize or combine data, but also to understand which factors cause the results of the studies to vary (i.e., publication date, study design, possibility of selection bias), and how these factors affect the associations calculated from the data of all the studies combined (Rothman and Greenland, 1998).

Meta- and pooled analyses are a valuable technique in epidemiology; however, in addition to calculating a summary RR, they should follow standard techniques (Stroup et al., 2001) and analyze the factors that contribute to any heterogeneity between the studies.

Bias in epidemiologic studies

One key reason that the results of epidemiologic studies cannot directly provide evidence for cause-and-effect is the presence of bias. Bias is defined as "any systematic error in the design, conduct or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of disease" (Gordis, 2000, p. 204). In other words, sources of bias are factors or research situations that can mask a true association or cause an association that does not truly exist. As a result, the extent of bias, as well as its types and sources, is one of the most important considerations in the interpretation of epidemiologic studies. Since it is not possible to fully control human populations, perfectly measure their exposures, or control for the effects of all other risk factors, bias will exist in some form in all epidemiologic studies of human health. Laboratory studies, on the other hand, more effectively manage bias because of the tight control the researchers have over most study variables.

One important source of bias occurs in epidemiologic studies when a third variable confuses the relationship between the exposure and disease of interest because of its relationship to both. Consider an example of a researcher whose study finds that people who exercise have a lower risk of diabetes compared to people who do not exercise. It is known that people who exercise more also tend to consume healthier diets and healthier diets may lower the risk of diabetes. If the researcher does not control for the impact of diet, it is not possible to say with certainty that the lower risk of diabetes is due to exercise and not to a healthier diet. In this example, diet is the confounding variable.

Cause versus association and evaluating evidence regarding causal associations

Epidemiologic studies can help suggest factors that may contribute to the risk of disease, but they are not used as the sole basis for drawing inferences about cause-and-effect relationships. Since epidemiologists do not have control over the many other factors to which people in their studies are exposed, and diseases can be caused by a complex interaction of many factors, the results of epidemiologic studies must be interpreted with caution. A single epidemiologic study is rarely unequivocally supportive or non-supportive of causation; rather, a weight is assigned to the study based on the validity of its methods and all relevant studies (epidemiology, *in vivo*, and *in vitro*) must be considered together in a weight-of-evidence review to arrive at a conclusion about possible causality between an exposure and disease.

In 1964, the U.S. Surgeon General published a landmark report on smoking-related diseases (HEW, 1964). As part of this report, the Surgeon General outlined nine criteria for evaluating epidemiologic studies (along with experimental data) for causality. In a more recent edition of this report, these criteria have been reorganized into seven criteria. In the earlier report, which was based on the commonly-referenced Hill criteria (Hill, 1965), coherence, plausibility, and analogy were considered as distinct items, but are now summarized together because they have been treated in practice as essentially reflecting one concept (HHS, 2004). Table 1 provides a list and brief description of each criterion.

Table 1. Criteria for evaluating whether an association is causal (HHS, 2004)

Criteria	Description
Consistency	Repeated observation of an association between exposure and disease in multiple studies of adequate statistical power, in different populations, and at different times.
Strength of the association	The larger (stronger) the magnitude and statistical strength of an association between exposure and disease, the less likely such an effect is the result of chance or unmeasured confounding.
Specificity	The exposure is the single cause or one of a few causes of disease.
Temporality	The exposure occurs prior to the onset of disease.
Coherence, plausibility, and analogy	The association cannot violate known scientific principles and the association must be consistent with experimentally demonstrated biologic mechanisms.
Biologic gradient	The observation that the stronger or greater the exposure, the stronger or greater the effect, also known as a dose-response relationship.
Experiment	Observations that result from situations in which natural conditions imitate experimental conditions. Also stated as a change in disease outcome in response to a non-experimental change in exposure patterns in populations.

The criteria were meant to be applied to statistically significant associations observed in the cumulative epidemiologic literature (i.e., if no statistically significant association is observed for an exposure, then the criteria are not relevant). It is important to note that these criteria were not intended to serve as a checklist, but as guide to evaluate associations for causal inference. Theoretically, it is possible for an exposure to meet all seven criteria, but still not be deemed a causal factor. Also, no one criterion can provide indisputable evidence for causation, nor can any single criterion, except for temporality, rule out causation.

In summary, the judicious consideration of these criteria is useful in evaluating epidemiologic studies, but they cannot be used as the sole basis for drawing inferences about cause-and-effect relationships. In line with the criteria of coherence, plausibility, and analogy, epidemiologic studies are considered along with *in vivo* and *in vitro* studies in a comprehensive weight-of-evidence review. Epidemiologic support for causality is usually based on high-quality studies that report consistent results across many different populations and study designs and are supported by experimental data collected from *in vivo* and *in vitro* studies.

Biological response versus disease in human health

When interpreting research studies, it is important to distinguish between a reported biological response and an indicator of disease. This is relevant because exposure to ELF EMF may elicit a biological response that is simply a normal response to environmental conditions. This response, however, may not be a disease, cause a disease, or be otherwise harmful. There are many exposures or factors encountered in day-to-day life that elicit a biological response, but the response is neither harmful nor the cause of disease. For example, as a person walks from a dark room indoors to a sunny day outdoors, the pupils of the eye naturally constrict to limit the amount of light passing into the eye. This constriction of the pupil is a biological response to the change in light conditions. Pupil constriction, however, is neither a disease itself, nor is it known to cause disease.

3 The WHO 2007 Report: Methods and Conclusions

The WHO is a scientific organization within the United Nations system with the mandate to provide leadership on global health matters, shape health research agendas, and set norms and standards. The WHO established the International EMF Project in 1996, in response to public concern about exposure to ELF EMF and possible adverse health outcomes. The Project's membership includes 8 international organizations, 8 collaborating institutions, and over 54 national authorities. The overall purpose of the Project is to assess health and environmental effects of exposure to static and time-varying fields in the frequency range of 0 Hz to 300 Gigahertz. A key objective of the Project is to evaluate the scientific literature and make periodic status reports on health effects to be used as the basis for a coherent international response, including the identification of important research gaps and the development of internationally acceptable standards for ELF EMF exposure.

In 2007, the WHO published their Environmental Health Criteria (EHC) 238 on EMF summarizing health research in the ELF range. The EHC conducted their review using standard scientific procedures, as outlined in its Preamble and described above in Section 2. The Task Group responsible for the report's overall conclusions consisted of 21 scientists from around the world with expertise in a wide range of scientific disciplines. They relied on the conclusions of previous weight-of-evidence reviews,[5] where possible, and mainly focused on evaluating studies published after an IARC review of ELF EMF and cancer in 2002.

The WHO Task Group and IARC use specific terms to describe the strength of the evidence in support of causality between specific agents and cancer. These categories are described here because, while they are meaningful to scientists who are familiar with the IARC process, they can create an undue level of concern with the general public. *Sufficient evidence of carcinogenicity* is assigned to a body of epidemiologic research if a positive association has been observed in studies in which chance, bias, and confounding can be ruled out with reasonable confidence. *Limited evidence of carcinogenicity* describes a body of epidemiologic research

[5] The term weight-of-evidence review is used in this report to denote a systematic review process by a multidisciplinary, scientific panel involving experimental and epidemiologic research to arrive at conclusions about possible health risks. The WHO EHC on EMF does not specifically describe their report as a weight-of-evidence review. Rather, they describe conducting a health risk assessment. A health risk assessment differs from a weight-of-evidence review in that it also incorporates an exposure and exposure-response assessment.

where the findings are inconsistent or there are outstanding questions about study design or other methodological issues that preclude making a conclusion. *Inadequate evidence of carcinogenicity* describes a body of epidemiologic research where it is unclear whether the data is supportive or unsupportive of causation because there is a lack of data or there are major quantitative or qualitative issues. A similar classification system is used for evaluating *in vivo* studies and mechanistic data for carcinogenicity.

Summary categories are assigned by considering the conclusions of each body of evidence (epidemiologic, *in vivo*, and *in vitro*) together. As identified in Figure 3, categories include (from highest to lowest risk): *carcinogenic to humans*; *probably carcinogenic to humans*; *possibly carcinogenic to humans*; *not classifiable as to its carcinogenicity to humans*; and *probably not carcinogenic to humans*. These categories are intentionally meant to err on the side of caution, giving more weight to the possibility that the exposure is truly carcinogenic and less weight to the possibility that the exposure is not carcinogenic. The category *possibly carcinogenic to humans* denotes exposures for which there is limited evidence of carcinogenicity in epidemiologic studies and less than sufficient evidence of carcinogenicity in studies of experimental animals. *In vitro* research is not described in Figure 3 because it provides ancillary information; it is used to a lesser degree in evaluating carcinogenicity and is classified simply as strong, moderate, or weak.

	Epidemiology Studies				Animal Studies			
	Sufficient evidence	Limited evidence	Inadequate evidence	Evidence suggesting lack of carcinogenicity	Sufficient evidence	Limited evidence	Inadequate evidence	Evidence suggesting lack of carcinogenicity
Known Carcinogen	✓							
Probable Carcinogen		✓			✓			
Possible Carcinogen		✓				✓	✓	
Not Classifiable			✓			✓	✓	
Probably not a Carcinogen				✓				✓

Sufficient evidence in epidemiology studies—A positive association is observed between the exposure and cancer in studies, in which chance, bias and confounding were ruled out with "reasonable confidence."

Limited evidence in epidemiology studies—A positive association has been observed between the exposure and cancer for which a causal interpretation is considered to be credible, but chance, bias or confounding could not be ruled out with "reasonable confidence."

Inadequate evidence in epidemiology studies—The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.

Evidence suggesting a lack of carcinogenicity in epidemiology studies—There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. The results from these studies alone or combined should have narrow confidence intervals with an upper limit close to the null value (e.g. a relative risk of 1.0). Bias and confounding should be ruled out with reasonable confidence, and the studies should have an adequate length of follow-up.

Sufficient evidence in animal studies—An increased incidence of malignant neoplasms is observed in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or indifferent laboratories or under different protocols. An increased incidence of tumors in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide sufficient evidence.

Limited evidence in animal studies—The data suggest a carcinogenic effect but are limited for making a definitive evaluation, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; etc.

Inadequate evidence in animal studies—The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available

Evidence suggesting a lack of carcinogenicity in animal studies—Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic.

Figure 3. Basic IARC method for classifying exposures based on potential carcinogenicity. Note that in 2019, IARC removed the category *Probably not a Carcinogen* (Group 4), as only one chemical had ever been assigned to that category. https://monographs.iarc.who.int/wp-content/uploads/2019/07/2019-SR-001-Revised_Preamble.pdf. Accessed March 18, 2022

The IARC has reviewed over 1,000 substances and exposure circumstances to evaluate their potential carcinogenicity. Eighty percent of exposures fall in the categories *possibly carcinogenic* (31 percent) or *not classifiable* (48 percent).[6] This occurs because it is nearly impossible to prove that something is completely safe, and few exposures show a clear-cut or probable risk, so most agents will end up in either of these two categories. Throughout the history of the IARC, only one agent has been classified as *probably not carcinogenic*, which illustrates the conservatism of the evaluations and the difficulty in proving the absence of an effect beyond all doubt.

The WHO report provided the following overall conclusions with regard to ELF EMF:

> New human, animal, and in vitro studies published since the 2002 IARC Monograph, 2002 [*sic*] do not change the overall classification of ELF as a possible human carcinogen (WHO, 2007, p. 347).
>
> Acute biological effects [i.e., short-term, transient health effects such as a small shock] have been established for exposure to ELF electric and magnetic fields in the frequency range up to 100 kHz that may have adverse consequences on health. Therefore, exposure limits are needed. International guidelines exist that have addressed this issue. Compliance with these guidelines provides adequate protection. Consistent epidemiological evidence suggests that chronic low-intensity ELF magnetic field exposure is associated with an increased risk of childhood leukaemia. However, the evidence for a causal relationship is limited, therefore exposure limits based upon epidemiological evidence are not recommended, but some precautionary measures are warranted (WHO, 2007, p. 355).

The WHO concluded the following regarding specific diseases:

Childhood cancers. The WHO report paid particular attention to childhood leukemia because the most consistent epidemiologic association in the area of ELF EMF and health research has been reported between this disease and TWA exposure to high magnetic-field levels. Two pooled analyses reported an association between childhood leukemia and TWA magnetic-field exposure >3 to 4 mG (Ahlbom et al., 2000; Greenland et al., 2000). These data, categorized as limited epidemiologic evidence, resulted in the classification of magnetic fields as possibly carcinogenic by the IARC in 2002.

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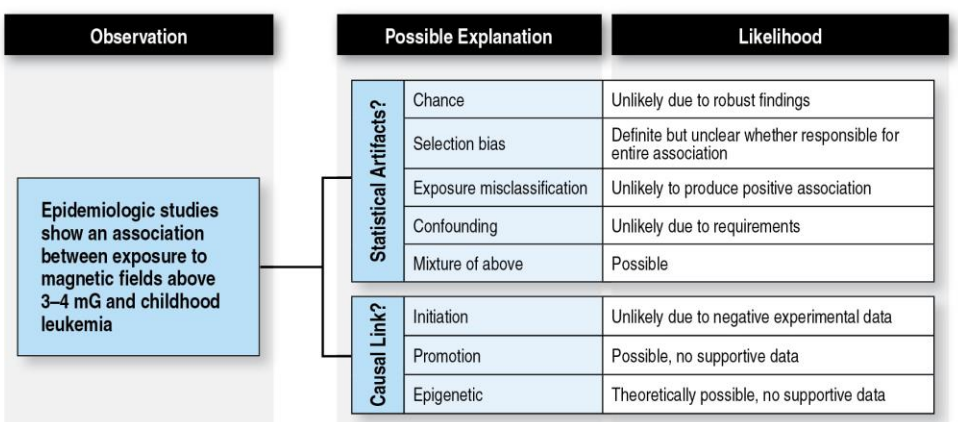
[6] https://monographs.iarc.fr/agents-classified-by-the-iarc/. Accessed March 18, 2022.

The WHO report systematically evaluated several factors that might be partially, or fully, responsible for the consistent association, including: chance, misclassification of magnetic-field exposure, confounding from hypothesized or unknown risk factors, and selection bias (*see* Figure 4). The authors concluded the following:

- Chance is an unlikely explanation since the pooled analyses had a large sample size and decreased variability.
- Control selection bias probably occurs to some extent in these studies and would result in an overestimate of the true association, but would not explain the entire observed association.
- It is less likely that confounding occurs, although the possibility that some yet-to-be identified confounder is responsible for the association cannot be fully excluded.
- Exposure misclassification would likely result in an underestimate of the true association, although it is not entirely clear.

The WHO concluded that reconciling the epidemiologic data on childhood leukemia and the negative experimental findings (i.e., no hazard or risk observed) through innovative research is currently the highest priority in the field of ELF EMF research. The WHO stated, however, that the public health impact of magnetic fields on childhood leukemia would likely be minimal if the association was determined to be causal given that few children are expected to have long-term *average* magnetic-field exposures greater than 3 to 4 mG.



Source: Adapted from Schüz and Ahlbom (2008)

Figure 4. Possible explanations for the observed association between magnetic fields and childhood leukemia.

Fewer studies have been published on magnetic fields and childhood brain cancer compared to studies of childhood leukemia. The WHO Task Group described the results of these studies as inconsistent and limited by small sample sizes and recommended a meta-analysis to clarify the research findings.

Breast cancer. The WHO concluded that the more recent studies they reviewed on breast cancer and ELF EMF exposure were higher in quality compared with earlier studies, and for that reason, they provide strong support to previous consensus statements that magnetic-field exposure does not influence the risk of breast cancer. In summary, the WHO stated "[w]ith these [more recent] studies, the evidence for an association between ELF magnetic-field exposure and the risk of female breast cancer is weakened considerably and does not support an association of this kind" (WHO, 2007, p. 9). The WHO recommended no further research with respect to breast cancer and magnetic-field exposure.

Adult leukemia and brain cancer. The WHO concluded, "[i]n the case of adult brain cancer and leukaemia, the new studies published after the IARC monograph do not change the conclusion that the overall evidence for an association between ELF [EMF] and the risk of these disease remains inadequate" (WHO, 2007, p. 307). The WHO panel recommended updating the existing European cohorts of occupationally-exposed individuals and pooling the epidemiologic data on brain cancer and adult leukemia to confirm the absence of an association.

In vivo research on carcinogenesis. The WHO concluded the following with respect to *in vivo* research: "[t]here is no evidence that ELF [EMF] exposure alone causes tumours. The evidence that ELF field exposure can enhance tumour development in combination with carcinogens is inadequate" (WHO, 2007, p. 10). Recommendations for future research included the development of a rodent model for childhood acute lymphoblastic leukemia (ALL) and the continued investigation of whether magnetic fields can act as a co-carcinogen.

Reproductive and developmental effects. The WHO concluded that, overall, the body of research does not suggest that maternal or paternal exposures to ELF EMF cause adverse reproductive or developmental outcomes. The evidence from epidemiologic studies on miscarriage was described as inadequate and further research on this possible association was recommended, although low priority was given to this recommendation.

Neurodegenerative diseases. The WHO reported that the majority of epidemiologic studies have reported associations between occupational magnetic-field exposure and mortality from Alzheimer's disease and amyotrophic lateral sclerosis (ALS), although the design and methods of these studies were relatively weak (e.g., disease status was based on death certificate data, exposure was based on incomplete occupational information from census data, and there was no control for confounding factors). The WHO concluded that there is inadequate data in support of an association between magnetic-field exposure and Alzheimer's disease or ALS. The panel highly recommended that further studies be conducted in this area, particularly studies where the association between magnetic fields and ALS is estimated while controlling for the possible confounding effect of electric shocks.

Cardiovascular disease. It has been hypothesized that magnetic-field exposure reduces heart rate variability, which in turn increases the risk for acute myocardial infarction (AMI). With one exception (Savitz et al., 1999), however, none of the studies of cardiovascular disease morbidity and mortality that were reviewed show an association with exposure. Whether a specific association exists between exposure and altered autonomic control of the heart remains speculative and overall the evidence does not support an association. Experimental studies of both short- and long-term exposure indicate that while electric shock is an obvious health hazard, other hazardous cardiovascular effects associated with ELF EMF are unlikely to occur at exposure levels commonly encountered environmentally or occupationally.

4 Current Scientific Consensus

The following sections identify and describe epidemiologic and *in vivo* studies related to ELF EMF and health published between December 2018 and December 2021. The purpose of this section is to evaluate whether the findings of these recent studies alter the conclusions published by the WHO in their 2007 report, as described in Section 3. A previous Exponent report summarized the literature through December 2018 (Exponent, 2019) and concluded that those results did not provide sufficient evidence to alter the basic conclusion of the WHO EHC published in 2007.

A structured literature search was conducted using PubMed, a search engine provided by the National Library of Medicine and the National Institutes of Health that includes over 33 million up-to-date citations from MEDLINE and other life science journals for biomedical articles (http://www.pubmed.gov). A well-defined search strategy was used to identify English language literature indexed between December 2018 and December 2021.[7] All fields (e.g., title, abstract, keywords) were searched with various search strings that referenced the exposure and disease of interest.[8] A researcher with experience in this area reviewed the titles and abstracts of these publications for inclusion in this evaluation. The following specific inclusion criteria were applied:

1. **Outcome**. Epidemiologic studies evaluated cancer; reproductive or developmental effects; neurodegenerative diseases; or cardiovascular disease; *in vivo* studies evaluated carcinogenicity. Research on other outcomes was not included (e.g., psychological effects, behavioral effects, hypersensitivity).
2. **Exposure**. Studies evaluated ELF EMF at a frequency of 50 or 60-Hz.
3. **Exposure assessment methods**. Studies evaluated exposure beyond self-report of an activity or occupation, and estimated exposure through various methods including calculated

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7 Since the literature search was performed at the end of December 2021, and there is sometimes a delay between the publication date of a study and the date it is indexed in PubMed, it is possible that some studies published prior to December 2021 are not included in this update.

8 EMF OR magnetic fields OR electric fields OR electromagnetic OR power frequency OR transmission line AND cancer (cancer OR leukemia OR lymphoma OR carcinogenesis) OR neurodegenerative disease (neurodegenerative disease OR Alzheimer's disease OR amyotrophic lateral sclerosis OR Lou Gehrig's disease) OR cardiovascular effects (cardiovascular OR heart rate) OR reproductive outcomes (miscarriage OR reproduction OR developmental effects).

EMF levels using distance from power lines, measured TWA exposure, and average exposure estimated from JEMs.

4. **Study design**. Study design included epidemiologic studies, meta-analyses, pooled analyses, human experimental studies, and *in vivo* studies of carcinogenicity. The review relies on the conclusions of the WHO with regard to *in vivo* studies in the areas of reproduction, development, neurology, and cardiology. Further, this report relies on the conclusions of the WHO report (as described in Section 3) regarding mechanistic data from *in vitro* studies since this field of study is less informative to the risk assessment process (IARC, 2002).
5. **Peer-review**. The study must have been peer-reviewed and published. Therefore, no conference proceedings, abstracts, or non-peer reviewed on-line materials were included.

Epidemiologic studies are evaluated below first by outcome (childhood cancer; adult cancer; reproductive or developmental effects; neurodegenerative disease; and cardiovascular effects), followed by an evaluation of *in vivo* research on carcinogenesis. Tables 2 through 9 list the relevant studies that were published from December 2018 through December 2021 in these areas.

Childhood health outcomes

Childhood leukemia

In 2002, the IARC assembled and reviewed research related to ELF EMF to evaluate the strength of the evidence in support of carcinogenicity. The IARC expert panel noted that when studies with the relevant information were combined in a pooled analysis (Ahlbom et al., 2000; Greenland et al., 2000), a statistically significant two-fold association was observed between childhood leukemia and estimated average exposure to high levels of magnetic fields (i.e., greater than 3 to 4 mG of average 24- and 48-hour exposure). This evidence was classified as limited evidence in support of carcinogenicity, falling short of sufficient evidence because chance, bias, and confounding could not be ruled out with reasonable confidence. Largely as a result of the findings related to childhood leukemia, the IARC classified magnetic fields as *possibly carcinogenic*, which, as noted previously, is a category that describes exposures with limited epidemiologic evidence and inadequate evidence from *in vivo* studies. The classification of *possibly carcinogenic* was confirmed by the WHO in their 2007 review.

Since the WHO conducted their review, childhood leukemia continues to be a main focus of ELF EMF epidemiologic research. Kheifets et al. (2010a) provided an update to the analyses conducted by Ahlbom et al. (2000) and Greenland et al. (2000) by reporting the results of a pooled analysis of seven case-control studies of childhood leukemia and ELF EMF published between 2000 and 2010. Although the authors included a large number of cases (n=10,865) in this analysis, only 23 cases had measured fields and 3 cases had calculated fields in the highest exposure category (≥3 mG). A moderate and statistically not significant association was reported for the highest exposure category (OR 1.44, 95% CI 0.88-2.36), which was weaker than the association reported in the previous pooled analyses (Ahlbom et al., 2000; Greenland et al., 2000).

More recently, several case-control studies from the United States (Crespi et al., 2016), France (Sermage-Faure et al., 2013), Denmark (Pedersen et al., 2014a, 2014b, 2015), and the United Kingdom (Bunch et al., 2014, 2015; Swanson and Bunch, 2018) assessed the risk of childhood leukemia in relation to residential proximity to high-voltage power lines. None of these studies reported consistent overall associations between childhood leukemia development and residential distance to high-voltage power lines. The largest of these studies (Bunch et al., 2014) was an update of an earlier study in the United Kingdom (Draper et al., 2005) and included over 53,000 childhood cancer cases diagnosed between 1962 and 2008 and over 66,000 healthy children as controls. Overall, the authors reported no association between childhood leukemia development and residential proximity to power lines with any of the voltage categories. The statistical association reported in the earlier study (Draper et al., 2005) was no longer apparent in the updated analysis (Bunch et al., 2014).

These case-control studies had large sample sizes and were population-based studies requiring no subject participation, which minimizes the potential for selection bias. The main limitation of these studies was the reliance on distance to power lines as the main exposure metric, which is known to be a poor predictor of actual residential magnetic-field exposure. Several observers in the scientific literature discussed the limitations of distance as an exposure proxy in the context of the French study by Sermage-Faure et al. (Bonnet-Belfais et al., 2013; Clavel et al., 2013). In addition, Chang et al. (2014) provided a detailed discussion of the limitations of exposure assessment methods based on geographical information systems. Swanson et al. (2014) also concluded, based on their analysis of data from the British study (Bunch et al., 2014), that geocoding information not based on exact address, but only on post code information, is "probably not acceptable for assessing magnetic-field effects" (Swanson et al., 2014, p. N81).

Additional research reviewed in Exponent (2019) also has not provided consistent or compelling evidence of an association (e.g., Magnani et al., 2014; Salvan et al., 2015; Tabrizi and Bigdoli, 2015; Tabrizi and Hossein, 2015; Su et al., 2016; Kheifets et al. 2017, Amoon et al., 2018a, 2018b; Kyriakopoulou et al., 2018). In their 2015 report, SCENIHR concluded that the epidemiologic data on childhood leukemia and EMF exposure reviewed for the report "are consistent with earlier findings of an increased risk of childhood leukaemia with estimated daily average exposures above 0.3 to 0.4 μT [microtesla] [i.e., 3 to 4 mG]" and noted that "no mechanisms have been identified and no support is existing [*sic*] from experimental studies that could explain these findings, which, together with shortcomings of the epidemiological studies prevent a causal interpretation" (SCENIHR, 2015, p. 164).

Recent studies (December 2018 through December 2021)

Crespi et al. (2019) examined the same California study population as Crespi et al. (2016) to investigate the separate and combined relationship between distance from high-voltage power lines and calculated magnetic-field exposure and childhood leukemia risk. The authors reported that neither residential proximity to high-voltage power lines (<50 meters, ≥200 kilovolts [kV]) nor calculated magnetic fields (≥0.4 μT [≥4 mG]) alone were associated with childhood leukemia; however, an association was observed for study subjects with both residential proximity to high-voltage power lines and high calculated magnetic-field levels (Crespi et al., 2019). No associations were observed with low-voltage power lines. The authors considered their study as "hypothesis generating" and noted that the observed associations could be spurious findings due to small sample sizes or confounding. The authors concluded that their findings "argue against magnetic fields as a sole explanation" for an association between distance and childhood leukemia and "in favor of some other explanation" linked to the power lines (Crespi et al., 2019, p. 535).

In further analyses of data from the same California childhood cancer epidemiologic study, Amoon et al. (2019, 2020) assessed the role of residential mobility and dwelling type in estimating the potential effect of magnetic-field exposure on childhood leukemia risk. Amoon et al. (2019) reported that residential mobility had some impact on the association between magnetic-field exposure and childhood leukemia but concluded that confounding by residential mobility is "unlikely to be the primary driving force behind previously observed largely consistent, but unexplained associations" (Amoon et al., 2019, p. 7). Amoon et al. (2020) reported that while race, ethnicity, and socioeconomic status were associated with dwelling type (e.g., single-family home, apartment, duplex, mobile home), dwelling type was not associated with childhood leukemia, and thus did not appear to be a confounder in the relationship between magnetic-field exposure and childhood leukemia risk in this study. The authors reported potential differences in the strength of the association between childhood leukemia and magnetic-field exposure by dwelling type and recommended additional research in this area.

Auger et al. (2019a) examined the relationship between residential proximity to high-voltage transmission lines and transformer stations during pregnancy of the mother and risk of childhood cancer in the offspring in a cohort of 784,000 children born in Québec and followed for one decade after birth. No statistically significant associations were reported between distance to high-voltage power lines or transformer stations and any cancer outcomes, including hematopoietic cancer, and solid tumors (Auger et al., 2019a). The authors concluded that their results "suggest an absence of a causal link between [EMF] from high voltage power sources and the risk of cancer in children" (Auger et al., 2019a, p. 6).

Núñez-Enríquez et al. (2021) conducted a case-control study to assess the relationship between residential magnetic-field exposure and B-lineage acute lymphoblastic leukemia (B-ALL) in Mexico City, Mexico. The study included children less than 16 years of age (290 cases and 407 controls). Exposure to magnetic-field exposure was assessed using 24-hour measurements in the participants' bedrooms. The authors reported statistically significant associations between B-ALL and 24-hour magnetic-field exposures ≥ 0.4 μT [4 mG] and ≥ 0.6 μT [6 mG]; however, non-statistically significant associations were reported for 24-hour magnetic field exposures ≥ 0.2 μT [2 mG], ≥ 0.3 μT [3 mG], and ≥ 0.5 μT [5 mG]. The authors concluded that "to date, a clear mechanism through which exposure to ELF- MFs [magnetic fields] may be associated with leukemia has not been established. Therefore, it is possible that other factors related to ELF- MF exposure, which we could not identify in the present study, may be relatively more relevant as risk factors for childhood leukemia development" (Núñez-Enríquez et al., 2021, p. 9). Reliance on 24-hour measurements, the large proportion of participants with higher magnetic-field exposures (14% of cases and 11% of controls had 24-hour exposures ≥ 0.3 μT [3 mG]), and the ability to analyze the most common childhood leukemia subtype (B-ALL) separately are among the study's strengths. The statistically significantly higher frequency of infections during the first year of life among cases, compared the controls, may be indicative of potential confounding. The hospital-based selection of controls may be a source of selection bias, if the catchment areas of the hospitals used to recruit controls were different than those of the hospitals where the leukemia cases were treated and recruited. Participation rate was also lower among cases than among controls, representing another potential source of selection bias.

Recent pooled analyses of epidemiologic studies of childhood leukemia and magnetic-field exposure indicated weak and statistically non-significant associations. Swanson et al. (2019) examined 41 studies to assess the trends in childhood leukemia risk over time. The authors reported a statistically non-significant decline in risk from the mid-1990s until the present, which they stated was "unlikely to be solely explained by improving study quality but may be due to chance" (Swanson et al., 2019, p. 470). The authors concluded, however, that the current body of literature on EMF "argue against health effects of MFs [magnetic fields] at these exposure levels" (Swanson et al., 2019, p. 485). Talibov et al. (2019) conducted a pooled analysis of 11 case-control studies examining the relationship between parental occupational exposure to ELF magnetic fields and childhood leukemia. No statistically significant association was found for paternal or maternal exposure by leukemia sub-type or overall, and no association was observed when additional exposure categories were used. The authors concluded that their study "suggests that parental ELF-EMF exposure plays no relevant role in the aetiology of childhood leukemia" (Talibov et al., 2019, p. 752).

Amoon et al. (2022) conducted a pooled analysis of and included original data from epidemiologic studies of residential exposure to magnetic fields and childhood leukemia published after the 2010 pooled analysis (Kheifets et al., 2010a). The study compared the exposures of 24,994 children with leukemia to those of 30,769 controls without leukemia to measured or calculated magnetic fields at their residences in California, Denmark, Italy, and the United Kingdom (Amoon et al., 2022). The exposures of these two groups to magnetic fields were found to not significantly differ, so the authors reported "[u]nlike previous pooled analyses, we found no increased risk of leukemia [above 0.4 μT]" and "[i]n conclusion, our results do not show the risk increase observed in previous pooled analysis and, over time, show a decrease in effect to no association between MF and childhood leukemia."

Investigators from Korea conducted a systematic review and meta-analysis of exposure to ELF-MF and childhood cancer (Seomun et al., 2021). The authors included 30 studies in their meta-analyses and reported that "[c]hildren exposed to 0.2-, 0.3-, and 0.4-μT ELF-MFs [magnetic fields] had a 1.26 (95% CI 1.06-1.49), 1.22 (95% CI 0.93-1.61), and 1.72 (95% CI 1.25-2.35) times higher odds of childhood leukemia." The authors did not specifically evaluate the change in association between ELF magnetic fields and childhood leukemia over time, and the overall results were likely influenced by the larger number of earlier studies.

Assessment

In summary, while most of the large and methodologically advanced studies published within the last decade (e.g., Bunch et al., 2014, Pedersen et al., 2014a, 2014b, 2015; Crespi et al., 2016; Kheifets et al., 2017, Crespi et al., 2019) showed no statistically significant associations between estimates of exposures from power lines, and recent pooled analyses indicated weaker and statistically non-significant associations, the association between childhood leukemia and magnetic fields observed in some earlier studies remains unexplained. Thus, the results of recent studies do not change the classification of the epidemiologic data as limited. In their most recent review of the research, SSM concluded that,

> Regarding the exposure to ELF magnetic fields and the development of childhood leukaemia, associations have been observed, but a causal relationship has not been established (SSM, 2021, p. 6).

In 2020, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) published a review of the research related to potential health effects of EMF exposure; the Commission's objective was to identify any data gaps in the body of literature on which they based their exposure guidelines (see Section 6) (ICNIRP, 2020). Regarding the research on childhood leukemia, ICNIRP did not recommend further epidemiologic studies on this topic, noting that any additional studies would be "unlikely to advance the knowledge, as they will potentially be affected by the same types of biases as existing studies" (ICNIRP, 2020, p. 535). ICNIRP (2020) did recommend "[f]urther studies on mechanisms and biological data from childhood leukemia experimental models" while also stating, "there is no support from animal experiments and there are no mechanistic data that can provide an explanation for any effect on biological structures at the exposure levels that have been identified in epidemiological studies"

(ICNIRP, 2020, p. 536). The lack of evidence of a plausible biological mechanism between magnetic-field exposure and childhood leukemia development has been noted in other recent publications (e.g., Habash et al., 2019) and is discussed in the sub-section on *in vivo* studies related to carcinogenesis.

Table 2. Relevant studies of childhood leukemia (December 2018 - December 2021)

Author	Year	Study Title
Amoon et al.	2019	The sensitivity of reported effects of EMF on childhood leukemia to uncontrolled confounding by residential mobility: a hybrid simulation study and an empirical analysis using CAPS data.
Amoon et al.	2020	The role of dwelling type when estimating the effect of magnetic fields on childhood leukemia in the California Power Line Study (CAPS).
Amoon et al.	2022	Pooled analysis of recent studies on magnetic fields and childhood leukaemia.
Auger et al.	2019a	Residential exposure to electromagnetic fields during pregnancy and risk of child cancer: a longitudinal cohort study.
Crespi et al.	2019	Childhood leukemia risk in the California Power Line Study: magnetic fields versus distance from power lines.
Núñez-Enríquez et al.	2021	Extremely low-frequency magnetic fields and the risk of childhood B-lineage acute lymphoblastic leukemia in a city with high incidence of leukemia and elevated exposure to ELF magnetic fields.
Seomun et al.	2021	Exposure to extremely low-frequency magnetic fields and childhood cancer: a systematic review and meta-analysis.
Swanson et al.	2019	Changes over time in the reported risk for childhood leukemia and magnetic fields.
Talibov et al.	2019	Parental occupational exposure to low-frequency magnetic fields and risk of leukaemia in the offspring: findings from the Childhood Leukaemia International Consortium (CLIC).

Childhood brain cancer

Compared to the research on magnetic fields and childhood leukemia, there have been fewer studies of childhood brain cancer. The data are less consistent and limited by even smaller numbers of exposed cases compared with studies of childhood leukemia. The WHO review recommended the following:

> As with childhood leukaemia, a pooled analysis of childhood brain cancer studies should be very informative and is therefore recommended. A pooled analysis of this kind can inexpensively provide a greater and improved insight into the existing data, including the possibility of selection bias and, if the

> studies are sufficiently homogeneous, can offer the best estimate of risk (WHO 2007, p. 18).

Addressing these recommendations, researchers conducted both a meta-analysis (Mezei et al., 2008) and a pooled analysis (Kheifets et al., 2010b) of available studies. The meta-analysis by Mezei et al. (2008) reported no overall association, but reported a statistically non-significant weak association with calculated or measured magnetic fields above 3 to 4 mG based on a sub-analysis of five studies. The pooled analysis by Kheifets et al. (2010b) included data from 10 studies of childhood brain cancer or central nervous system (CNS) cancer with long-term measurements, calculated fields, or spot measurements of residential magnetic-field exposure published from 1979 to 2010. Similar to childhood leukemia, few cases of childhood brain cancer had estimated magnetic-field exposures greater than 3 to 4 mG. None of the analyses showed statistically significant increases, and while some categories of high exposure had an OR >1.0, the overall patterns were not consistent with an association and no dose-response trends were apparent. The authors concluded that their results provide little evidence for an association between magnetic fields and childhood brain tumors.

Several of the same epidemiologic studies discussed in the childhood leukemia section investigated the potential relationship between residential proximity to overhead and underground transmission lines and childhood brain cancer (Bunch et al., 2014, 2015, 2016; Pedersen et al., 2015; Crespi et al., 2016). None of these studies reported any consistent association between distance to power lines and childhood brain cancer risk. Su et al. (2018) published a meta-analysis of epidemiologic studies that investigated the association between parental exposure to ELF magnetic fields and nervous system tumors in their offspring. The authors reported no consistent associations between maternal or paternal exposure to ELF magnetic fields and neuroblastoma or CNS tumors.

Recent studies (December 2018 through December 2021)

The previously discussed study on childhood leukemia by Auger et al. (2019a) also investigated the association between exposure to EMF during pregnancy and the occurrence of CNS tumors in the offspring. The authors reported a statistically non-significant association between a residential distance of 80 meters from a transformer station and CNS tumors. When the analysis was stratified by gender, the authors reported an association for males only. No associations were observed with distance to transmission lines. The authors concluded that "[r]esidential proximity to transformer stations is associated with a borderline risk of childhood cancer, but the absence of an association with transmission lines suggests no causal link" (Auger et al., 2019a).

The meta-analysis of Seomun et al. (2021) described above also included studies of childhood brain cancer. No statistically significant associations were reported; the OR was 0.95 (95% CI 0.59-1.56) for magnetic-field exposure >0.2 μT, and 1.25 (95% CI 0.45-3.45) for magnetic-field exposure >0.4 μT.

Assessment

Overall, the weight-of-evidence does not support an association between magnetic-field exposures and the development of childhood brain cancer. The results of the two recent studies do not alter the classification of the epidemiologic data in this field as inadequate, as they did not report any consistent and convincing evidence for an association. This is in line with the 2015 SCENIHR review, which concluded that "no association has been observed for the risk of childhood brain tumours" (SCENIHR, 2015, p. 158).

Table 3. Relevant studies of childhood brain cancer (December 2018 - December 2021)

Authors	Year	Study
Auger et al.	2019a	Residential exposure to electromagnetic fields during pregnancy and risk of child cancer: a longitudinal cohort study.
Seomun et al.	2021	Exposure to extremely low-frequency magnetic fields and childhood cancer: a systematic review and meta-analysis.

Adult health outcomes

Breast cancer

The WHO reviewed studies of breast cancer and residential magnetic-field exposure, electric blanket usage, and occupational magnetic-field exposure. These studies did not report consistent associations between magnetic-field exposure and breast cancer. The WHO concluded that the recent body of research on this topic was less susceptible to bias compared with previous studies, and as a result, it provided strong support to previous consensus statements that magnetic-field exposure does not influence the risk of breast cancer. Specifically, the WHO stated:

> Subsequent to the IARC monograph a number of reports have been published concerning the risk of female breast cancer in adults associated with ELF magnetic field exposure. These studies are larger than the previous ones and less susceptible to bias, and overall are negative. With these studies, the evidence for an association between ELF exposure and the risk of breast cancer is weakened considerably and does not support an association of this kind (WHO 2007, p. 307).

The WHO recommended no specific research with respect to breast cancer and magnetic-field exposure. Research in this area provided additional support for the WHO's conclusion that there is no association between exposure to ELF EMF and breast cancer development. A large case-control study that investigated the risk of several types of adult cancers and residential distance to high-voltage power lines reported no association between female breast cancer and residential distance to power lines or estimated exposure to magnetic fields (Elliott et al., 2013). Several occupational epidemiologic studies of female and male breast cancers also provided no support for an association between ELF EMF exposure and breast cancer development (Sorahan, 2012; Li et al., 2013; Koeman et al., 2014; Grundy et al., 2016).

Recent studies (December 2018 through December 2021)

No published epidemiologic studies examining the potential relationship between ELF EMF and breast cancer development were identified within the time period of this report.

Assessment

As no new published studies were identified during the time period of this report, the conclusion that there is no association between ELF EMF and breast cancer, as expressed by the WHO and other reviewing agencies, continues to be valid. The review by SCENIHR (2015) concluded that overall studies on "adult cancers show no consistent associations" (p. 158). The SSM concluded in two recent annual reports that, with respect to female breast cancer, "now it is fairly certain that there is no causal relation with exposure to ELF magnetic fields" (SSM, 2016, p. 7), and with respect to male breast cancer, "[t]o date, there is no established link between ELF-MF [magnetic field] exposure and breast cancer in men" (SSM, 2018, p. 49).

Adult brain cancer

Brain cancer was studied along with leukemia in many of the occupational studies of ELF EMF. The findings were inconsistent, and there was no pattern of stronger findings in studies with more advanced methods, although a small association could not be ruled out. The WHO classified the epidemiologic data on adult brain cancer as inadequate and recommended 1) updating the existing cohorts of occupationally-exposed individuals in Europe, and 2) pooling the epidemiologic data on brain cancer and adult leukemia to confirm the absence of an association.

The WHO stated the following:

> In the case of adult brain cancer and leukaemia, the new studies published after the IARC monograph do not change the conclusion that the overall evidence for an association between ELF [EMF] and the risk of these disease remains inadequate (WHO 2007, p. 307).

Overall, the epidemiologic studies of ELF EMF and adult brain cancer that were reviewed in our previous reports predominantly support no association with brain cancer in adults but remain limited due to the exposure assessment methods and insufficient data available on specific brain cancer subtypes. Two Swedish case-control studies discussed in Exponent (2019) investigated the relationship between occupational exposure to ELF EMF and glioma (Carlberg et al., 2017) and meningioma (Carlberg et al., 2018). In Carlberg et al. (2017), the authors reported no overall association between glioma and cumulative exposure to ELF EMF and a marginally significant association with the highest average exposure category. Sub-analyses examining the association by tumor grade and exposure period did not show consistent associations. In Carlberg et al. (2018), no trend or association was reported between meningioma development and exposure to ELF EMF using any of the exposure metrics or exposure periods.

Recent studies (December 2018 through December 2021)

Carlberg et al. (2020) evaluated a potential link between occupational exposure to magnetic fields and acoustic neuroma. Similar to previous papers (Carlberg et al., 2017, 2018), the authors in Carlberg et al. (2020) relied on data from previously published case-control studies in Sweden (Hardell et al., 2006, 2013). Carlberg et al. (2020) included 310 cases and 3,485 controls during the time periods of 1997 to 2003 and 2007 to 2009 and assessed average and cumulative magnetic-field exposure using the participants' questionnaire responses and a previously developed JEM (Turner et al., 2014). The authors reported no statistically significant associations between acoustic neuroma and either average or cumulative magnetic-field exposure, regardless of the exposure period examined (1 to 14 years or 15+ years). The authors concluded that "occupational ELF-EMF was not associated with an increased risk for acoustic neuroma" (Carlberg et al., 2020, p. 1).

Carles et al. (2020) conducted a case-control epidemiologic study to investigate the association between residential proximity to power lines and brain tumor development from 1965 to 2006 among adults in France. The authors included 490 cases (gliomas and meningiomas combined) and 980 controls in their study. Exposure was assessed using the distance from the residence to the nearest power line and the voltage of the power lines as surrogate indicators of magnetic-field exposure. Several statistically significant associations were reported, although the associations were not consistent across brain tumor types or exposure metrics, and no clear exposure-response trend was observed. Statistically significant associations were reported between living <50 meters from power lines of any voltage for more than 15 years and all brain tumors, as well as meningiomas; between ever living <50 meters from a power line of any voltage and glioma; and between ever living <50 meters from a high-voltage power line (<200 kV) and both glioma and all brain tumors. No statistically significant associations were observed between any tumor type and living <50 meters from very high voltage power lines (≥200 kV) or living near power lines of any voltage for more than 5 years and more than 10 years. In addition, no statistically significant associations were observed for assessed magnetic-field exposure ≥0.3 μT [3 mG]). Souques et al. (2020) highlighted several methodological limitations in the Carles et al. (2020) study, including the potential for exposure misclassification due to inaccuracies of the geolocation method used to ascertain residential distance to power lines and the study's failure to account for underground lines, which would result in lower exposure levels, and concluded that due to these limitations, the results of the Carles et al. (2020) study were "meaningless and unusable" (Souques et al. 2020, p. 2).

Khan et al. (2021) reported results on newly diagnosed brain cancer cases in a cohort study of 256,372 individuals who lived in residential buildings with indoor transformer stations in Finland. Exposure to magnetic fields was assessed based on the location of the participants' apartment in relation to the location of the transformer station in the building; those participants who lived for at least 1 month in an apartment located directly above a transformer room or that shared a wall with a transformer room were considered exposed (n=9,636 exposed individuals). The authors reported no association between magnetic-field exposure and meningioma based on residential location and a non-statistically significant association with glioma. No association was reported between brain tumors and duration of residence near transformers. Limitations of the study include the low number of cases and the exposure assessment method, which did not account for personal behavior and time spent in the apartment that may influence personal exposure, or potential confounding exposures. Its prospective design, the minimized potential for selection bias (no contact was required with the study subject), and the previously validated exposure classification system (Okokon et al., 2014) are among the strengths of the study.

Assessment

Recent studies do not provide support for an association between exposure to magnetic fields and brain cancer development. As mentioned above, the most recent SCENIHR report states that, overall, studies on "adult cancers show no consistent associations" (SCENIHR, 2015, p. 158).

Table 4. Relevant studies of adult brain cancer (December 2018 - December 2021)

Authors	Year	Study
Carlberg et al.	2020	Case-control study on occupational exposure to extremely low-frequency electromagnetic fields and the association with acoustic neuroma.
Carles et al.	2020	Residential proximity to power lines and risk of brain tumor in the general population.
Khan et al.	2021	A cohort study on adult hematological malignancies and brain tumors in relation to magnetic fields from indoor transformer stations.
Souques et al.	2020	Letter to editor regarding "residential proximity to power lines and risk of brain tumor in the general population" by Carles C. and coll.

Adult leukemia and lymphoma

There is a vast literature on adult leukemia and ELF EMF, most of which is related to occupational exposure. Overall, the findings of these studies are inconsistent—some studies report a positive association between measures of ELF EMF and leukemia and other studies show no association. No pattern has been identified whereby studies of higher quality or design are more likely to produce positive or negative associations. The WHO subsequently classified the epidemiologic evidence for adult leukemia as inadequate. They recommended updating the existing European occupational cohorts and updating a meta-analysis on occupational magnetic-field exposure. Subsequently, Kheifets et al. (2008) provided an update to two meta-analyses they published in the 1990s. Their updated meta-analysis indicated that pooled risk estimates from more recent studies were lower than in past meta-analyses and that no consistent pattern was observed by leukemia subtypes. Thus, the combined results were not in support of a causal association between occupational EMF exposure and adult leukemia.

Studies reviewed in Exponent (2019) did not provide evidence to change the WHO conclusion (Talibov et al., 2015; Huss et al. 2018a). In the same study as their retrospective cohort analysis of the Swiss National Cohort, Huss et al. (2018a) conducted a meta-analysis of epidemiologic studies of occupational exposure to ELF magnetic fields and acute myeloid leukemia, in which the authors reported a weak overall association.

Recent studies (December 2018 through December 2021)

The Finnish cohort study by Khan et al. (2021), described above, also reported results on the potential association between magnetic-field exposures from indoor transformer stations in residential buildings and development of hematological neoplasms, including lymphoma and leukemia. Based on very small number of cases (n=4), a statistically significant association was reported for ALL; this association was observed to increase with duration of exposure. No associations were reported for other leukemia subtypes or for lymphoma or multiple myeloma, and the risk level for these diseases decreased with increasing duration of exposure. As discussed above, the study's limitations include the low number of cases and the lack of personal exposure data or information on potential confounding exposures.

Researchers from Australia (Odutola et al., 2021) conducted a systematic review and meta-analysis of various occupational exposures and follicular lymphoma, a common non-Hodgkin lymphoma subtype; only two studies were identified that specifically investigated occupational ELF magnetic-field exposure (Koeman et al., 2014; Huss et al., 2018a). No consistent pattern was observed in these studies.

Assessment

Recent studies did not provide substantial evidence for an association between EMF and leukemia overall, leukemia sub-types, or lymphoma in adults. Thus, the previous conclusion that the evidence is inadequate for adult leukemia remains appropriate. While some scientific uncertainty remains on a potential relationship between adult lymphohematopoietic malignancies and magnetic-field exposure because of continued deficiencies in study methods, the current database of studies provides inadequate evidence for an association (EFHRAN, 2012; SCENIHR, 2015).

Table 5. Relevant studies of adult leukemia (December 2018 - December 2021)

Authors	Year	Study
Khan et al.	2021	A cohort study on adult hematological malignancies and brain tumors in relation to magnetic fields from indoor transformer stations.
Odutola et al.	2021	A systematic review and meta-analysis of occupational exposures and risk of follicular lymphoma.

Reproductive and developmental effects

In 2002, two studies received considerable attention because of a reported association between peak magnetic-field exposure greater than approximately 16 mG and miscarriage: a prospective cohort study of women in early pregnancy (Li et al., 2002) and a nested case-control study of women who miscarried compared to their late-pregnancy counterparts (Lee et al., 2002). These two studies improved on the existing body of literature because average exposure was assessed using 24-hour personal magnetic-field measurements (earlier studies on miscarriage were limited because they used surrogate measures of exposure, including visual display terminal use, electric blanket use, or wire code data). The Li et al. (2002) study, however, was criticized by the National Radiological Protection Board *inter alia* because of the potential for selection bias, a low compliance rate, measurement of exposure after miscarriages, and apparent selection of exposure categories after inspection of the data (NRPB, 2002). The scientific panels that considered these two studies concluded that the possibility of this bias precludes making any conclusions about the effect of magnetic fields on miscarriage (NRPB, 2004; FPTRPC, 2005; WHO, 2007). The WHO concluded, "[t]here is some evidence for increased risk of miscarriage associated with measured maternal magnetic-field exposure, but this evidence is inadequate" and recommended further epidemiologic research (WHO, 2007, p. 254).

Following the publication of these two studies, a hypothesis was put forth that the observed association may be the result of behavioral differences between women with healthy pregnancies that went to term (i.e., less physically active) and women who miscarried (i.e., more physically active after miscarriage) (Savitz, 2002). It was proposed that physical activity is associated with an increased opportunity for peak magnetic-field exposure, and the nausea experienced in early, healthy pregnancies, and the cumbersomeness of late, healthy pregnancies, would reduce physical activity levels, thereby decreasing the opportunity for environmental exposure to peak magnetic fields while doing activities in one's community. This hypothesis received empirical support from studies that reported consistent associations between activity (mobility during the day) and various metrics of peak magnetic-field exposure measurements (Mezei et al., 2006; Savitz et al., 2006; Lewis et al., 2015). These findings suggest that the association between maximum magnetic-field exposure and miscarriage was due to differing activity patterns of the cases and controls, not to a magnetic-field effect on embryonic development and viability.

Studies on ELF EMF exposure and reproductive or developmental effects published subsequent to the WHO 2007 report included ones focusing on miscarriage or stillbirth (Auger et al., 2012; Shamsi Mahmoudabadi et al., 2013; Wang et al., 2013; Li et al., 2017) and birth outcomes (Mahram and Ghazavi, 2013; de Vocht and Lee, 2014; de Vocht et al., 2014; Eskelinen et al., 2016; Sadeghi et al., 2017; Sudan et al., 2017; Migault et al., 2018). These additional publications provided little new insight on pregnancy and reproductive outcomes and did not change the classification of the data from earlier assessments as inadequate. Recommendations for future studies included, among others, the selection of appropriate study populations, the assessment and control for potential confounding by the mothers' physical activity, the careful characterization of exposure, and the analysis of various exposure metrics in the study (Lewis et al., 2016).

Recent studies (December 2018 through December 2021)

Exponent (2019) included a summary of Li et al. (2017), in which the authors examined the association between magnetic-field exposure and miscarriage in a cohort of 913 pregnant women in California. Exposure was assessed using 24-hour personal magnetic-field measurements collected on a single day during pregnancy, and the 99th percentile value observed during the 24-hour measurement period was used as the exposure of interest by the authors. The authors reported an increased risk of miscarriage in women with higher magnetic-field exposure (i.e., the 99th percentile value during the 24-hour measurement of ≥2.5 mG) compared to women with lower magnetic-field exposure (<2.5 mG) when measurements were collected on a typical day (defined as a day reflecting the participants' typical pattern of work and leisure activities during pregnancy). They reported no association, however, among those women whose magnetic-field exposure was measured on a non-typical day, and no trend was observed for miscarriage risk with increasing magnetic-field exposures >2.5 mG. The authors did not report the overall TWA for the 24-hours of exposure that could be compared to previous studies. As discussed in Exponent (2019), there are several notable limitations of this study, including the collection of only one measurement over a single 24-hour period during pregnancy, a lack of information on the exact timing of the measurement (i.e., whether the measurement day preceded or followed the occurrence of miscarriage among cases), and a lack of measured mobility during the measurement day, a potential major source of confounding in the study (e.g., Savitz, 2002; Mezei et al., 2006; Savitz et al., 2006). Recently, Grimes and Heathers (2021) published an evaluation of the Li et al. (2017) paper and concluded that "this work exemplifies a number of deeply unsound methodological choices that nullify its strong conclusion." The limitations discussed by Grimes and Heathers (2021) include the exclusion of over half of the study population resulting in a disproportional selection of subjects by exposure status, and the inappropriate dichotomization of the data.

Canadian researchers analyzed a population-based sample of 2,164,246 infants born in Quebec, Canada, between 1989 and 2016, to assess the relationship between residential proximity to ELF EMF and risk of birth defects (Auger et al., 2019b). The authors calculated distance to the nearest high-voltage transmission line or transformer station using geocoded postal codes of the mother's residence at birth and used hospital records to identify defects present at the time of birth. No strong or consistent associations were reported. Weak, positive associations were observed between a residential address within 50 meters from transmission lines and genital, clubfoot, or sense organ defects; however, reduced risks were observed for noncritical heart defects and congenital hip dislocation. The study's limitations include the lack of information on exposure to other agents and on risk factors that are known to potentially cause birth defects (e.g., mothers' smoking habits).

Researchers in Iran conducted a cross-sectional study to evaluate the relationship between residential proximity to high-voltage power lines and female infertility (Esmailzadeh et al., 2019). The authors included 462 cases and 471 controls with no history of infertility in their study. Exposure was assessed by measuring the distance to the nearest high-voltage power lines using geographic information systems and aerial evaluations. The authors reported an association between infertility and living within 500 meters of the power lines compared to living more than 1,000 meters away. One of the main limitations of the study was the cross-sectional design, which does not allow to determine whether exposure to the magnetic fields occurred before or after the outcome of interest (i.e., infertility). Another severe limitation of the paper was the use of residential address within 500 meters of power lines as a surrogate for EMF exposure; beyond approximately 100 meters, no elevation of ELF EMF levels can be expected. Therefore, no valid conclusions can be drawn from the study with respect to exposure to EMF and infertility.

Researchers in China evaluated the association between magnetic-field exposure and fetal growth in a cohort study of 128 pregnant women using 24-hour personal magnetic-field measurements taken during the third trimester of pregnancy (Ren et al., 2019). The authors reported associations between prenatal magnetic-field exposure and fetal growth indicators (lower birth weight, thinner skinfold, and smaller head, arm, and abdominal circumference) for newborn girls, but not for newborn boys. While the use of personal exposure measurements is an improvement in exposure assessment methods compared to many earlier studies, the collection of only one measurement over a single 24-hour period during pregnancy may result in exposure misclassification, as day-to-day changes in exposure cannot be captured in one 24-hour measurement period.

A cohort study conducted among female patients of a Massachusetts fertility clinic examined the relationship between personal magnetic-field exposure levels and pregnancy outcomes (Ingle et al., 2020). The study included 119 women (age 18 to 46 years), recruited from 2012 to 2018 while undergoing fertility treatment. Exposure assessment was based on personal exposure measurements taken in three 24-hour time periods separated by several weeks; the study participants also completed a time-activity diary documenting their daily activities. The authors reported no statistically significant associations between magnetic-field exposure levels and the included main outcomes measures (e.g., implantation, clinical pregnancy, live birth, and pregnancy loss). The study's strengths include the prospective design, the use of personal exposure monitors, and the collection of repeated measurements; its limitations include the relatively small sample size.

Data from previously conducted cohort studies in California were analyzed to assess whether maternal exposure to magnetic fields is associated with the development of attention-deficit/hyperactivity disorder (ADHD) in their offspring (Li et al., 2020). The study included 1,482 mother-child pairs from 1996 to 1998 and 2006 to 2012. Exposure assessment was based on 24-hour personal magnetic-field measurements collected on a single day during the first or second trimester of pregnancy and the authors used the 90th percentile value observed during the 24-hour measurement period as the exposure metric of interest. Cohort members with ADHD diagnoses were identified through medical records. The authors reported a statistically significant association between exposure to magnetic fields ≥ 1.3 mG and ADHD diagnosis in their offspring; a stronger association was observed for children with a diagnosis persisting into adolescence. As noted above, measurements taken over a single 24-hour period during pregnancy represents a limitation of the study. Further, the specific exposure metric (90^{th} percentile) and cut-point (1.3 mG) used in the study are unconventional and have not typically been used in previous epidemiologic studies of potential health effects of EMF. The authors' use of an unusual cut-point was recently called into question by others in the research community; as a result, in February 2021, the primary author of Li et al. (2020) issued a notice of retraction and replacement for the study, based on "errors in the statistical analyses" (Li, 2021). The author reported that the journal editors requested that the researchers re-analyze the study data using continuous and categorical exposure levels, rather than the 1.3 mG cut-point, which was poorly defined and explained by the authors. In the notice of retraction, Li (2021) stated that based on the updated analyses, "the associations were inconsistent and nonlinear, [therefore] limiting interpretations" and that the findings "should be interpreted with caution."

Researchers in Iran conducted a cross-sectional study to evaluate the relationship between exposure to magnetic fields and levels of reproductive hormones in 122 male power plant workers aged 20 to 50 years (Suri et al., 2020). Each worker completed a general health questionnaire and provided a blood sample used to determine serum levels of free testosterone, luteinizing hormone, and follicle stimulating hormone. TWA exposure of each employee was calculated based on measurements taken at the workstations and rest areas of the employees and categorized into tertiles. The authors reported no statistically significant differences in the serum levels of any of the three hormones examined when compared across the three exposure groups. The study's cross-sectional design precludes any causal interpretation.

Another Iranian cross-sectional study examined the relationship between maternal exposure to electromagnetic fields, including power lines and various radiofrequency field sources (e.g., mobile phones, Wi-Fi, cordless phones), and speech problems in offspring (Zarei et al., 2019). The study included 110 mothers of children 3 to 7 years of age with speech problems who had been referred to a speech treatment center and 75 mothers of children defined as "healthy" by the authors (no additional details provided). Questionnaire based information was used for exposure assessment to determine "whether they [study subjects] had been exposed to different sources of electromagnetic fields" (Zarei et al., 2019, p. 62); no additional details were provided on exposure assessment. Statistically significant associations were reported between offspring with speech problems and maternal "history of exposure to high tension power lines" before and during pregnancy (Zarei et al., 2019, p. 63). The study's limitations include the small overall sample size and the small number of exposed subjects; the lack of information on control selection; the use of self-reported and poorly described questionnaire-based information for exposure assessment; and the potential for selection bias, as mothers were enrolled in the study using "convenience sampling."

Chinese researchers conducted a case-control study to evaluate the relationship between exposure to electrical appliances and electronic equipment in early pregnancy and congenital heart disease (CHD) in the offspring (Zhao et al., 2021). The study included 585 cases and 1,754 controls born without birth defects. Occupational and residential exposure to selected electrical appliances and electronic equipment (mobile phone, television, computer, induction cooker, microwave oven) 3 months before pregnancy and during the first trimester of pregnancy was determined based on personal interviews with the mothers during their hospital stay for childbirth. The authors reported statistically significant associations between offspring with CHD and maternal exposure to computers, induction cookers, and microwave ovens before and during pregnancy; a decrease in offspring with CHD was observed for mothers who reported wearing a radiation protection suit during the time periods under study, which might block radiofrequency fields not ELF magnetic fields. The study's limitations include a high potential for recall bias because mothers who have given birth to infants with CHD may be more likely to recall the events leading up the diagnosis compared to mothers who gave birth to healthy children and thus have less reason to recall such memories. In addition, statistically significant differences between the cases and controls were reported for several potentially confounding variables (e.g., drinking, passive smoking, and folic acid supplement). Most important, the appliances that were assessed in this study are known sources of radiofrequency fields and exposures to ELF-EMF would be relatively minor.

Migault et al. (2020) conducted a pooled analysis of two previously published French cohort studies (Vandentorren et al., 2009; Ancel et al., 2014) to examine the relationship between maternal exposure to magnetic fields during pregnancy and the risk of adverse birth outcomes. A JEM was used to assess occupational maternal exposure to magnetic fields during three separate periods of gestational age. The authors reported no association between cumulative magnetic-field exposure and prematurity among the two highest exposure categories; conversely, an increased risk of prematurity was observed for the lower exposure category. No consistent associations were observed between cumulative magnetic-field exposure and being small for gestational age. The authors concluded that "due to the heterogeneity of the results regarding exposure levels, the associations observed cannot be definitely explained by ELF-EMF exposure" (Migault et al., 2020, p. 27). The study's limitations include the heterogeneity in study populations between the two included studies, low portion of mothers with high magnetic-field exposure (3% to 4%), and missing information on other occupational exposures that could explain the observed associations (e.g., chemical agents).

Assessment

The recent epidemiologic studies evaluated do not provide substantial new evidence in support of an association between EMF and reproductive or developmental outcomes and thus the classification of the data as inadequate remains appropriate. Studies in this research area still suffer from limitations in study design, sample size, and exposure assessment method. The most recent review by SCENIHR concluded that "recent results do not show an effect of ELF MF [magnetic field] exposure on reproductive function in humans." (SCENIHR, 2015). Regarding research on reproductive or developmental outcomes, ICNIRP concluded in their 2020 review of potential research gaps that "[s]ubsequent [epidemiologic] studies [after 2010] do not support the hypothesis that ELF-MFs [magnetic fields] are related to adverse pregnancy outcomes, and the older laboratory studies did not find an association between ELF-MFs and reproduction and/or development … Overall, the evidence gathered so far does not indicate any data gaps that require research for guideline development" (ICNIRP, 2020, p. 534).

Table 6. Relevant studies of reproductive and developmental effects (December 2018 - December 2021)

Authors	Year	Study
Auger et al.	2019b	Maternal proximity to extremely low frequency electromagnetic fields and risk of birth defects.
Esmailzadeh et al.	2019	Exposure to electromagnetic fields of high voltage overhead power lines and female infertility.
Grimes and Heathers	2021	Association between magnetic field exposure and miscarriage risk is not supported by the data.
Ingle et al.	2020	Association of personal exposure to power-frequency magnetic fields with pregnancy outcomes among women seeking fertility treatment in a longitudinal cohort study.
Li et al.	2017	Exposure to magnetic field non-ionizing radiation and the risk of miscarriage: a prospective cohort study.
Li et al.	2020	Association between maternal exposure to magnetic field nonionizing radiation during pregnancy and risk of attention-deficit/hyperactivity disorder in offspring in a longitudinal birth cohort.
Li et al.	2021	Notice of retraction and replacement. Li et al. Association between maternal exposure to magnetic field nonionizing radiation during pregnancy and risk of attention-deficit/hyperactivity disorder in offspring in a longitudinal birth cohort. JAMA Netw Open. 2020;3(3):e201417.
Migault et al.	2020	Maternal cumulative exposure to extremely low frequency electromagnetic fields, prematurity and small for gestational age: a pooled analysis of two birth cohorts.
Ren et al.	2019	Prenatal exposure to extremely low frequency magnetic field and its impact on fetal growth.
Suri et al.	2020	Relationship between exposure to extremely low-frequency (ELF) magnetic field and the level of some reproductive hormones among power plant workers.
Zarei et al.	2019	Mother's exposure to electromagnetic fields before and during pregnancy is associated with risk of speech problems in offspring.
Zhao et al.	2021	Risk of congenital heart disease due to exposure to common

Authors	Year	Study
		electrical appliances during early pregnancy: a case-control study.

Neurodegenerative diseases

Research into the possible effect of magnetic fields on the development of neurodegenerative diseases began in 1995; the majority of research since then has focused on Alzheimer's disease and a specific type of motor neuron disease called ALS, which is also known as Lou Gehrig's disease. Early studies on ALS, which had no obvious biases and were well conducted, reported an association between ALS mortality and estimated occupational magnetic-field exposure. The scientific review panels, however, were hesitant to conclude that the associations provided strong support for a causal relationship. Rather, they felt that an alternative explanation (i.e., electric shocks received at work) may be the source of the observed association.

The majority of the studies reviewed by the WHO reported statistically significant associations between occupational magnetic-field exposure and mortality from Alzheimer's disease and ALS, although the design and methods of these studies were relatively weak (e.g., disease status was based on death certificate data, exposure was based on incomplete occupational information from census data, and there was no control for confounding factors). Furthermore, there were no biological data to support an association between magnetic fields and neurodegenerative diseases. The WHO panel concluded that there are inadequate data in support of an association between magnetic fields and Alzheimer's disease or ALS. The panel recommended more research in this area using improved methods; in particular they recommended studies that enrolled incident Alzheimer's disease cases (rather than ascertaining cases from death certificates), as well as studies that estimated electrical shock history in ALS cases.

Following the research recommendations of the WHO, scientists conducted epidemiologic research that studied exposure to ELF EMF and development of neurodegenerative diseases. Overall, these studies, including those reviewed in Exponent (2019) (e.g., Yu et al., 2014; Fischer et al., 2015; Koeman et al., 2015, 2017; Vergara et al., 2015; Pedersen et al., 2017; Vinceti et al., 2017; Checkoway et al., 2018), did not provide consistent and convincing support for an association. Several meta-analyses of these studies reported weak to no evidence of an association between occupational exposure to ELF magnetic fields and neurodegenerative disease (Zhou et al., 2012; Vergara et al., 2013; Capozella et al., 2014; Huss et al., 2018b;

Jalilian et al., 2018; Röösli and Jalilian, 2018). The authors of several of these meta-analyses concluded that potential within-study biases, evidence of publication bias, and uncertainties in the various exposure assessments greatly limit the ability to infer an association, if any, between occupational exposure to magnetic fields and neurodegenerative disease.

Several studies have examined the potential role of electric shocks in occupational environments as a possible explanation for the weak and inconsistent association between ELF EMF and ALS. The studies that addressed the issue of electric shocks in the development of neurodegenerative and neurological diseases presented no convincing evidence for an association (Das et al., 2012; Grell et al., 2012; van der Mark et al., 2014; Brouwer et al., 2015; Ingre et al., 2015; Bozzoni et al., 2016).

Recent studies (December 2018 through December 2021)

Gervasi et al. (2019) conducted a case-control epidemiologic study to evaluate the relationship between residential proximity to overhead power lines and risk of Alzheimer's disease and Parkinson's disease in Italy. The study included 9,835 cases of Alzheimer's dementia and 6,810 cases of Parkinson's disease, and four controls matched to each case on sex, year of birth, and municipality of residence. Exposure assessment was based on residential distance from the nearest overhead power line (>30 kV). The authors reported a weak, statistically not significant association between residences within 50 meters of overhead power lines and both Alzheimer's disease and Parkinson's disease. The study's strengths include the large study population and the inclusion of potential confounders. The characterization of exposure using residential distance to power lines, however, is a primary limitation of the study.

Peters et al. (2019) assessed the potential relationship between occupational exposure to both ELF magnetic fields and electric shock with ALS in a multi-country European case-control study that included 2,704 cases and 1,323 controls. Occupational exposure was assessed using a JEM. Statistically significant associations were observed between ALS and ever having been exposed above background levels to either magnetic fields or electric shocks. No clear exposure-response trend was observed, however, with exposure duration or cumulative exposure.

Filippinni et al. (2020) conducted a case-control study in Italy, including 95 cases and 1,235 controls, to evaluate the association between ALS and various environmental and occupational factors, including electromagnetic fields. Questionnaire-based information was used to assess occupational and residential exposures to electric and magnetic fields. The authors reported a statistically significant association between ALS and proximity to overhead power lines. The association between ALS and occupational exposure to EMF was not statistically significant; occupational use of electric and electronic equipment was associated with a statistically non-significant decreased risk of ALS development. The study's limitations include the possibility of selection bias due to the low overall response rate (<20%) and the potential for exposure misclassification as a result of reliance on a self-reported information to assess exposures.

Researchers in New Zealand conducted a case-control study, including 319 cases and 604 controls, to assess the association between occupational exposure to electric shocks, magnetic fields, and motor neuron disease [MND], including ALS (Chen et al., 2021). Exposure was assessed based on the participants' occupational history obtained using questionnaires and previously developed JEMs for electric shocks and magnetic fields. The authors reported no association between MND and exposure to magnetic fields when examining any of the exposure metrics (e.g., ever/never exposed, duration of exposure, cumulative exposure level). Positive associations were reported between MND and a job with the potential for electric shock exposure.

Gunnarsson and Bodin (2018) conducted a meta-analysis of occupational risk factors for development of ALS and reported statistically significant associations between occupational exposure to EMF and ALS and between jobs that involve working with electricity and ALS. The authors noted a "slight" publication bias and some study heterogeneity (Gunnarsson and Bodin, 2018, p. 10). Significant associations were also reported between ALS and heavy physical work, exposure to metals (including lead) and chemicals (including pesticides), and working as a nurse or physician. Gunnarsson and Bodin (2019) updated their previous meta-analysis (Gunnarsson and Bodin, 2018) to also include Parkinson's disease and Alzheimer's disease. A weak statistically significant, association was reported between exposure to EMF and Alzheimer's disease; no association was observed for Parkinson's disease. When the authors combined the studies of ALS and Alzheimer's disease, a stronger association with EMF was observed in those studies published prior to 2005 compared to studies published more recently. The authors opined that there is "an evident publication bias" in the studies published before 2005.

Huang et al. (2020) conducted a meta-analysis of 43 epidemiologic studies to investigate potential occupational risk factors for dementia or mild cognitive impairment. The authors included five cohort studies and seven case-control studies related to magnetic-field exposure. Positive associations were reported between dementia and work-related magnetic-field exposures in both types of studies. The authors, however, provided no information on the occupations held by the study participants, their magnetic-field exposure levels, or how magnetic-field levels were assessed. The authors also reported a high level of heterogeneity among studies. This analysis adds little to the weight of the evidence for an association between dementia and magnetic fields due to its limitations.

Filippini et al. (2021) conducted a meta-analysis to assess the dose-response relationship between residential exposure to magnetic fields and ALS. The authors identified six ALS epidemiologic studies that assessed exposure to residential magnetic fields by either distance from overhead power lines or magnetic-field modelling. They reported a decrease in risk of ALS in the highest exposure categories for both distance-based and modeling-based exposure estimates. The data were also used to conduct dose-response analyses for modelled magnetic field estimates; the authors reported that their dose-response analyses "showed little association between distance from power lines and ALS." The authors noted that their study was limited by small sample size, the potential for residual confounding, and by "some publication bias."

Jalilian et al. (2021) conducted a meta-analysis of occupational exposure to ELF magnetic fields and electric shocks and development of ALS including 27 studies from Europe, the United States, and New Zealand. A weak statistically significant association was reported between magnetic-field exposure and ALS; no association was observed between electric shocks and ALS. "Moderate to high" heterogeneity and indications of publication bias was identified for the study's magnetic-field exposure and ALS and the authors noted that "the results should be interpreted with caution" (Jalilian et al., 2021, p. 1).

Grebeneva et al. (2021) evaluated morbidity among electric power company workers in Kazakhstan. The authors included three groups of "exposed" workers who worked at electric substations (a total of 161 workers) and controls "who were not associated with exposure to electromagnetic fields (114 people)." Morbidity was assessed "based on analyzing the sick leaves of employees" from 2010 to 2014 and expressed as "incidence rate per 100 employees."

The authors reported higher "incidence rate" of "diseases of the nervous system" in two of the exposed categories compared to the non-exposed group. No meaningful conclusions from the study could be drawn, however, because no specific diagnoses within "diseases of the nervous system" were presented in the paper. The study also had a small sample size and short follow up period. In addition, no measured or calculated magnetic-field levels were presented by the authors.

Assessment

In recent years, multiple studies examined the potential relationship between EMF, electric shocks, and neurodegenerative diseases. Many of these studies represented methodological improvements (e.g., increased sample size, improved exposure assessment, inclusion of incidence cases) compared to previous studies. In spite of these methodological improvements, the overall evidence from these studies provided no consistent or convincing support for a causal association. The most recent SCENIHR report (2015) concluded that newly published studies "do not provide convincing evidence of an increased risk of neurodegenerative diseases, including dementia, related to ELF MF [magnetic field] exposure" (SCENIHR, 2015, p. 186). In their 2020 review of research data gaps, ICNIRP concluded, "[f]urther epidemiological and experimental studies on Alzheimer's disease and ALS would be useful" (ICNIRP, 2020, p. 535).

Table 7. Relevant studies of neurodegenerative disease (December 2018 - December 2021)

Authors	Year	Study
Chen et al.	2021	Associations of occupational exposures to electric shocks and extremely low-frequency magnetic fields with motor neurone disease.
Filippini et al.	2020	Environmental and occupational risk factors of amyotrophic lateral sclerosis: a population-based case-control study.
Filippini et al.	2021	Residential exposure to electromagnetic fields and risk of amyotrophic lateral sclerosis: a dose-response meta-analysis.
Gervasi et al.	2019	Residential distance from high-voltage overhead power lines and risk of Alzheimer's dementia and Parkinson's disease: a population-based case-control study in a metropolitan area of Northern Italy.
Grebeneva et al.	2021	Evaluating occupational morbidity among energy enterprise employees in industrial region of Kazahstan.
Gunnarsson and Bodin	2018	Amyotrophic lateral sclerosis and occupational exposures: a systematic literature review and meta-analysis.
Gunnarsson and	2019	Occupational exposures and neurodegenerative diseases – a

Authors	Year	Study
Bodin		systematic literature review and meta-analysis.
Huang et al.	2020	Association of occupational factors and dementia or cognitive impairment: a systematic review and meta-analysis.
Jalilian et al.	2021	Amyotrophic lateral sclerosis, occupational exposure to extremely low frequency magnetic fields and electric shocks: a systematic review and meta-analysis.
Peters et al.	2019	Associations of electric shock and extremely low-frequency magnetic field exposure with the risk of amyotrophic lateral sclerosis.

Cardiovascular disease

A hypothesis asserts that magnetic-field exposure reduces heart rate variability, which in turn increases the risk for AMI. In a large cohort of utility workers, Savitz et al. (1999) reported an association with arrhythmia-related deaths and deaths due to AMI among workers with higher magnetic-field exposure. Previous and subsequent studies did not report a statistically significant increase in cardiovascular disease mortality or incidence related to occupational magnetic-field exposure (WHO, 2007).

The WHO concluded:

> Experimental studies of both short- and long-term exposure indicate that, while electric shock is an obvious health hazard, other hazardous cardiovascular effects associated with ELF fields are unlikely to occur at exposure levels commonly encountered environmentally or occupationally. Although various cardiovascular changes have been reported in the literature, the majority of effects are small and the results have not been consistent within and between studies. With one exception [Savitz et al., 1999], none of the studies of cardiovascular disease morbidity and mortality has shown an association with exposure. Whether a specific association exists between exposure and altered autonomic control of the heart remains speculative. Overall, the evidence does not support an association between ELF exposure and cardiovascular disease." (WHO, 2007, p. 220)

As discussed in Exponent (2019), Elmas (2016) summarized some of the literature examining the effects of EMF exposure on the heart. The review included studies that assessed the relationship between long-term occupational exposure and heart rate, as well as several studies examining short-term exposure and various health impacts. The author concluded that "despite these studies, the effects of EMFs on the heart remain unclear" and that there is "not yet any consensus in these works about possible mechanisms by which effects of EMF exposure may occur" (Elmas, 2016, p. 80).

Recent studies (December 2018 through December 2021)

The study by Grebeneva et al. (2021), described above, also evaluated the occurrence of "diseases of the circulatory system" among other diseases and reported higher "incidence rate" of these conditions in two of the exposed categories compared to the non-exposed group. No meaningful conclusions from the study can be drawn due to the same limitations discussed above.

Assessment

The conclusion that there is no association between magnetic fields and cardiovascular diseases has not changed. Regarding research on cardiovascular outcomes, ICNIRP concluded in their 2020 review of potential research gaps that "the research available at the time the ICNIRP 2010 Guidelines were drafted provided convincing null findings, which suggest there are no data gaps in this area that require research" (ICNIRP, 2020, p. 534).

Table 8. Relevant studies of cardiovascular disease (December 2018 - December 2021)

Authors	Year	Study
Grebeneva et al.	2021	Evaluating occupational morbidity among energy enterprise employees in industrial region of Kazahstan.

In vivo studies related to carcinogenesis

In the field of ELF EMF research, a number of research laboratories have conducted studies that exposed rodents, including those with a particular genetic susceptibility to cancer, to high levels of magnetic fields over the course of the animals' lifetime and performed tissue evaluations to assess the incidence of tumors in many organs. These studies are known as chronic bioassays.

In addition to these studies, magnetic-field exposure was administered alone (to test for the ability of magnetic fields to act as a complete carcinogen). Other studies exposed animals to a known carcinogen at the same time they were exposed to magnetic fields to assess their cancer-promoting capability.

Another type of study exposed animals to magnetic fields and examined biological processes of only indirect relevance to the development of cancer but are nonetheless of interest to scientists. These studies investigated biomarkers of damage to deoxyribonucleic acid (DNA) and factors affecting the oxidation of DNA and other molecules. Recently, the scope of these studies was expanded to investigate the potential therapeutic benefits of EMF exposure on the development of tumors implanted in animals.

The overall conclusion of the WHO regarding animal studies was that “[o]verall there is no evidence that ELF exposure alone causes tumours. The evidence that ELF field exposure can enhance tumour development in combination with carcinogens is inadequate” (WHO, 2007, p. 322).

The state of this research as reviewed by the WHO and more recent publications reviewed in the Exponent (2019) report are summarized.

Chronic bioassays

The WHO review (2007) described four large-scale, long-term studies of rodents exposed to magnetic fields over the course of their lifetime that did not report increases in any type of cancer (Mandeville et al., 1997; Yasui et al., 1997; Boorman et al., 1999a, 1999b; McCormick et al., 1999). No directly relevant animal model for childhood ALL existed at the time of the WHO review. Some animals, however, develop a type of lymphoma similar to childhood ALL and studies exposing these predisposed transgenic mice to ELF magnetic fields did not report an increased incidence of this lymphoma type (Harris et al., 1998; McCormick et al., 1998; Sommer and Lerchl, 2004). Following the release of the WHO review, Bernard et al. (2008) reported that magnetic-field exposure did not affect development of the most common form of childhood leukemia induced in a rat model by a chemical carcinogen.

As evaluated in Exponent (2019), subsequent chronic bioassays from the Ramazzini Institute were entirely consistent with prior studies (Soffritti et al., 2016a, 2016b), but a small study of shorter duration reported some differences between exposed and control groups among female mice, but not males (Qi et al., 2015). Serious limitations in the design, conduct, and reporting of these more recent studies, however, undercut the weight given to the results of these studies.

Carcinogenic agents plus magnetic fields (combined)

Studies investigated whether exposure to magnetic fields can promote cancer or act as a co-carcinogen in treated animals in combination with known cancer-causing agents, such as ionizing radiation, ultraviolet radiation, or other chemicals. While no effects were observed in these studies on chemically-induced, pre-neoplastic liver lesions, leukemia or lymphoma, skin tumors, or brain tumors (WHO, 2007, Tables 78-79), the WHO noted that incidence of 7,12-dimethylbenz[a]anthracene (DMBA)-induced mammary tumors was increased with magnetic-field exposure in a series of experiments in Germany (Löscher et al., 1993, 1994, 1997; Mevissen et al., 1993a, 1993b, 1996a, 1996b, 1998; Baum et al., 1995; Löscher and Mevissen, 1995), suggesting that magnetic-field exposure increased the proliferation of mammary tumors initiated by this chemical carcinogen. These results were not replicated in a subsequent series of experiments in a laboratory in the United States (Anderson et al., 1999; Boorman et al., 1999a, 1999b), possibly due to differences in experimental protocols and the species strain. In Fedrowitz et al. (2004) and Fedrowitz and Löscher (2008), exposure enhanced mammary tumor development in one sub-strain (Fischer 344 rats), but not in another sub-strain that was obtained from the same breeder, which argues against a promotional effect of magnetic fields.[9]

Exponent (2019) evaluated studies reported by the Ramazzini Institute that reported weak evidence for interactions between magnetic fields and exposure to ionizing radiation (Soffritti et al., 2015; 2016a) and formaldehyde (Soffritti et al., 2016b) but the methods and limitations of these studies are similar to other reports from the Ramazzini Institute that reported no effects of magnetic field alone and merit little weight.

Magnetic-field effects on cellular processes potentially relevant to cancer

Some studies reviewed by the WHO reported an increase in genotoxic effects among exposed animals (e.g., DNA strand breaks in the brains of mice [Lai and Singh, 2004]), although the results have not been replicated. More recent studies in which animals were exposed to higher

[9] The WHO concluded with respect to the German studies of mammary carcinogenesis, "[i]nconsistent results were obtained that may be due in whole or in part to differences in experimental protocols, such as the use of specific substrains" (WHO 2007, p. 321).

levels of magnetic fields for longer exposure periods reported no increase in damage to DNA (Saha et al., 2014; Korr et al., 2014). Indicators of biological processes that might lead to DNA damage are constantly investigated, but while short-term effects on indicators of oxidation in tissues show some effects at very high levels (100,000 mG), effects at lower (but still high) levels (1,000 mG) are inconsistent and longer exposures do not result in greater responses (Akdag et al., 2013; Glinka et al., 2013; Hassan and Abdelkawai, 2014; Manikonda et al., 2014).

Studies reviewed in Exponent (2019) had scattered results in this category. Alcaraz et al. (2014) reported an increase in micronuclei in erythrocytes of mice following exposure to a 2,000 mG, 50-Hz, magnetic field, which had not been reported by others at lower levels of magnetic fields and was unaffected by concomitant antioxidant treatment. Wilson et al (2015) reported that magnetic field up to 3,000 mG did not increase mutations in blood cells of mice or a dose-related increase in testes. A follow up study reported no increase the amount of DNA breaks produced by X-rays or affect the repair of DNA damage caused by X-rays (Woodbine et al., 2015).

Exponent (2019) also evaluated studies that reported effects of magnetic field on oxidative indicators in the blood of rats and mice at field levels of 80,000 to 200,000 mG (Li et al., 2015; Luo et al., 2016).

In summary, the WHO concluded the following with respect to *in vivo* research related to cancer: "[t]here is no evidence that ELF [EMF] exposure alone causes tumours. The evidence that ELF field exposure can enhance tumour development in combination with carcinogens is inadequate" (WHO, 2007, p. 322). Subsequent research, as reviewed in Exponent (2019) and below, has not provided any clear support for the idea that magnetic fields promote the development of tumors initiated by carcinogenic chemicals or that magnetic fields have any confirmed effect on oxidative processes that might damage DNA or other cellular components linked to cancer.

Recent *in vivo* studies of carcinogenesis (December 2018 through December 2021)

Cancer bioassays

As noted above, past large-scale, long-term bioassays of magnetic-field exposures reported that lifetime exposure to magnetic fields do not initiate or promote tumor development in rodents. No new studies of this type have been published in the most recent evaluation period.

Carcinogenic treatments plus magnetic fields (combined)

The Ramazzini Institute republished some data from its previous research (Soffritti and Giuliani, 2019), which was reviewed in Exponent (2019).

Other investigators developed a new model for childhood leukemia by inserting the gene ETV6-RUNX1 into fertilized mouse embryos (Rodriquez-Hernandez et al., 2017). This gene is found in about 25% of children with ALL. They observed that about 11% of the mice born with this gene developed leukemia if raised under ordinary laboratory conditions in which bacterial and viral infections were common. In a subsequent pilot study by Campos-Sanchez et al. (2019), these genetically-modified mice were exposed to a 50-Hz magnetic fields at 15,000 mG. The authors were unable to assess an effect because of the small number of mice studied, the low frequency of disease development, and the lack of sham controls. No further research on this animal model has been published.

EMF effects on cellular processes potentially relevant to cancer

While the case could be made that almost any biochemical process might be related to cancer, historically, processes relating to damage to DNA and chromosomes have been given the most attention and weight (IARC, 1999).

Aslankoc et al. (2018) assessed epididymal sperm count, motility, and DNA damage in male Wistar rats (8 rats randomly assigned per group) exposed to a 50-Hz electric field at 10 kV/m or sham control exposure for 23 hours per day and 0.1 milliliters (ml) of physiological serum via oral gavage for 30 days. There were no significant differences between the control group and electric-field treated animals on overall body temperature, testicular temperature, testicular weight, testosterone, follicle-stimulating hormone, luteinizing hormone, and catalase. Relative to control animals, rats exposed to electric fields had increased body weight and body weight gain, higher comet scores for epididymal spermatozoa, increased malondialdehyde (MDA) levels, and more apoptotic cells in terminal deoxynucleotidyl transferase (TdT) dUTP Nick-End Labeling (TUNEL) analysis. In addition, rats exposed to electric fields had reduced epididymal sperm count and sperm motility, superoxide dismutase (SOD), and glutathione peroxidase.

The explanation for these results would seem to be the “vacuolisation, germ cell decrease in the seminiferous epithelium … oedema and vascular congestion in the interstitial tissue.” Based on these findings, the authors concluded that exposure to 50-Hz electric fields for 23 hours per day for 30 days resulted in DNA damage and oxidative stress that may have adversely affected male fertility. The histological results, however, support an alternative explanation. That is, the intermittent contact of the testes (with lower resistance than the feet) with the metal floor electrode led to current flow, and perhaps even spark discharges, which were the primary source of damage to the testes. In addition, the investigators did not consider that such a very strong electric field from high-voltage electrodes would be stressful to the rats because of the physical stimulation of the body fur and vibrissae and the generation of ozone (e.g., Goheen et al., 2004). The study also included two other groups: electric-field exposed plus the antioxidant resveratrol, and only resveratrol. In general, resveratrol treatment partially ameliorated the effects of electric fields. This study is limited by the use of a single electric-field dose, poor exposure assessment, absence of experimenter blinding, and no functional confirmation of infertility (i.e., breeding), which contrast to the otherwise thorough and well-done assessment of male reproductive tissues and physiology.

Magnetic- and electric-field treatments on tumor growth

In recent years, multiple studies have investigated the therapeutic potential of magnetic-field and electric-field exposures in the treatment of experimentally-induced tumors.

Yadamani et al. (2018) injected TUBO breast cancer cells in mice (8 per group) and 14 days later compared the morphology of cells from a single tissue section from the tumor of one control mouse with a single tissue section from the tumor of another mouse exposed to a 40,000 mG, 50-Hz magnetic field for 90 minutes per day for 14 days. The study stated that compared to control mice, treated mice showed decreases in the number of core cells, blood vessels, and cell structural appearance, which was accompanied by apoptosis. This study is limited by the use of a single magnetic-field level, the incomplete reporting of results, and an analysis of just one mouse each from the control and treatment group. In addition, the authors did not specify whether animals were randomly assigned to exposure or control groups or were handled similar to the exposed group (sham controls), and they provided little detail on experimental methods, including the coding of the samples to prevent bias in the analysis of the samples and data. No weight can be given to this study given the multiple limitations of the methods and analyses.

Rageh et al. (2020) tested whether magnetic fields would enhance the anti-tumor action of cisplatin, a drug used to treat solid tumors of the breast, lung, and neck. Ehrlich carcinoma tumor cells were subcutaneously injected into the right flank of female BALB/c mice and 14 days later randomly assigned to groups of 10 mice in: 1) a control group; 2) groups of mice treated with doses of cisplatin (3 or 6 milligrams per kilogram [mg/kg] intraperitoneal); 3) a group exposed to 3 mg/kg cisplatin and a 50,000 mG, 500-Hz magnetic field for 30 minutes, and 4) a group treated just with the magnetic field. Mice were administered cisplatin on experimental days 1, 4, and 8, while magnetic-field exposure occurred daily for 2 weeks. The growth of tumors was assessed by tumor volume and tumor and kidney tissues were analyzed by histologic and biochemical tests.

Cisplatin at low and high doses, and the combination of low dose cisplatin and magnetic-field exposure, significantly decreased tumor volumes. Perhaps contrary to expectation, the high dose of cisplatin was significantly less effective than the low dose of cisplatin in reducing tumor volume; the addition of the magnetic field to the low dose had little effect. Four interrelated metrics used to evaluate DNA damage as measured in comet assays of tumors and kidneys were similar in both tissues. There were no differences between the DNA damage metrics of mice exposed to magnetic fields alone and the DNA damage metrics of control mice in tumor tissue. In kidney tissue, mice exposed to magnetic fields alone had a significantly higher percent of DNA in tail than control mice, with no other significant differences observed in other comet parameters for kidney tissue. The concurrent administration of cisplatin and magnetic fields, however, significantly increased the DNA damage to the tumors, but had little effect on the damage to the kidney compared to low dose cisplatin. The authors report that damage to the kidney (nephrotoxicity) is a common effect of cisplatin administration.

Contrary to the author's global summary of the study results "the magnetic field … reduce[s] the nephrotoxicity [of cisplatin]," the DNA damage as indicated by all metrics showed that the low dose cisplatin + magnetic-field treatment was marginally greater, not lower, than the damage from low dose cisplatin alone. The study also measured a positive correlation between indices of DNA damage and MDA and negative correlations with antioxidant enzyme SOD, glutathione (GSH) level, and tumor volume, but no analysis of magnetic-field data was included in the paper. This study is limited by the use of a single magnetic-field dose, inadequate description of methods, including magnetic-field exposure, the lack of sham-exposed controls, the lack of randomization of mice to groups or blind analysis of data, no specification of counts of Ehrlich carcinoma tumor cells transplanted into animals, incomplete presentation of data, and unclear summaries and analyses of most results. No weight can be given to the results of this study regarding magnetic fields.

Orel et al. (2021) exposed Walker-256 carcinosarcoma-bearing rats (n=10 per group) to 50-Hz EMF plus doxorubicin (DOX) (a drug used to treat hematologic and solid tumors) or DOX alone, to assess the therapeutic potential of these combined treatments. The rats were not randomly allocated to control and treatment groups. Rats were implanted with carcinosarcoma cells (2 x 10^6 microliters medium 199) in the right hind dorsum. Two days following implantation, animals were administered 1.5 mg/kg DOX intravenously. Rats in the EMF condition were anesthetized and exposed to a 2 kV/m, 50-Hz electric field and a magnetic field of 164 mG [2,040 Amperes/meter], for 80 minutes every 2 days for a total of five exposures, but the control animals to which they were compared were not handled similarly or anesthetized, which would have qualified as a sham control.

Although not discussed by the authors, EMF treatment alone produced a dramatic reduction in tumor growth (volume) over the 14 days of the study compared to untreated rats, and treatment with DOX and DOX + EMF produced further reductions in tumor growth. Tumor-bearing animals with no treatment, DOX, or EMF alone had significantly reduced body weight gain relative to DOX + EMF treated animals. Survival rates of tumor-bearing rats did not differ; however, all intervention groups showed improved survival relative to controls. The authors also examined the histological structure of the liver and blood components indicative of hepatic redox processes. All treatments reduced the activity of antioxidant enzymes SOD, CAT, and GSH activity of the liver and increased liver enzymes (alanine aminotransferase and aspartate aminotransferase) in the blood. Another indicator of liver damage, thiobarbituric acid reactive substances (TBARS), was increased in control rats with tumors and those treated with DOX; however, EMF alone or EMF+ DOX reduced this measure of toxicity by about 60%. Although the description of the methods and clarity of the analysis was better in this study than the Rageh et al. (2020) study, it shared limitations (single dose of EMF, no randomization, no blinded analysis, and no sham-exposed control group). The latter omission is serious because the repeated handling and anesthesia of the EMF-treated groups produced stress not experienced by rats in the control group and the DOX alone group, and the isoflurane anesthesia administered with EMF could have affected the metabolism and toxicity of DOX as well as measures of redox status. Thus, it is impossible to separate the effects attributed to EMF from those of the co-administered anesthetic.

Occupational biomarker studies

Bagheri Hosseinabadi et al. (2019) performed a cross-sectional study[10] of 102 thermal power plant workers and 136 office workers in Shahroud, Iran, that measured aspects of DNA damage in blood lymphocytes in these groups by the comet assay as well as indicators of programmed cell destruction (apoptosis) by flow cytometry. Measured electric fields and magnetic fields and self-estimated time spent at workstations were used to compute TWA exposures. The analyses ranked the power plant workers by exposure into three groups and 50 cells from each subject were classified for DNA characteristics for five inter-related indices from the alkaline comet assay. The EMF measurements and comet assays were performed by separate persons and the comet assays were analyzed in a blinded fashion.

Differences between power plant workers for four of five of these indices from the comet assay by level of magnetic-field exposure were reported, but not on the most commonly reported measure of damage—length of the comet tail. Data from flow cytometry also indicated significant differences between the plant worker groups on cellular apoptosis but not measured DNA damage. Comparisons of power plant and office workers on these comet assay measures showed small numerical differences between these groups with great variability. Statistical differences between these exposed groups were reported for three of the five indices. No explanation was given for the authors’ failure to report the results of flow cytometry analyses of the comparison group of office workers.

Zendehdel et al. (2019) performed a cross-sectional study of workers at an electric generating plant. They reported a statistically significant difference in DNA strand breaks measured by the comet assay in blood cells between 29 power plant workers and a support group of 28 members. Although the two groups of workers were similar with respect to age, length of work experience, and smoking status, the investigators made no effort to compare the workers with regard to exposure to the many chemical exposures within in a coal-fired power plant that have been

[10] In a cross-sectional study, the investigators determine the study subjects’ exposure and outcome status at the same time; thus, these types of studies are not suitable to draw any conclusion on a potential causal association.

associated with indicators of DNA damage (Celik et al., 2007) or social or economic factors. In addition, Zendehdel et al. (2019) reported no attempt to prevent bias in the collection and analysis of the samples by investigators by standard procedures for blinding. The authors did not report the time separating the measurement of the magnetic field and blood drawing.

Zendehdel et al. (2020) reported further cross-sectional analyses of data collected in their previous study (Zendehdel et al., 2019). In this latest study they compared measurements of the Fourier transform infrared (FITR) absorption spectra of DNA and hemoglobin extracted from the blood of workers in the powerhouse. The population consisted of controller workers with a mean exposure to magnetic fields of about 100 mG [10 µT] for 70% of their work time (n=29) and administrators in the powerhouse with somewhat lower mean magnetic-field exposure (60 mG [6 µT]) (n=29). Measurements of ELF magnetic fields were obtained from 78 stations in the power production site. Median exposure to magnetic fields of controllers was 8.5 mG [0.85 µT] (range of 40 to 500 mG [4 to 50 µT]) while median exposure to magnetic field of administrators was 5 mG [0.5 µT]. Participants in both groups were males employed at the powerhouse for 5 to 12 years, were between the ages of 30 and 46, and had similar smoking histories. No data on workplace use, exposure to solvents, or airborne emissions from the power generating plant were provided. The total hemoglobin concentration was reported only for controller subjects and was stated to be significantly lower than the levels of administrative subjects. Wave numbers associated with COO glutamic acid in the FITR spectra were reported to be marginally (14%) lower in controllers compared to administrators. Differences between the two groups in six molecular characteristics of DNA also were statistically significant, but neither the direction of the difference nor the data were shown.

Since this paper is among the first to apply the FITR spectroscopy to the study of these biomolecules from the environment, it should have confirmed that these changes were related to or indicative of functional changes and had overcome known problems of this method (Han, 2018). For example, the authors could have compared molecular changes in DNA measured in this study to the measures of DNA damage obtained from the comet assays of the same subjects in the earlier study. Or, they could have confirmed that exposure of DNA and hemoglobin *in vitro* to magnetic fields produced the same specific changes to the molecules as reported in human subjects. This study is limited by its retrospective cross-sectional design and other major failures in the design and analysis, including no substantiated relevance to biological endpoints of interest, and no clear support that the reported changes had any relationship to magnetic-field levels experienced by these groups (e.g., correlation between measurements on individual subjects with long-term measurements).

Another cross-sectional study examined 15 male workers who maintain 225-kV and 400-kV transmission lines, who also live near these lines and substations, and 25 male controls (Touitou et al., 2020). No details on the controls were provided. The exposed workers had 1 to 20 years of experience in this type of work. The workers' magnetic-field exposures were measured at 30 second intervals for 1 week; the average magnetic-field levels of the exposed workers was 9 mG and the exposure of controls averaged 0.9 mG. From 10 PM to 8 AM, 13 blood samples were drawn from each participant, and chromogranin A (CgA), a general, non-specific marker that is elevated by neuroendocrine tumors and by stimulation of the adrenal gland by stress, was measured in each sample. The CgA levels were observed to decrease steadily at the same rate from a nighttime peak in both the exposed and control groups. The results did not indicate that elevated exposure to magnetic fields had any significant effect on this indicator.

In weighing the findings of the studies that measured DNA damage and related parameters, it is important to note that the measurement of DNA characteristics of single cells in the comet assay is a specialized and highly technical process that requires considerable experience. None of the laboratories that performed the sample analyses appeared to have demonstrated expertise, nor the historical database necessary, to carry out these complex tests, and none of the data reported in these studies met the criteria required to confirm a clear positive response (OECD, 2015).

Oxidative indicator studies

Normal cellular processes produce reactive oxygen and other oxidant species, and while they are effectively managed by other cellular functions, when they are produced in great excess, they can be damaging to DNA and other cell components and may support some carcinogenic processes. Several studies investigated a variety of indicators of oxidative stress in blood samples. It is important, however, not to simply assume that substances that increase oxidative stress are harmful, and antioxidants, including some vitamins, are beneficial. For example, there are clinical trials and other studies that report antioxidants may damage DNA (Fox et al., 2012), may not protect against cancer in humans (Goodman et al., 2011), and may increase cancer risk and tumor progression (Sayin et al., 2014).

Bagheri Hosseinabadi et al. (2020) conducted a double-blind randomized control trial to assessing whether administration of vitamin E (400 units), vitamin C (1,000 milligrams [mg]), or a combination in cocoa milk, attenuated DNA fragmentation below that of a randomly selected control group. The subjects were recruited from a thermal power plant in Semnan, Iran, and. Participants (n=91; 21 to 24/group) were employed at the thermal power plant for at least 2 years (technicians, engineers, operators, and office workers). In this study, the average magnetic-field exposure was 16.5 μT (165 mG) and electric-field exposure was 22.5 V/m, but these exposures did not differ between the employees who were allocated to the control group or groups that were treated with vitamins. EMF measurements and sample collection were similar to those used in the previous study (Bagheri Hosseinabadi et al., 2019). The study did not report when the EMF measurements were taken or the times when blood sample collections were made before and after the treatment period. Employees working more than 10 years at the plant had significantly more tail DNA on the comet assay than workers employed for shorter durations, and there were no differences in pre-treatment levels of any DNA measure reported for the groups. After the treatment period, post-measurements of apoptosis did not differ from pre-treatment levels following any treatments. In contrast, several post-treatment comet assay indicators in the vitamin C, vitamin E, and vitamins C+E groups were significantly lower than in the post-treatment control group. Administration of 400 units of vitamin E predicted a greater decreased DNA damage on comet assay better than other intervention groups; however, there was a significant decrease in comet indices for all groups, except control. Because of the short duration of this study and absence of follow-up with participants, it cannot be determined if these findings have any relevance to a long-term benefit of these supplements or the cocoa milk to workers, or any relationship to EMF, chemical, or other conditions in this population, or to past or future risks of cancer. While Bagheri Hosseinabadi et al. (2020) provides information on vitamin supplements, it provided no insight on the role magnetic fields may have in cell DNA attributes. Data from the same study subjects were later analyzed for measures of antioxidant vitamins on oxidative stress and proinflammatory cytokines (Bagheri Hosseinabadi et al., 2021a), and also were not related to measurements of magnetic fields. The results also appear inconsistent with a lack of effect of antioxidants on mutation frequencies of mice exposed to magnetic fields (Alcaraz et al., 2014).

Bagheri Hosseinabadi et al. (2021b) analyzed the same samples (or workers) as evaluated for DNA damage in the earlier Bagheri Hosseinabadi et al. (2019) cross-sectional study of power plant workers. In this study, they report that MDA, SOD, and catalase indicators of oxidative stress increased with the mean level of magnetic-field exposure of three groups within the plant. The results were quite similar for the three groups segregated by level of electric-field exposure. In contrast, the overall total antioxidant capacity measure did not differ between the three groups of workers. The study did not provide sufficient data and analyses to assess whether the differences in the indicators resulted from just the magnetic field, just the electric field, or both fields. The similarity in the results also could occur because work locations closer to equipment would tend to increase both electric-field and magnetic-field exposure, as well temperate and airborne exposures. The authors acknowledged the limitations of the cross-sectional design of the study and discussed similarities and differences in the outcomes of earlier studies.

Assessmen

No new long-term cancer bioassay studies, the gold standard for identifying carcinogens in animals, were reported in this period. No other studies that combined exposure to carcinogens + magnetic fields were reported. One study reported a spectrum of effects in the testes of male rats exposed to a 10 kV/m electric field, including DNA damage, for which conducted currents and discharges from contact with one of the exposure electrodes is a plausible explanation, not the induction of an electric field in tissue through the air (Aslankoc et al., 2018).

The idea that magnetic fields might enhance the effect of drugs used to treat cancer was explored in three studies in which animals were injected with tumor cells and then given chemical chemotherapy alone, magnetic field alone, or both. Two studies reported that the magnetic field alone at levels of 40,000 mG (Yadamani et al., 2018) or 50,000 magnetic + 2 kV/m electric fields (Orel et al., 2021) reduced the growth of tumors. The third study reported that magnetic fields exposure enhanced the effect of an anti-tumor drug on tumor volume (Rageh et al., 2020).

Recent studies also investigated two potential mechanisms related to carcinogenesis: genotoxicity and oxidative stress. Three investigators performed cross-sectional studies of workers in a substation, arc welding, electrical power plant, and high-voltage transmission line workers to compare markers of damage to DNA damage or neuroendocrine tumors in blood samples from workers with varying EMF exposures. Two studies reported small differences in comet assay measures of DNA damage between groups of workers that were not fully consistent within the studies (Bagheri Hosseinabadi et al., 2019; Zendehdel et al., 2019, 2020). A much smaller study (Touitou et al., 2020), reported no differences between exposed and unexposed workers with a history of 1 to 20 years of work at a utility on a biomarker for stress and neuroendocrine tumors despite a 10-fold difference in their measured exposures to magnetic fields.

A cross-sectional study of workers in a thermal power plant reported lower levels, of DNA damage measured by the comet assay when taking vitamins than a control group but included no analyses of EMF exposure (Bagheri Hosseinabadi et al., 2020). A second cross-sectional study by this group reported measures of oxidative stress were elevated in thermal power plant workers categorized by higher magnetic- and electric-field exposures, but the analysis was insufficient to isolate EMF from other likely exposures (Bagheri Hosseinabadi et al., 2021b). A third study of power plant workers tested whether antioxidant vitamins had an effect on blood levels of proinflammatory cytokines. Reductions were reported but these results were not related to levels of magnetic-field exposure and so were not informative (Bagheri Hosseinabadi et al., 2021a).

Overall, the *in vivo* studies of EMF published since the last update do not alter the WHO's conclusion that the overall evidence from *in vivo* studies does not support the role of EMF exposure in genotoxic effects and continues to show that there is inadequate evidence of carcinogenicity due to EMF exposure. The quality of most studies, however, leaves much to be improved, so the recommendation that "further studies on mechanisms and biological data from childhood leukemia experimental models are recommended" is appropriate (ICNIRP, 2020, p. 535).

Table 9. Relevant *in vivo* studies related to carcinogenesis (December 2018 - December 2021)

Authors	Year	Study
Campos-Sanchez et al.	2017	Novel ETV6-RUNX1 mouse model to study the role of ELF-MF in childhood B-acute lymphoblastic leukemia: a pilot study.
Aslankoc et al.	2018	The impact of electric fields on testis physiopathology, sperm parameters and DNA integrity-The role of resveratrol.
Bagheri Hosseinabadi et al.	2019	DNA damage from long-term occupational exposure to extremely low frequency electromagnetic fields among power plant workers.
Zendehdel et al.	2019	DNA effects of low level occupational exposure to extremely low frequency electromagnetic fields (50/60 Hz).

Authors	Year	Study
Bagheri Hosseinabadi et al.	2020	The effect of vitamin E and C on comet assay indices and apoptosis in power plant workers: A double blind randomized controlled clinical trial
Orel et al.	2020	Effects induced by a 50 Hz electromagnetic field and doxorubicin on Walker-256 carcinosarcoma growth and hepatic redox state in rats.
Rageh et al	2020	Magnetic fields enhance the anti-tumor efficacy of low dose cisplatin and reduce the nephrotoxicity.
Touitou et al.	2020	Evaluation in humans of ELF-EMF exposure on chromogranin A, a marker of neuroendocrine tumors and stress.
Zendehdel et al.	2020	Quality assessment of DNA and hemoglobin by Fourier transform infrared spectroscopy in occupational exposure to extremely low-frequency magnetic field.
Bagheri Hosseinabadi et al.	2021a	The effects of antioxidant vitamins on proinflammatory cytokines and some biochemical parameters of power plant workers: A double-blind randomized controlled clinical trial.
Bagheri Hosseinabadi et al.	2021b	Oxidative stress associated with long term occupational exposure to extremely low frequency electric and magnetic fields.

5 Reviews Published by Scientific Organizations

A number of national and international scientific organizations have published reports or scientific statements with regard to the possible health effects of ELF EMF since January 2006. Although none of these documents represents a cumulative weight-of-evidence review of the caliber of the WHO review published in June 2007, their conclusions are of relevance. In general, the conclusions of these reviews are consistent with the scientific consensus articulated in Section 4.

The following list indicates the scientific organization and a link to the online reports or statements. Although not listed below, the recent *Report on Carcinogens* from the NTP did not list either ELF EMF as "Known To Be Human Carcinogens" or "Reasonably Anticipated To Be Human Carcinogens" (NTP, 2021).

- **The European Health Risk Assessment Network on Electromagnetic Fields Exposure**
  - http://efhran.polimi.it/docs/IMS-EFHRAN_09072010.pdf (EFHRAN, 2010 [*in vitro* and *in vivo* studies])
  - http://efhran.polimi.it/docs/D2_Finalversion_oct2012.pdf (EFHRAN, 2012 [human exposure])
- **The Health Council of Netherlands**
  - http://www.gezondheidsraad.nl/en/publications/bioinitiative-report-0 (HCN, 2008a)
  - http://www.gezondheidsraad.nl/en/publications/high-voltage-power-lines-0 (HCN, 2008b)
  - http://www.gezondheidsraad.nl/sites/default/files/200902.pdf (HCN, 2009a)
  - http://www.gezondheidsraad.nl/en/publications/advisory-letter-power-lines-and-alzheimer-s-disease (HCN, 2009b)

- **The Health Protection Agency (United Kingdom)**
    - http://www.hpa.org.uk/Publications/Radiation/DocumentsOfTheHPA/RCE01PowerFrequencyElectromagneticFieldsRCE1/ (HPA, 2006)
- **The International Commission on Non-Ionizing Radiation Protection**
    - http://www.icnirp.de/documents/LFgdl.pdf (ICNIRP, 2010)
    - https://www.icnirp.org/cms/upload/publications/ICNIRPlfgaps2020.pdf (ICNIRP, 2020)
- **The Scientific Committee on Emerging and Newly Identified Health Risks (European Union)**
    - http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_007.pdf (SCENIHR, 2007)
    - http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_022.pdf (SCENIHR, 2009)
    - http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_041.pdf (SCENIHR, 2015)

The Swedish Radiation Protection Authority (SSI)

- https://www.stralsakerhetsmyndigheten.se/contentassets/d5e931cff47b498099d7bcddae5ec6a7/200501--reports-from-ssis-international-independent-expert-group-on-electromagnetic-fields-2003-and-2004 (SSI, 2005)
- https://www.stralsakerhetsmyndigheten.se/contentassets/54f003dfe0ec4a24a9b212963841983f/200704-recent-research-on-emf-and-health-risks.-fourth-annual-report-from-ssis-independent-expert-group-on-electromagnetic-fields-2006 (SSI, 2006)
- https://www.stralsakerhetsmyndigheten.se/contentassets/119df5b843164b93be8f7143321af021/200812-recent-research-on-emf-and-health-risks.-fifth-annual-

report-from-ssis-independent-expert-group-on-electromagnetic-fields-2007 (SSI, 2007)

- https://www.stralsakerhetsmyndigheten.se/contentassets/119df5b843164b93be8f7143321af021/200812-recent-research-on-emf-and-health-risks.-fifth-annual-report-from-ssis-independent-expert-group-on-electromagnetic-fields-2007 (SSI, 2008)

- **The Swedish Radiation Safety Authority (SSM)**
  - https://www.stralsakerhetsmyndigheten.se/contentassets/921664c245584802811f517dbba81e7d/200936-recent-research-on-emf-and-health-risks.-sixth-annual-report-from-ssms-independent-expert-group-on-electromagnetic-fields-2009 (SSM, 2009)
  - https://www.stralsakerhetsmyndigheten.se/contentassets/63e6735284dc4634830c4dd6003d9b07/201044-recent-research-on-emf-and-health-risk-seventh-annual-report-from-ssms-independent-expert-group-on-electromagnetic-fields-2010 (SSM, 2010)
  - https://www.stralsakerhetsmyndigheten.se/contentassets/7f20edcd0b024940bca450d596568e30/201319-eighth-report-from-ssms-scientific-council-on-electromagnetic-fields (SSM, 2013)
  - https://www.stralsakerhetsmyndigheten.se/contentassets/08b2f497b3ad48cf9e29a1d0008e7d82/201416-recent-research-on-emf-and-health-risk-ninth-report-from-ssms-scientific-council-on-electromagnetic-fields-2014 (SSM, 2014)
  - https://www.stralsakerhetsmyndigheten.se/contentassets/ee7b28e0fee04e80bcaf84c24663a004/201519-recent-research-on-emf-and-health-risk---tenth-report-from-ssms-scientific-council-on-electromagnetic-fields-2015 (SSM, 2015)
  - https://www.stralsakerhetsmyndigheten.se/contentassets/98d67d9e3301450da4b8d2e0f6107313/201615-recent-research-on-emf-and-health-risk-eleventh-report-from-ssms-scientific-council-on-electromagnetic-fields-2016 (SSM, 2016)

- https://www.stralsakerhetsmyndigheten.se/contentassets/f34de8333acd4ac2b22a9b072d9b33f9/201809-recent-research-on-emf-and-health-risk (SSM, 2018)
- https://www.stralsakerhetsmyndigheten.se/contentassets/ea182ee131d049f1b3b1140dd0fbc0f8/201908-recent-research-on-emf-and-health-risk-thirteenth-report-from-ssms-scientific-council-on-electromagnetic-fields-2018.pdf (SSM, 2019)
- https://www.stralsakerhetsmyndigheten.se/contentassets/47542ee6308b4c76b1d25ae0adceca15/2020-04-recent-research-on-emf-and-health-risk---fourteenth-report-from-ssms-scientific-council-on-electromagnetic-fields-2019.pdf (SSM, 2020)
- https://www.stralsakerhetsmyndigheten.se/contentassets/fce87121bd5e47ca95ad16d93d03f638/202108-recent-research-on-emf-and-health-risk.pdf (SSM, 2021)

6 Standards and Guidelines

Following a thorough review of the research, scientific agencies develop exposure standards to protect against known health effects. The major purpose of a weight-of-evidence review is to identify the lowest exposure level below which no health hazards have been found (i.e., a threshold). Exposure limits are then set well below the threshold level to account for any individual variability or sensitivities that may exist.

Several scientific organizations have published guidelines for exposure to ELF EMF based on acute health effects that can occur at very high field levels. ICNIRP reviewed the epidemiologic and experimental evidence and concluded that there was insufficient evidence to warrant the development of standards or guidelines on the basis of hypothesized long-term adverse health effects such as cancer; rather, the guidelines put forth in their 2010 document set limits to protect against acute health effects (i.e., the stimulation of nerves and muscles) that occur at much higher field levels. ICNIRP recommends a residential screening value of 2,000 mG and an occupational exposure screening value of 10,000 mG (ICNIRP, 2010). If exposure exceeds these screening values, then additional dosimetry evaluations are needed to determine whether basic restrictions on induced current densities are exceeded. For reference, in a national survey conducted by Zaffanella and Kalton (1998) for the National Institute for Environmental Health and Safety's EMF Research and Public Information Dissemination program, only about 1.6% of the general public in the United States experienced exposure to magnetic fields of at least 1,000 mG during a 24-hour period.

The International Committee on Electromagnetic Safety (ICES) also recommends limiting magnetic-field exposures at high levels because of the risk of acute effects, although their guidelines are higher than ICNIRP's guidelines; the ICES recommends a residential exposure limit (Exposure Reference Level) of 9,040 mG and an occupational exposure limit of 27,100 mG for 60-Hz magnetic fields (ICES, 2019, 2020). Both guidelines incorporate large safety factors.

The ICNIRP and ICES guidelines provide guidance to national agencies and only become legally binding if a country adopts them into legislation. The WHO strongly recommends that countries adopt the ICNIRP guidelines or use a scientifically sound framework for formulating any new guidelines (WHO, 2006).

There are no national or state standards in the United States limiting exposures to ELF EMF based on health effects. Florida and New York have enacted standards to limit magnetic fields at the edge of the right-of-way from transmission lines (NYPSC, 1978, 1990; FDER, 1989; FDEP, 1996). The basis for these limits, however, was to maintain the status quo so that fields from new transmission lines would be no higher than those produced by existing transmission lines.

In a 1985 decision, the Massachusetts Energy Facilities Siting Board (EFSB) approved an edge-of-ROW level of 85 mG as a benchmark for comparing different design alternatives. Since then, this benchmark has not served as a generally applicable standard or guideline. Instead, the EFSB has encouraged the use of practical and cost-effective designs to minimize magnetic-field levels along the edges of transmission line rights-of-way. This approach is consistent with recommendations of the WHO (2007) for addressing ELF EMF.

Table 10. Screening guidelines for EMF exposure

Organization	Exposure (60 Hz)	Magnetic field guideline
ICNIRP	Occupational	10,000 mG
	General Public	2,000 mG
ICES	Occupational	27,100 mG
	General Public	9,040 mG

Sources: ICNIRP, 2010; ICES, 2019, 2020.

7 Summary

A significant number of epidemiologic and *in vivo* studies have been published on ELF EMF and health since the WHO 2007 report was released. The weak statistical association between high, average magnetic fields and childhood leukemia reported in two pooled analyses in 2000 (Ahlbom et al., 2000; Greenland et al., 2000) has not been appreciably strengthened by later research. To the contrary, the strength of the association has diminished over time, and the latest pooled analysis of epidemiology studies published on this topic in the past 10 years that analyzed populations of cases and controls three to five times larger than the original pooled analyses reported "no association between MF [magnetic fields] and childhood leukemia" (Amoon et al., 2022). Thus, the conclusion by the WHO in 2007, that there is "[c]onsistent epidemiological evidence" of an association between magnetic-field exposure and childhood leukemia development (WHO 2007, p. 355), is inconsistent with newer data. The previously reported association in some studies remains unexplained and unsupported by experimental studies. The recent *in vivo* experimental studies confirm the lack of experimental data for genotoxic effects of ELF EMF that would support a leukemogenic or other cancer. Publications on other cancer and non-cancer outcomes evaluated provided no substantial new information to alter the previous conclusion that the evidence is inadequate to conclude that ELF EMF exposure is harmful at typical environmental levels.

In conclusion, when recent studies are considered in the context of previous research, they do not provide evidence to alter the conclusion that ELF EMF exposure at the levels we encounter in our everyday environment is not a cause of cancer or any other disease process.

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