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Childhood leukemia and proximity to nuclear power plants: A systematic review and meta-analysis

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ABSTRACT

Objective: To evaluate the association between childhood leukemia and residential proximity to nuclear power plants (NPP).
Methods: We performed a systematic review by searching the MEDLINE database for published studies of childhood leukemia incidence and proximity to NPP. The primary analysis included children <15 years of age living within 25 km of a NPP, and the secondary analysis focused exposure of children <5 years of age living within 5 km of such facilities.
Results: A meta-analysis including eight studies (1,665 cases) of childhood leukemia within 25 km of NPPs produced a pooled estimate of 1.00 (95% confidence interval (CI) = 0.95–1.05). A secondary analysis of a subset of three case-control studies (53 cases) examining the risk in children <5 years of age within 5 km of a NPP produced a meta-estimate of 1.45 (95% CI = 0.74–2.86), and an analysis of the same parameters using four studies (76 cases) from ecological/cohort studies generated a significantly elevated pooled estimate of 1.33 (95% CI = 1.05–1.68).
Conclusion: Meta-estimates for ecological/cohort and case-control studies did not provide evidence of an increase in leukemia incidence in children <15 years of age living <25 km of a NPP. A subset of studies including children <5 years of age living <5 km from a NPP produced significantly elevated estimates for ecological/cohort studies. Continuing to undertake large-scale studies of populations surrounding nuclear facilities is encouraged to refine potential risks and better understand methodological nuances.

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1. Background

Childhood leukemia is the most common type of childhood cancer, representing more than a third of all cancer diagnoses in children below 15 years of age [1]. This particular cancer is unique both in its short latency period and average incident peak early in life, around two to four years of age [2]. Genetic links, such as Down's syndrome, neurofibromatosis, and Fanconi's anemia, have been identified as risk factors for leukemia, but are believed to be responsible for less than 10% of all leukemia cases [3].

Studies in various populations, including atomic bomb survivors, nuclear power workers, and children exposed to nuclear fallout, have convincingly indicated increased leukemia risks from exposures to low levels of radiation [4]. Recently, Kaatsch [5,6] conducted a case-control study (known as the Kinderkrebs in der Umgebung von Kernkraftwerken or, more commonly as, the KiKK study) in Germany and noted a higher than expected risk of leukemia in children less than five years of age living within five kilometres of nuclear power plants (NPPs). Such findings have renewed concerns and invited research efforts into better understanding the nature of a possible link between childhood leukemia and residential proximity to a NPP. Yet subsequent investigations have been unable to replicate such results: Bithell [7] followed a similar protocol of children five years and under living within five kilometres of a NPP and were not able to identify a positive association.

In light of recent conflicting results, numerous researchers have encouraged the pooling of international data on childhood leukemia cases in close proximity to NPPs to increase statistical power [8,9]. Moreover, Muirhead [10] recommended a systematic review to be undertaken to help understand strengths and limitations of each study in hopes to better understand the issue globally. Although a meta-analysis [11] was conducted relatively recently, all of the studies used to generate meta-rates were published pre-2000, thus excluding updated findings.

Interest in nuclear power may have tempered since the Fukushima Daiichi meltdown in 2011, but there are still 435 nuclear reactors currently generating electricity in 30 countries, with 72 new nuclear plants presently under construction in 15 countries [12]. Gaining a better understanding of a potential association between nuclear power and childhood leukemia would be important to protect the health of populations currently living within close proximity to such facilities and also in the consideration of siting new NPPs.

We have conducted a systematic review to identify all analytical studies investigating incidence of childhood leukemia and proximity to NPPs, as well as performed a meta-analysis to assess any such association.

2. Materials and methods

2.1. Study identification

We followed PRISMA [13,14] and MOOSE [15] guidelines, as well as the Cochrane Handbook [16], for performing and recording information for a systematic review. One of us[1] (WM) undertook the review by first searching the MEDLINE database for studies published in peer-reviewed journals as of July 31, 2015. Broad search terms were used to maximize search results: (childhood leukemia) AND (nuclear power). Once all search results were compiled and assessed, we examined the reference list of selected studies, as well as a meta-analysis [11] and three reviews [9,17,18] on this topic identified during the search, for any additional publications that satisfied all eligibility criteria.

The following inclusion criteria were established and applied to all results from the MEDLINE search:

- Study must be original research of an ecological, cohort or case-control study design;
- Primary outcome must be incidence of childhood leukemia, including at least one group of children <15 years of age;
- Exposure must be residential proximity to NPPs (i.e. electricity-generating facilities), either at diagnosis or birth, and it must be made clear where cases reside;
- Study estimates must include Standardized Incidence Ratios (SIRs) for ecological and cohort studies or Odds Ratios (ORs) for case-control studies for either individual NPP sites or grouping of sites;
- If study estimates are not provided, necessary information to calculate estimates and confidence intervals (CIs) must be available; and
- Published in a peer-reviewed journal in English.

First, we examined titles and abstracts, and, only if deemed relevant, undertook a review of the full text. All eligible studies were assigned a unique identification code. Fig. 1 provides the numbers of studies identified at each stage of the search, as well as reasons for excluding studies.

Risk estimates were recorded (or calculated) separately, where permitted, for various exposure and age groups. Estimates were calculated for exposed children living at intervals of 5 km up to 25 km from a NPP at either time of diagnosis or birth. To be clear, these are arbitrary intervals [19]: a distance of 5 km was selected to correspond with Kaatsch [5,6], which spurred several studies of similar design in other countries [7,20,21]. Proximity at less than 25 km was used as a surrogate for "exposed", for comparability across published research on this subject. Tables 1 and 2 present information extracted from each of the eligible studies.

Preference was given to defining exposure by residence at birth, since residence at birth would better account for higher sensitivities of the fetus to radiation and provide time for latency periods of leukemia, compared to residence at diagnosis [8]. The primary analysis defined exposure as children <15 years living within 25 km of a NPP and the secondary analysis focused on the most sensitive exposure and age [9]: children <5 years living within 5 km. Lastly, while the focus of the current study is on exposure to NPPs specifically, estimates were included for proximity to nuclear reprocessing sites as a sensitivity analysis; studies of such sites have identified childhood leukemia excesses, so understanding the effect of these sites

[1] Although published guidance on systematic reviews recommends multiple authors to be involved in the review, using one author was necessary to satisfy academic requirements. CG verified the included and excluded studies.