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Ian Fairlie

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Childhood cancers near German nuclear power stations: the ongoing debate

Ian Fairlie*

London, United Kingdom

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In late 2007, the significant KiKK study (Kinderkrebs in der Umgebung von KernKraftwerken = Childhood Cancer in the Vicinity of Nuclear Power Plants) in Germany reported a 1.6-fold increase in all cancers and a 2.2-fold increase in leukaemias, among children living within 5 km of all German nuclear power stations. The KiKK study by Kaatsch et al. was extensively described in a recent edition of Medicine Conflict and Survival. It has triggered much discussion as to the cause(s) of these increased cancers. This article reports on recent developments on the KiKK study, including responses by German radiation agencies, and recent epidemiological studies near United Kingdom and French nuclear installations. It reflects the current debate and concludes with advice to policy-makers on radiation risks on the relative merits of the KiKK study. An accompanying article outlines a possible explanation for the increased cancers and makes recommendations for future research.

Keywords: cancer; carbon-14; congenital malformations; discharges; embryo; emissions; foetus; leukaemia; nuclear power stations; radiation; radioactivity; radionuclides; relative risk; tritium; untoward pregnancy outcomes

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Introduction

In the late 1980s and early 1990s, increased incidences of childhood leukaemias were reported near United Kingdom nuclear facilities at Windscale (now Sellafield), Burghfield and Dounreay. Various explanations were offered for these increases; however, the UK Committee on the Medical Aspects of Radiation in the Environment (COMARE) concluded that the cause or causes remained unknown but were unlikely to involve radiation exposures[1–6]. This was primarily because the then National Radiation Protection Board (now Health Protection Agency – Radiation Protection Division) had estimated that the radiation doses from these facilities were too low by at least three orders of magnitude, to explain the increased leukaemias.

*Email: ianfairlie@gmail.com

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As recently reported in *Medicine, Conflict and Survival*[7], the German KiKK study (Kinderkrebs in der Umgebung von KernKraftwerken = Childhood Cancer in the Vicinity of Nuclear Power Plants) has rekindled the debate over childhood leukaemia[8,9]. It reported a 2.2-fold increase in leukaemias and a 1.6-fold increase in solid cancers among children under five years old living within 5 km of all German nuclear power stations.

The KiKK epidemiology study commands attention for a number of reasons. First is its high statistical power as the low numbers and lack of statistical significance of many small studies tend to limit the information that can be derived from them. This power stems partly from its sheer size: it examined all cancers at the 16 nuclear reactor locations in Germany between 1980 and 2003, including 1592 under-fives with cancer and 4735 controls, with 593 under-fives with leukaemia and 1766 controls. It also stems from its case–control design and from the accuracy of its distance measurements. Second is its authority: it was commissioned in 2003 by the German Government's Bundesamt fur Strahlenschutz (BfS) which is the German Federal Office for Radiation Protection, roughly equivalent to the UK Health Protection Agency – Radiation Protection. The study was set in train after requests by German citizen groups. The study was carried out by an epidemiology team from the University of Mainz which could not be accused of being opposed to nuclear power. Third is the validity of its results as vouchsafed for by the German Government's BfS. It is now officially accepted in Germany that children living near nuclear power plants develop cancer and leukaemia more frequently than those living further away[10].

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The KiKK study found a clear association between cancer increases and proximity to NPPs. However the authors asserted that the increases could not be explained by radiation from NPPs as the estimated radiation risks from NPP emissions were too low to result in the observed cancer increases. A separate part of the KiKK study investigated potential confounders known to be leukaemogenic, for example, population movements. The question it examined was whether any of these confounders had a significant impact on the distance trend found in an analysis of the same data without confounders. The confounders were grouped into five categories. None of these confounder groups changed the distance trend within the limits of error. But the statistical power of this part of the KiKK study to detect the possible influence of confounders was low.

Report of external Expert Panel on KiKK: 10 December 2007

(This section and the following two sections have been prepared with translation and interpretation help from Dr A. Körblein.)

In 2001, the German Government's Federal Office for Radiation Protection (BfS) established an expert working group (Arbeitsgruppe) to advise it on the design of the KiKK study. Later this was reformulated to be

more independent of the BfS and the KiKK study team and renamed the Expert Panel (Expertengremium). It consisted of 12 scientists with expertise in epidemiology, child health, and radiation, who were representative of the differing views on radiation risks (see Box 1).

Box 1

Members of the external Expert Panel on KiKK
Dr I. Brüske-Hohlfeld, Institut für Epidemiologie, GSF, Neuherberg
Prof. Dr E. Greiser, Bremer Instituts für Präventionsforschung und Nuklearmedizin
Prof. Dr W. Hoffmann, University of Greifswald
Dr A. Körblein, Umweltinstitut München
Prof. Dr K.H. Jöckel, University of Duisburg-Essen
Dr H. Küchenhoff, Institut für Statistik der LMU München
Dr S. Pflugbeil, Präsident der Gesellschaft für Strahlenschutz e.V. Berlin
Dr H. Scherb, Institut für Biomathematik und Biometrie, GSF, Neuherberg
Dr K. Straif, International Agency for Research on Cancer, Lyon
Prof. Dr J.U. Walther, University of München
Prof. Dr S. Wirth, Helios Klinikum, Wuppertal
K. Wurzbacher, Umweltinstitut München

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In December 2007, the Expert Panel met to discuss the then forthcoming KiKK study. Its statement[11] confirmed that the KiKK study 'was the methodically the most elaborate and comprehensive investigation of the NPP – cancer relationship world-wide, and the association between NPP proximity and cancer risk was therefore sufficiently proved for Germany.' Although the Expert Panel considered the KiKK study was well designed, it criticized the study's interpretation of the results. In direct opposition to the KiKK study's assertion that radiation could not explain the increased cancers, the External Advisory Panel stated:

> all members are convinced that due to the particularly high radiation risks in small children and due to the insufficient data on emissions of power reactors, this relationship definitely cannot be excluded. Furthermore, several epidemiological causality criteria favour such an interrelation. The task of science now is to find an explanation for the difference between the epidemiological and radio-biological evidence.

Report of Epidemiological Quality Team: March 2008

During 2007, the German Government's Federal Office for Radiation Protection (BfS) appointed an independent team of three senior

epidemiologists to check specifically on the epidemiology of the KiKK study. The team consisted of Professors Dr Karl-Heinz Jöckel and Dr Eberhard Greiser from the University of Duisburg-Essen, and Professor Dr Wolfgang Hoffmann of the University of Greifswald. The team's report (Epidemiological Quality Inspection of the KiKK Studies Ordered by the Federal Office for Radiation Protection) is available (in German) at http://www.bfs.de/de/kerntechnik/kinderkrebs/Qualitaetspruefung.html.

The team's report gave a clean bill of health to the design and methodology of the KiKK study. However, it also disagreed with the view of the KiKK authors that a radiobiological cause for the increased cancers could be ruled out. The team's report stated instead that the dose and risk models assumed by the KiKK authors did not necessarily reflect the actual exposures and possible radiation risks. The team stated it was necessary to investigate the radiobiological plausibility of the findings under different exposure scenarios. More work was needed on the exact radiation doses to nearby people. Also more research was required on the biological effects of ionizing radiation in the light of the paradigm shift caused by new findings from radiation epidemiology, genetic medicine and molecular biology. It further suggested that a combination of genetic polymorphisms for reduced DNA repair and/or genetic radiosensitivity might provide a possible biological explanation for the KiKK findings.

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SSK Report: October 2008

Following the publication of the KiKK study in December 2008, the German Government commissioned its permanent advisory body on radiation risks, the Strahlenschutzkommission (SSK – a committee of 17 radiation scientists (see Box 2)), to evaluate the present state of radioecological and radiobiological knowledge 'in order to ascertain whether radiation could explain the KiKK findings of increased cancers near German NPPs'.

In its subsequent report, the SSK stated it was unable to explain the increased cancer risks; that there were likely to be multiple causes for the increases; and that radiation exposures were too low to be a causal factor. However, the SSK report did not discuss a number of matters which might appear to be necessary in view of its remit to examine whether radiation exposures could explain the cancer increases. For example, the SSK report did not discuss:

- the precise sources of radiation exposures from NPPs to nearby residents;
- the nature, size and chemical form of radioactive releases from NPPs;

Box 2

Members of the German Government's permanent Strahlenschutzkommission

Prof. Dr R. Michel, Chairman Universität Hannover
Prof. Dr N. Leitgeb, Technische Universität Graz
Prof. Dr B. Stöver, Universitäts-Klinikum Charité Berlin
Dr M.-J. Atkinson, Deutsches Forschungszentrum für Umwelt und Gesundheit GmbH
Prof. Dr Dr Bockisch, Universität Essen
Prof. Dr E.W. Breitbart, Kreiskrankenhaus Buxtehude
Prof. Dr F. Eckardt-Schupp, Deutsches Forschungszentrum für Umwelt und Gesundheit
PD Dr A.A. Friedl, Universität München
Dr R. Gellermann, HGN Hydrogeologie GmbH
Prof. Dr T. Herrmann, Technische Universität Dresden
Dr M. Horn, TÜV Rheinland Industrie Service GmbH
Dr P. Jacob, Deutsches Forschungszentrum für Umwelt und Gesundheit GmbH
Prof. Dr K.-H. Jöckel, Universitätsklinikum Essen
Dipl.-Phys. J. Kopp, Klinikum Augsburg
Dr F. Lange, GRS – Gesellschaft für Anlagen- und Reaktorsicherheit mbH
Prof. Dr P. Sahre, Verein für Kernverfahrenstechnik und Analytik Rossendorf e.V.
Prof. Dr H.E. Wichmann, Deutsches Forschungszentrum für Umwelt und Gesundheit

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- the episodic nature of these releases, and the resulting heterogeneous dose rates;
- the relative hazards of the main nuclides released from NPPs (H-3, C-14, Kr-85);
- the uncertainties in the estimated nuclide emissions from NPPs;
- the relative hazards of nuclide emissions to air and nuclide discharges to rivers;
- the uncertainties in the environmental, metabolic and dosimetric models used to estimate radiation doses from NPPs;
- the uncertainties in the radiation weighting factors and tissue weighting factors used to estimate 'effective' radiation doses;
- the resulting cumulative uncertainties in radiation doses from NPPs;
- the resulting cumulative uncertainties in radiation risks from NPPs.

In the view of this author, it is difficult to assess the KiKK findings and the radiation risks from NPPs without discussing at least some of the above matters. Therefore, the SSK's assertion that radiation doses were too low to be a cause of the increased cancers is unsupported: the SSK simply did not examine the matter.

Other studies on childhood leukaemias near NPPs. December 2008

The picture here is mixed. Previous UK[5,12] and French[13,14] studies have generally not found evidence of leukaemia increases, apart from one UK study[15]. However, since the KiKK study was published, more recent studies have suggested small increases may exist, albeit without statistical significance. Bithell et al.[16] found a small increase in child leukaemias near most UK NPPs and Laurier et al.[17] found a small increase near French NPPs. Within 5 km, Bithell et al observed 18 cases *vs.* 14.58 expected (RR = 1.30, $p = 0.169$ one-sided test). Within 10 km, Laurier et al. observed 25 cases *vs.* 20.6 expected, a 20 per cent increase relative to the 10–20 km zone (RR = 1.2, $p = 0.248$ one-sided test). In both cases, the numbers were low and not statistically significant at the $p = 0.05$ level (i.e. there was a greater than five per cent possibility that the observations could have occurred by chance).

The two studies concluded that there was 'no suggestion' or 'no evidence', respectively, of leukaemia increases near French and UK nuclear reactors. These conclusions are incorrect for the following reason. Where a study on disease incidence finds small increases which are not statistically significant, this does not mean that the effect being examined is discounted, as many laypeople might think. (It is a common misinterpretation that the p value is the probability that the null hypothesis (that is, of no effect) is true, so that an insignificant result means that the null hypothesis is likely to be true[18].) Instead statistical significance refers to the result of a statistical test[19]. Therefore, it would have been more accurate to have stated that small cancer increases were observed, but the numbers were too small to reach statistical significance, and that the studies were too weak to make definite conclusions.

Axelson[20] has also pointed out that many negative and non-positive studies, unlike positive studies, may be of questionable validity because they can obscure existing risks. He was critical of the selection phenomena and observational problems with exposure and outcome in many negative and non-positive studies.

The stated conclusions in the Laurier and Bithell studies may act to mislead members of the public into thinking that there are no increased leukaemias near French or UK nuclear power stations when in fact the question remains open, and the stronger KiKK evidence suggests the opposite.

This KiKK's findings have been confirmed by two meta-analyses: these combine the data of smaller studies in order to achieve statistical

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significance. Baker and Hoel[21] analysed data from 17 research papers world-wide covering 136 nuclear sites in the UK, Canada, France, the United States, Germany, Japan and Spain. In children up to nine years old, leukaemia death rates were from five to 24 per cent higher, and leukaemia incidence rates were 14 to 21 per cent higher. These findings were statistically significant. Körblein carried out a meta-analysis[22] of leukaemias near most NPPs in Germany, France and the UK. He also found a statistically significant increased risk of child leukaemias relative risk of leukaemia deaths near NPPs with a relative risk of 1.33 (single tailed $p = 0.0246$).

Conclusion: advice for policy makers

Policy makers need to be guided by the best available scientific evidence. This is particularly true as regards childhood leukaemia because it is a rare disease and requires statistically powerful (that is, numerically large) studies to obtain statistically significant results.

It is preferable for policy makers to rely on the KiKK study rather than the Bithell and Laurier studies for the following reasons. First, the KiKK study found statistically significant cancer increases. The *p*-values in the KiKK study were 0.0034 for all cancers and 0.0044 for leukaemias (both one-tailed), in other words well below the usually applied 0.05 level for statistical significance. Second, as discussed above, the KiKK findings have been supported by independent meta-analyses. Third, the KiKK study is a case–control study (for example, it examined 593 under-fives with leukaemia together with 1,766 controls) which means its findings take precedence over the Bithell and Laurier studies which were less reliable ecological studies. Finally, the KIKK study used much more accurate distance measures. It estimated distances between the actual homes of cancer cases and NPPs to within 25 m and allowed the study to examine the distance/risk relationship more accurately.

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Notes on contributor

Ian Fairlie is an independent consultant on radioactivity in the environment. He has worked for various UK government departments and regulatory agencies, and advises environmental NGOs, the European Parliament and local authorities. Between 2001 and 2004 he acted as Secretariat to the UK government's CERRIE Committee on internal emitters. Dr Fairlie wishes to thank Dr Alfred Körblein for his valued help in translating German documents and checking various drafts.

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