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LETTERS TO THE EDITOR

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Authors' response to: Childhood cancer and nuclear power plants in Switzerland: a census-based cohort study

From BEN D SPYCHER, CLAUDIA E KUEHNI, MARCEL ZWAHLEN and MATTHIAS EGGER* ON BEHALF OF THE SWISS NATIONAL COHORT STUDY GROUP AND THE SWISS PAEDIATRIC ONCOLOGY GROUP

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We thank Jürg Schädelin, Alfred Körblein and Giovanni Ghirga for their comments on the CANUPIS study (Childhood Cancer and Nuclear Power Plants in Switzerland). 1

Schädelin is surprised that 'a virtually identical result was obtained' in the Swiss and in the German KiKK study (Kinderkrebs in der Umgebung von Kernkraftwerken)² in the regression analyses of the inverse distance to the nearest nuclear power plant (NPP). He misinterprets numerically similar results that were reported on different scales: the results given on page 31 of our web appendix 2 are incidence rate ratios (IRRs) and not comparable to the KiKK study, which reported the untransformed regression coefficients. The regression coefficient in our study was 0.55 [95% confidence interval (CI) -1.22 to 2.32] in the resident cohort and -0.29(-2.36 to 1.79) in the birth cohort; clearly different from the 1.75 (95% lower confidence bound 0.65) in the German study. Schädelin also sees a discrepancy between our results for the resident cohort (using address of residence at diagnosis and showing a slight decrease of risk closer to NPPs) and the birth cohort (using address at birth and showing a slight increase of risk), but ignores the wide confidence intervals (which both include the null). We agree with Schädelin that the 1/distance model makes strong assumptions about the relation between distance and risk. Due to the sharp increase of the function as distances approach zero, the few cases in close proximity to the NPPs will strongly influence regression parameters. Whereas the assumption that potential effects of radioactive emissions are limited to their immediate proximity is plausible, the precise functional form between distance and cancer incidence is unknown.

Körblein pooled our data with results from two studies from Germany and the United Kingdom to

suggest that our study 'confirms the excess of leukaemia' observed in the latter studies. Given the large number of previous studies, the three studies included by Körblein represent a highly selected subset. For example, it is unclear why the French study by Laurier³ was not included. This study reported a standardized incidence ratio (SIR) for the 0- to 5-km zone around NPPs of 0.96 (95% CI 0.31-2.24).

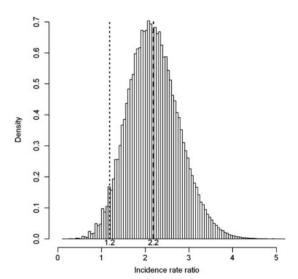


Figure 1 Sampling distribution of IRRs in the Swiss study assuming a true IRR of 2.2 as estimated in the German KiKK study. IRRs are for childhood leukaemia in 0- to 4-year olds comparing the 0- to 5-km zone with the >15-km zone around NPPs. The distribution is based on 10⁶ random draws from Poisson distributions of numbers of cases in each zone using the person-years and baseline incidence rate (in >15-km zone) from the Swiss study. The dotted and dashed lines represent the estimated IRR in the Swiss study (birth cohort) and the assumed true IRR respectively

In the UK the most recent figures (20 observed and 16.35 expected cases) published by the Committee on Medical Aspects of Radiation in the Environment (COMARE)⁴ differ from those used by Körblein. Of note, COMARE reported a combined SIR of 1.07 (95% CI 0.92–1.26) from a random-effects meta-analysis of 37 estimates from five countries.⁴

Körblein rightly points out that the 95% CI of the rate ratio estimate from the main analysis of childhood leukaemia in 0- to 4-year olds just includes the point estimate (2.19) of the German KiKK study. However, there is in fact considerable disagreement between the two studies. Assuming that the true IRR for leukaemia in 0- to 4-year olds comparing the 0- to 5-km zone with the >15-km zone around NPPs is indeed 2.2 (as estimated in the KIKK study), the probability of observing an IRR of 1.2 (as in our study) is 0.03 (Figure 1) and the power of rejecting the null hypothesis of no association at the 5% significance level is 76%.

Chirga argues that estimates of mean annual radiation doses originating from nuclear power plants (NPPs) are uncertain and that actual doses might fluctuate over time. He suggests that short spikes in emissions could increase the incidence of childhood cancer. Whereas we cannot exclude this possibility, we reiterate that our study provides little evidence that the rate of childhood cancer is higher in the proximity of NPPs. The few cases of cancer occurring in excess of the expected number of cases among children living in the 5-km zone around Swiss NPPs are well within statistical uncertainty, and so is the deficit of cases a few kilometres further afield. We agree with Chirga that our main exposure measure,

Euclidean distance of place of residence to nearest NPP, was crude and can only serve as a proxy for true radiation exposure.

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Conflict of interest: None declared.

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Added predictive ability of the information on job strain beyond the standard Framingham risk score

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Kivimaki *et al.* recently examined whether information on job strain improves risk prediction for coronary heart disease (CHD) beyond the standard Framingham risk score in a middle-aged low-risk working population. They observed that job strain was associated with an increased risk of CHD; however, when compared with the Framingham algorithm, adding job strain did not improve the model's predictive performance.

The authors are to be commended for re-estimating (or refitting) the Framingham model instead of directly applying the model to their population. A prediction model tends to perform better in data from which it was derived than on a new dataset. This difference in performance is an indication of the optimism in the apparent performance in the derivation set. In light of the correlations between job strain and currently established risk factors, the effect size estimated for job strain may be a reflection of information lost during inappropriate modelling of information on the currently established Framingham CHD risk factors. When β -coefficients derived from the Framingham study population are directly applied while the coefficient for job strain is obtained from the study sample, then job strain has a so-called home-advantage. In other words, the effect size for