Sufficient Statistical Power for CANUPIS?

(Study on Childhood Cancer and Nuclear Power Plants in Switzerland)

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To the editor:

CANUPIS, a Swiss study project on the incidence of childhood cancer near Swiss nuclear power plants (NPP) was presented in November 2008 (1). The Swiss study was prompted by the German KiKK-study (2), which found a doubling of leukaemia risk in children under the age of 5 years living within 5 kilometers of nuclear power plants at the time of the diagnosis.

The Swiss study seeks to confirm the German results for children below 5 years with respect to leukaemia and all cancers in a cohort study covering a 23-year period (1985–2007). Unlike the KiKK-study, the CANUPIS-study additionally covers children below the age of 16 years. The authors stated ***«Power calculations suggested that with the planned study design, we will have sufficient statistical power to show a doubling of risk for leukaemia in children under age 5 years, and a 40% increase in all cancers, as reported by the German study»*** (1). No statistical power calculations were mentioned for children <16 years.

On the basis of the demographical parameters specified by the authors (Swiss population of 7.5 million, about 1% of them living within 5 km of a nuclear power plant, of 429 cases with leukaemia and 1368 cases with «all cancers» aged <5 years, as well as of 981 cases with leukaemia and 2957 cases with «all cancers» aged <16 years), we were concerned whether statistical power reached conventional 80%-90% at a significance level p = 0.05. ***We were informed by the authors that power indeed was low with 51% only in the group of children <5 years with leukaemia*** (3). However power for doubling of incidence (rate ratio RR = 2.0) of all cancers in children <5 years was stated to be 94%, as well as 85% for leukaemia in children <16 years and 99% for the group «all cancers» <16 years (Table 1). Power figures in Table 1 could be confirmed, up to minor numerical deviations, using 10%-level two-sided one-sample Poisson tests, according to the method

Table 1. *CANUPIS-study: Calculated statistical power for rate ratio (RR) = 2.0 for leukaemia and «all cancers» in children living within 5 km of a Swiss NPP (3)*

	leukaemia	all cancers
age <5 years	**power 51% for RR 2.0**	**power 94% for RR 2.0**
age <16 years	**power 85% for RR 2.0**	**power 99% for RR 2.0**

Table 2. *Relative risk (RR) and excess relative risk (ERR) of leukaemia and «all cancers» for children living within 5 km of a German NPP (6)*

	leukaemia	all cancers
age <5 years	**RR 1.76 ERR 0.76**	**RR 1.54 ERR 0.54**
age <15 years	**RR 1.36 ERR 0.36**	**RR 1.22 ERR 0.22**

Table 3. *CANUPIS-study: Estimates of statistical power according to specified parameters (1) for appropriate rate ratios (RR) for leukaemia and «all cancers» in children living within 5 km of a Swiss NPP; 5%-level two-sided one-sample Poisson tests*

	leukaemia	all cancers
age <5 years	**power 51.5 % for RR 2.19**	**power 52.2% for RR 1.61**
age <16 years	**power 39.4% for RR 1.60**	**power 33.8% for RR 1.30**

Table 4. *CANUPIS-study: Minimal rate ratios necessary for statistical power of at least 80% according to specified parameters (1) for leukaemia and «all cancers» for children living within 5 km of a Swiss NPP; 10%-level two-sided one-sample Poisson tests*

	leukaemia	all cancers
age <5 years	**min. power 80% min. RR 2.59**	**min. power 80% min. RR 1.79**
age <16 years	**min. power 80% min. RR 1.95**	**min. power 80% min. RR 1.51**

of randomized uniformly most powerful tests (UMPUT) (4, 5).

It is unclear according to which published data this high rate ratio (RR = 2.0) was chosen by the Swiss investigators for power calculations both for leukaemia and all cancers in the 4 patient groups of the CANUPIS-study. According to the literature (6, 7), a RR of 2.0 is too high and, therefore, inappropriate for all but the group of children <5 years with leukaemia. In an earlier German study (6), excess relative risks (ERRs) of leukaemia and «all cancers» in children <15 years were found to be about half of the ERRs in children <5 years, respectively (Table 2). This tentative association was used to cut into halves the EERs of the KiKK study for children <5 years to estimate the ERRs for children <16 years in the CANUPIS-study (Table 3).

If calculations are done for appropriate rate ratios, estimates of power levels for all 4 groups studied in the ongoing CANUPIS-study are clearly far below the critical 80% level (Table 3). This means that the risk of false negative results for all groups is likely to be unacceptably high if the excess risk in Switzerland is similar to the risk observed in Germany. Minimal rate ratios necessary for at least 80% power are considerably higher than the rate ratios observed in German studies for all 4 patient groups (Table 4). Necessary rate ratios were even higher if conventional two-sided 5%-level tests were being used instead of the more liberal two-sided 10%-level tests or one-sided 5%-level tests.

An explanation for the choice of the rate ratio (RR) of 2.0 for all 4 groups as well as a publication of revised power calculations by the investigators of the CANUPIS-study on the basis of appropriate rate ratios and updated case numbers would be welcome.

The handicap of insufficient statistical power of the CANUPIS-study to confirm the KiKK-study results could be alleviated by supplementing the aims of the study. ***We therefore suggest that the statistical analysis should also address whether the findings of the Swiss study are significantly different from those of the German KiKK-study. This could be done by a formal comparison of the risk estimates and the corresponding confidence intervals of both studies. This addendum could protect against the misinterpretation of a probable negative result of CANUPIS as evidence of no carcinogenic effect (8) in the vicinity of Swiss nuclear power plants.*** Moreover, this kind of analysis would not compromise the ongoing project – it would, however, overcome to some degree the shortcomings of the actually underpowered confirmation trial design of the CANUPIS-study.

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