Reviewer's report

Title: Commentary: Childhood Cancer Near Nuclear Power Stations

Version: 3 **Date:** 5 August 2009

Reviewer: Alfred Koerblein

Reviewer's report:

Major Compulsory Revisions

p.3:

These conclusions are regrettable because low statistical significance (i.e. a p-value greater than 5%) should not be interpreted as measuring the probability of effect [26]. The word “significance” refers to a statistical test and not the effect being examined [27 28 29].

As already expressed in my first revision, I do not understand this sentence („low statistical significance .. should not be interpreted as measuring the probability of effect“). KiKK tests whether there is an increase of leukemias in the 0-5 km zone of NPS, in other words, whether proximity to NPS has an effect on leukemia rates. The effect is significant when the probability of this being a chance result is smaller than 5% ($p< 0.05$). So significance refers to the effect; the test is just a mathematical tool to determine the p-value.

I would advise to omit the sentence above since it will only cause confusion.

p.4:

More recently, Dr A Körblein has found that when the numbers of cases in the German and the Bithell et al study are added, the increase in the 5-km zone relative to the 5-10 km zone reaches statistical significance (RR =1.49 with 2-sided p-value=0.026) 32.

This should be an extra paragraph. First mention the RR observed in the British data (RR=1.52; $p>0.05$), then the RR in the German KiKK data (Kaatsch et al, Oct. 2008; RR=1.46; $p>0.05$), and the result of the combined analysis (RR=1.49; $p=0.026$).

p.4:

The KiKK study showed an increased risk of cancer in children under 5 years living near all nuclear power plants in Germany. The inner 5 km zone showed an increased risk (odds ratio 1.47; lower one-sided 95% confidence limit 1.16).

If „showed“ is understood as „observed“ the statement is not correct. It should be OR=1.61, lower 90% confidence limit 1.26 (see Spix et al. Table 4). The OR given above is the OR calculated from the continuous model (1/r). Instead of the OR I would give the regression coefficient of 1.18 (lower limit 90% CI: 0.46, see Spix et al Table 3). Also, I would replace lower one-sided 95% confidence limit by

lower 90% confidence limit.

p.4:

For all leukemias combined, the study showed a statistically significant trend for proximity to nuclear power stations with a positive regression coefficient of 1.75 [lower 95%-confidence limit 0.65].

I would first mention the result of the categorial analysis: OR (0-5 km) = 2.19 (lower 90% confidence limit 1.51, see Kaatsch et al Table V). Again use 90% CI instead of one-sided 95% CI. Then add the result of the regression analysis mentioned above (regression coefficient 1.75, lower limit 90% CI: 0.65, see Kaatsch Table III)

p.4:

A categorical analysis showed a statistically significant odds ratio of 2.19 (lower 95%-CL: 1.51) for residential proximity within 5 km compared to residence outside this area.

Use lower 90% CL instead

p.4:

These increased risks are statistically significant and are larger than the cancer increases observed near nuclear facilities in many other countries. The data indicate that the increased risks mainly lie within 5 km of NPPs though this does not necessarily mean that there are no increased risks beyond 5 km.

See:

http://www.ssk.de/werke/volltext/2008/ssk0806e.pdf,

Figure 1 (page 23) and page 22:

„For the 5-km radius zones around the nuclear power plants, a relative risk of childhood leukaemia of 2.27 was obtained (95%-CI: 1.45; 3.56). This result is highly significant (p=0.0003). Outside of the 5-km-radius zones, no significantly higher risk was found for any distance category (Fig. 1). The best estimates obtained lay between 0.95 (50-69 km radii) and 1.12 (30-49 km radii).“

So there is no evidence for increased risks in the distance zones beyond 5 km.

p.5:

The odds in table 2 were calculated by the KiKK authors using a linear relationship between distance and relative risk (that is, RR~e1/r).

using a linear relationship between distance and log(relative risk), that is, RR~exp(1/r).

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his is uncertain as the true relationship is unknown. For example, a quadratic relationship, (that is, $RR \sim e^{1/r^2}$) also fits the data.

I propose to drop this line

Further tests (the sum of squared residuals and goodness of fit) indicate that a quadratic relationship may actually fit the KiKK data better.

Why „may“? Either the fit is better or not.

I would advice to replace this sentence by:

A quadratic regression model, ie $RR \sim \exp(1/r^2)$ actually fits the data in Kaatsch's Table IV better (AIC=37.52) than a linear model (AIC=39.54) (A. Körblein, personal communiction).

Declaration of competing interests:

I have no competing interests.