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Health Protection
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Direction générale de la
protection de la santé

Room B43
Environmental Health Centre
Tunney's Pasture
Ottawa, Ontario
K1A 0L2

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Dr. Mary Paxton
American Petroleum Institute
1220 L Street, Northwest
Washington, D.C. 20005

Dear Mary,

As requested, I have read over the material you sent us on benzene risk estimation by C. Brown and R. Spirtas as well as the reply by K. Crump. My comments follow.

Spirtas and Brown¹ were asked to review Paxton et al.² Specifically, they addressed three issues: (1) the risk-group stratification, (2) the dose-response function and (3) combining data from Akron and St. Mary's locations. K. Crump³ commented on the differences between analyses by Paxton et al.², Crump⁴ and Brown and Spirtas¹.

As pointed out by Crump³, a higher log-likelihood does not necessarily mean a better fit. It only means that in total, the curve is closer to the observed points. However, this does not address potential lack-of-fit, particularly systematic departures of the estimated model from the observed data, and there could be other models with even higher log-likelihoods. One method for assessing lack of fit is to add more parameters to the model. If there is a significant increase in the log-likelihood, then the original model is not fitting the data as well as the new model. It would also be helpful if Crump³ had provided standard errors for the parameter estimates of the expanded models.

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- ¹ Brown C. and Spirtas R. (1993) A re-analysis of the leukemogenic risk associated with occupational benzene exposure in the pliofilm cohort. Unpublished.
 - ² Paxton M., Chinchilli V., Brett S, Rodricks J. (1993) Leukemia risk associated with benzene exposure in the pliofilm cohort. I. Mortality updata and exposure distribution, and II. Risk estimates, to appear in Risk Analysis.
 - ³ Crump K. (1993) Reconciliation of results of three statistical analyses of the risk of benzene exposure based on data from the pliofilm cohort. Unpublished.
 - ⁴ Crump K. (1993) Risk of benzene-induced leukemia derived from pliofilm cohort: effect of additional follow-up and new exposure estimates. J. Tox. Environ. Health, submitted.

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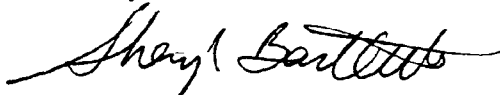
Mike Walker of the Biostatistics Section graphed the five curves fit by K. Crump³ for cumulative doses up to 50 ppm-years to view the differences for low doses and up to 3000 ppm-years to obtain a more global view. In the first figure, three of the models are quite similar. The exponential curve is somewhat flatter than these three though starts rising quickly at around 1000 ppm-years. The power curve raises quickly from the beginning and is much higher than the other four until 2500 ppm-years when the exponential curve overtakes it. It is puzzling that the power curve is so different from the others especially since the cumulative exposure for cases is not likely to exceed 3000 ppm-years. A graph of data would go a long way to clarify this issue. What about a plot of the relative risk in 500 ppm-year dose intervals? If you can provide this data, we would be happy to do some graphical comparisons. My FAX number is (613) 952-9798.

The method of stratifying risk-group did not lead to appreciable differences in parameter estimates for the exponential model and some small differences for the power function model (Paxton³, 1993). For all three sets of exposure estimates and for both models, the Spirtas strata yielded higher maximum log-likelihoods. It would be useful to know how the differences in parameter estimates translate into differences in estimated relative risks at specific cumulative exposures.

The only comment we have about the Akron and Combined analyses is that we believe that acute myelogenous leukaemia is the response of interest and would prefer to focus on that response.

I hope these comments are helpful to you. Please give me a call with any questions that arise.

Sincerely,

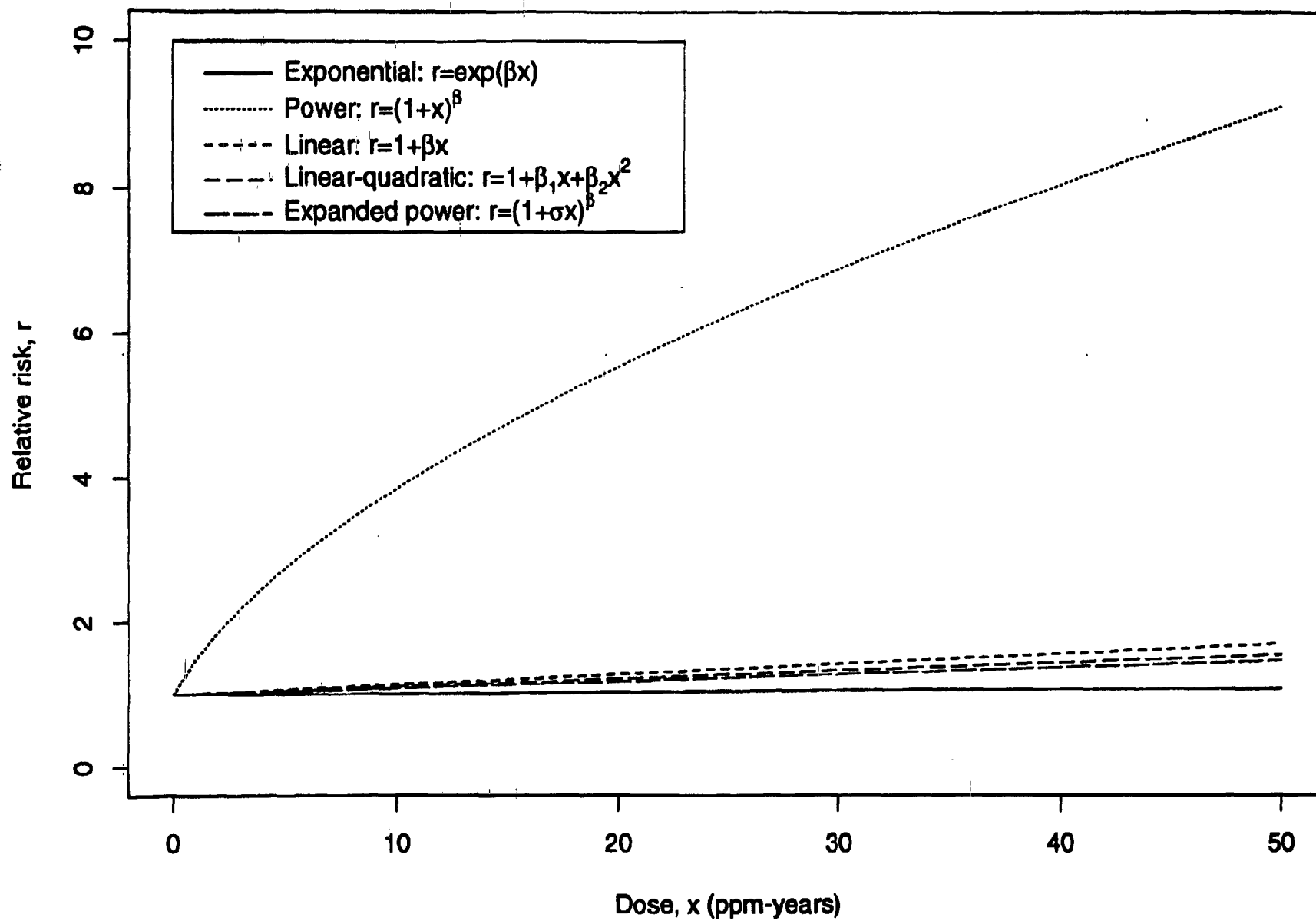


Sheryl Bartlett, PhD
Head, Biostatistics
Section
Environmental Health
Directorate
(613) 954-7787

cc. Dr. D. Krewski

³ Paxton, M. (1993) Exponential vs. Power function as dose-response in proportional hazards model. Unpublished table.

Benzene: relative risk vs. dose



Benzene: relative risk vs. dose

