



DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

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March 16, 2011

Charles Breckenridge, PhD
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Dear Dr Breckenridge:

Thank you for your letter of March 4. We appreciate your kind remarks on the value of our study now in press in EHP (Tanner et al 2011). A response to your comments and queries follows.

Regarding separate analyses of prevalent and incident cases, the division was appropriate for the analysis reported in our previous article (Kamel et al 2007), which was based on exposure data collected at enrollment in the AHS. Thus it was important to distinguish between prevalent cases who reported exposure after diagnosis and incident cases who reported exposure before diagnosis. The same difference does not exist for the nested case-control study (FAME) reported in our recent article (Tanner et al 2011), in which cases had all been diagnosed before the FAME Study exposure data were collected, *ie*, all were prevalent at the time of data collection. However, in the latter study we did conduct analyses stratified by time since diagnosis and found no meaningful differences between associations found for cases with more or less time elapsed between diagnosis and data collection. For cases with fewer than the median number of years between diagnosis and data collection, the ORs for paraquat were 2.6 (Wald 95% CI: 1.2 – 5.8) for men and women together and also 2.6 (1.2 – 6.0) for men only, while for cases with greater than the median number of years, the ORs were 2.5 (1.1 – 5.8) for men and women and 2.8 (1.2 – 6.6) for men.

You request analyses of the relationship of PD to paraquat based on the verified cases from the FAME study and exposure data collected at enrollment in the AHS. The AHS enrollment data consist of reports of use based on the response to a single question (“Have you ever mixed or applied paraquat?”), while the FAME study reported in Tanner et al (2011) collected a complete lifetime history of use on farms, so exposure metrics based on the latter are much less likely to involve misclassification. Thus the analyses you request are likely to be more biased than the ones in our article.

You ask whether we were able to establish a date of diagnosis for cases in the Tanner et al (2011) study. The answer is yes, we had such a date for all cases. Our exposure metrics, both ever use and lifetime days, were all calculated with respect to this date, *ie*, all the exposures that we considered preceded diagnosis.

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Finally, you ask about results based on proxy interviews. Relatively few study participants had such interviews (28 cases, 6 controls), limiting our ability to analyze this group separately. We did conduct analyses excluding these 34 participants, again with no material change in results: ORs for paraquat were 2.6 (1.3 – 5.0) for men and women together and 2.7 (1.4 – 5.3) for men only.

We hope that these comments address your concerns.

Sincerely,

A handwritten signature in black ink, appearing to read 'Freya Kamel', with a stylized, cursive script.

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Kamel, Tanner et al. Pesticide exposure and self-reported Parkinson's disease in the Agricultural Health Study. *Am J Epidemiol* 2007; 165:364-74.

Tanner, Kamel et al. Rotenone, paraquat, and Parkinson's disease. *Environ Health Perspect* 2011; DOI:10.1289/ehp.1002839.

Case ID: 220300429

SYNG-PQ-01638564