Reviewer's report

Title: Self-reported parkinsonian signs in the EPIC-Norfolk cohort

Version: 1 Date: 15 April 2005

Reviewer: Yoav Ben-Shlomo

Reviewer's report:

General

This paper reports opportunistic data from a large and important prospective cohort established to examine associations between dietary intake and cancer. It is at the moment mainly a descriptive paper on the prevalence of parkinsonian symptoms by age and compared to subjects with or without a diagnosis of PD. Such papers are helpful and rarely published as either researchers fail to write up the data and/or journals are less interested in publishing them. In general, such papers should be encouraged but I do have some comments which I feel should be addressed first and which I hope will result in a better and more useful publication. As a small aside I would like to suggest that the authors misuse the term “signs” and in fact mean “symptoms”. I may be wrong but I believe that a symptom is a subjective complaint whilst a sign is evidence elicited by a third party (usually a clinician and supposedly more objective) supporting or refuting the presence of pathology. Patients can have symptoms but no signs and vice versa. Sometimes the distinction can be blurred. For example in box 1 bradykinesia and rigidity are signs (you need to undertake passive limb movements to determine if they are present) but difficulty getting out of bed is a symptom. By definition the study is examining self-reported symptoms which we hope are indicative or correlate well with clinical signs. I would suggest the paper is altered to make this distinction.

I appreciate that some of the suggestions I have made below will require additional work but I feel that this will make the paper a more useful publication for other researchers to build on.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The authors fail to describe their statistical methods adequately other than state that they used a non-parametric method. They should report exact p-values in table 2 rather than merely having a footnote that all signs are p<0.01. If they feel that the data do show a linear trend with age then they should report the percentage increase (with 95% CIs) for a 10 year increase in age as an additional column to the table. For some reason they do not report the trend values for the combination of signs.

2. They authors should state the follow-up period for obtaining PD diagnosis from hospital and death records since the baseline assessment. Whilst self-reported PD may be specific it would be helpful to check its sensitivity by cross-checking this with reported PD drug consumption. Does the EPIC dataset have medication data? If YES this would be a helpful addition.

3. One important finding which is not discussed is the high percentage of missing data (40%). It is important to try and understand why this occurred so that future studies can improve on this. I have some concerns about the validity of assuming that missing means absence of symptom. Do the authors have their own thoughts given their large experience in undertaking surveys particularly in elderly populations. Other than age, have they looked for other predictors of missingness e.g. gender, order effect of questions. Some subjects may feel that having answered yes already to one or two questions they cannot be bothered to complete the rest. What is the mean number of
symptoms in subjects with or without missing having adjusted for age group? How could we do better in the future? I would welcome the thoughts of the authors.

4. The authors discuss the likelihood of a healthy cohort effect. It would be relatively simple and helpful to use the prevalence survey of Schrag et al (BMJ) and calculate an expected number of cases adjusting for age and hence a standardised ratio for cases with and without the self-reported symptoms. This would quantify the potential bias.

5. There was no justification made for why they choose 5 or more symptoms as diagnostic of PD. Other studies have suggested a lower cut-off I believe.

6. I had some concerns about the validity of the self-reported symptoms for subjects under 65 years. As the authors point out most previous studies are undertaken in older populations as they are usually part of a door to door survey and hence it is not cost-effective to screen younger subjects. The authors report that only micrographia and walking slower show age related increases which is worrying. It is possible for example that the tremor question is detecting subjects with benign essential tremor who will be younger. The low reported frequency of tremor in the PD cases also makes me worried about this question. The authors argue that the lower prevalence of tremor in their cohort may be due to a selection bias. This is true but it would not explain the low rate amongst cases. Tremor dominant cases are if anything milder than those with more predominant akinetic/rigid presentations.

7. The authors should report their search strategy and inclusion/exclusion criteria in the methods section with details of how they undertook their review. I was surprised that for example they did not include the following papers (same project) Screening Parkinson’s disease: A validated questionnaire of high specificity and sensitivity Movement Disorders Volume 10, Issue 5, Date: September 1995, Pages: 643-649; J. Duarte, L. E. Clavera, J. De Pedro-Cuesta, A. P. Sempere, F. Coria, D. B. Calne; Field validation of a method for population screening of parkinsonism Movement Disorders Volume 17, Issue 2, Date: March/April 2002, Pages: 258-264 Maria Dolores Sevillano, Jess de Pedro-Cuesta, Jacinto Duarte, Luis Erik Clavera.

8. I am aware of other papers in this area.

8. I found the discussion of the other papers on the last page of the paper rather difficult to follow. Either they should summarise the study population characteristics in a table or merely highlight possible methodological reasons for discrepancies in their results rather than take us through every study.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The authors provide data on the characteristics of subjects who did or did not drop out in table 1 but yet make no comment on these data or provide any results from hypothesis testing

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Discretionary Revisions (which the author can choose to ignore)

1. Making the paper more informative. I was surprised that the authors did not present the data on the diagnostic utility (sensitivity, specificity etc) of each symptom and their combinations. Perhaps they intend to submit these results as a separate publication, though given the data in table 2 the reader could calculate the all ages measures themselves anyway. Furthermore I suspect in the absence of a true gold standard (either pathology or examination by a movement disorder specialist) it may be hard to publish such a paper. I would suggest that this paper would be more informative if these data were included as an extra table but this decision must rest with them.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research
interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

No conflict of interest