Reviewer's report

Title: Schizophrenia, urbanization and the geographical distance to nearest major road

Version: 1 Date: 26 August 2005

Reviewer: Eadbhard O'Callaghan

Reviewer's report:

General

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

This manuscript address an important point in the epidemiology of schizophrenia and should be classified as an article of importance in its field. It is innovative and clever. The methods are appropriate and well described, and there is sufficient detail (for those fortunate enough to have such data) to replicate the study. The data are sound and well controlled. The manuscript adheres to the standards for reporting and the discussion and conclusions are well balanced and adequately supported by the data (possible proviso, please see below).

The writing is acceptable but could certainly do with some revisions to make it easier for readers. I believe that the manuscript should be accepted for publication.

The manuscript comes from the worlds current leaders in the epidemiology of the psychoses and it with some trepidation I ask for some clarification on a methodological point. If the point is relevant then I would suggest that the authors somewhat temper their conclusions and if irrelevant, we might ask them to explain more clearly why it is irrelevant—in the text, as I suspect many other readers might fall into the same trap as myself.

The paper is based on a reasonable and good hypothesis about the mechanism of the urban/rural effect. But I think there's an important issue here about the probable correlation between their measure of 'urbanicity' and 'distance to nearest road'; i.e. those two things are probably strongly correlated with each other. Perhaps it is my inability to read properly, but I can't find any analysis of this correlation in the paper.

When they look at 'distance to nearest road' without adjusting for urbanicity (first adjustment in the table), 'distance to nearest road' has a weak effect - though it is not a consistent or dose-response type effect. Then they adjust for urbanicity (second adjustment in the table): this is the part I don't fully understand. Because of the likely correlation between the 'distance to nearest road' and urbanicity, the authors are, essentially, adjusting for the very factor they are examining, thus ensuring they get a completely negative result - which they do. So the question is are they are over-adjusting? which is a recognized pitfall in these studies which are awash with data. Adjusting for
what you're looking for is a particular pity, because it dooms you to failure.

In this case, can you really conclude that 'distance to nearest road' is not the mechanism involved in urbanicity? Is it not that 'distance to nearest road' appears to have a weak effect (first adjustment in table) and this effect is not independent of urbanicity (second adjustment in table); i.e. the fact that the association between 'distance to nearest road' and schizophrenia disappeared after adjusting for urbanicity suggests some kind of link between the urbanicity and 'distance to nearest road' -unsurprising. And, (contrary to their conclusions) this observation (the disappearance of the association between 'distance to nearest road' and schizophrenia, when they adjust for urbanicity - which correlates with 'distance to nearest road') provides a kind of passive support for the notion that traffic pollution may, in fact, explain part of the mechanism accounting for excess of schizophrenia in urban areas! It certainly doesn't contradict it, or rule it out.

Based on these data, then, I think they all they could conclude is that 'distance to nearest road' does not have a significant effect on risk of schizophrenia independent of the effect of urbanicity. Of course, given the weakness of the observed association between 'distance to nearest road' and schizophrenia prior to adjustment for urbanicity (the first adjustment in the table), other factors must be additionally or alternatively implicated in the overall urban excess.

This, then, leads us to the classic psychiatry conclusion: while we cannot definitively confirm the effect of 'distance to nearest road' on risk of schizophrenia, we cannot rule it out either - and the data suggest that multiple factors may be involved in the urban/rural effect on risk of schizophrenia; these may or may not include 'distance to nearest road'.

In summary, the only firm conclusion I can draw from these data is that any effect of 'distance to nearest road' on risk of schizophrenia is not independent of 'urbanicity' - and, at best, the weak observed association between 'distance to nearest road' and schizophrenia suggests that 'distance to nearest road' may explain some of the mechanism whereby urbanicity increases risk, but it does not explain it all.

It is important that this point be clarified. If on the other hand it is the ignorance of the reviewer – others may also 'misread' the interpretation. Either way, it would help if it was clarified.

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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)

The second point is minor. The manuscript could do with a 'spring clean'. There are numerous changes of tense (e.g. Abstract, Methods sentence 1 (present) sentence 2 (past) which could easily be cleaned up and since this is likely to be a highly cited manuscript, is certainly worth the effort.

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Discretionary Revisions (which the author can choose to ignore)

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No

**Declaration of competing interests:**

I have no competing interests