Author's response to reviews

Title: Space-time clustering of childhood malaria at the household level: a dynamic cohort

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Version: 4 Date: 4 October 2006

Author's response to reviews: see over
1st Reviewer’s report

Title: Space-time clustering of childhood malaria at the household level: a dynamic cohort

Version: 1 Date: 9 March 2006

Reviewer: Andrew B. Lawson

Reviewer’s report:

General
The paper is clear and well written

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

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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) not clear why Satscan as not used for temporal clustering?

>> This is well taken and our responses are the following:
Indeed, we could have used Satscan for purely temporal clustering: First, in this study we aimed to detect spatio-temporal clusters, not only temporal clusters; second, we have used classical ARIMA analysis in order to show the (already observed) seasonality and detect trend or other temporal patterns, such as moving average or auto-regressive process. These temporal patterns cannot be rigorously analyzed by Satscan. Furthermore, the space-time permutation model analysis is automatically adjusted for both temporal trends and temporal clusters. We have added this clarification in the subsection statistical analysis’ Method section, to prece our interest on spatio-temporal clusters.

2) GIS systems don't provide statistical capabilities and so the comments on page 5 2nd paragraph are really incorrect ...these should be changed.

>> This is very relevant and changes have been added:
"The development of geographical information systems (GIS) has been an indispensable asset to this approach [12]. Together with the progress of statistical methods for spatial analysis, GIS have improved studies for the detection of clusters at high risk of diseases, over space and time."

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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 whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes

Declaration of competing interests: none
Title: Space-time clustering of childhood malaria at the household level: a dynamic cohort

Version: 3 Date: 12 September 2006

Reviewer: Mary Ann Lansang

Reviewer's report:

General

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

(1) Page 9, 1st sentence on "re-infection" vs. "persistent infection"--the authors should provide evidence to show that the prevalence of antimalarial drug resistance is not so high in the village as to negate their assertion that positive malarial smears are re-infections rather than persistent infections. This is critical because the authors define "malaria infection incidence" as "new positive thick blood films" (page 9). Page 14, 1st paragraph, seems to suggest the existence of chloroquine resistance. If they cannot show data on drug resistance, it would be safer for them to refer to "prevalence rates" rather than "incidence".

>> This is a very important concern, and we have added more data on the usage pattern of chloroquine at the Bancoumana site, during the whole study period (1996-2001), and provided the rate of treatment failure over the five years of the study. Chloroquine has been efficacious during the study period, therefore we think appropriate to use the incidence rate for the purpose of this paper. We did add in the "Results" section ("time series" subsection) page 10:

"Chloroquine was efficacious against falciparum malaria during the study period. The dynamic of rate of Good Clinical Therapeutic Responses was 86.7% in 1996, 88.3% in 1997, 97.2 in 1998, 97.1% in 1999, 94.4% in 2000 and 92.5% in 2001."

(2) Page 9, last paragraph under "Variables"--what other covariates were used in the analyses in addition to "thatched roofs"? Did they, for example, include no. of or distance from breeding sites (e.g., temporary backwaters)? age group? other variables?

>>

- We included the "thatched roofs" in the model.
- In order to take into account the "age" covariate and the difference between children and adult infection, the study design did limit the inclusion to children; Because in malaria endemic areas, malaria incidence in adults population are very low.
- Because of the presence of the medical team, the access to treatment was similar all the children. The presence of the study team at the local community health care hospital, have changed the malaria treatment behaviors, and the proportion of self medication was significantly reduced from 1997 (6.5%) to 2000 (0.8%). These data have been added into the paper. We did add in the "Discussion" section page 13: "Correct usage of chloroquine as the first line drug for malaria treatment has reduced significantly the self medication in the village of Bancoumana. The proportion of malaria self medication went from 6.5% in 1997 to 3.8% in 1998, 3.7% in 1999, and 0.8% in 2000 [18]. This was able to reduce chloroquin-resistant malaria parasites at the study site of Bancoumana."
- Anopheles breeding sites are numerous and various (and not only backwaters). During this
study it was not possible to investigate upstream all the breeding sites without any indications. Furthermore the aim of this study was to localize high risk zones. These high risk zones are indications for further field investigations.

First, the association between malaria risk and rainfall is complex (see for example Craig and al. Parasitology Today 1999;15(3):105-11). Second, because of the obvious seasonality of malaria infection in this village, this seasonality was taken into account by the space-time permutation model, which was automatically adjusted for both temporal trends and temporal clusters.

(3) Page 16, 1st paragraph states: "The major risk factors in this village are...", and yet the Methods section only clearly states the inclusion of thatched roofs in the model. No data are shown on the association to age, access to treatment, precipitation levels, breeding sites. These results should be presented.

>> See response to (2). These results are now presented. Following the reviewer's comments, we decide to change this paragraph on the classical covariates and to place it in the "method" section ("variables" subsection).

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) Y axes of Figures should be labeled properly. It is not clear what the measure of "incidence" is in these graphs.

>> Following this recommendation, we labeled the x- and y-axis in the legend of the figures 1 to 7.

(2) Page 7, last sentence and reference under "Study location"—please choose a better citation such as an existing malaria registry, local health statistics, rather than unspecified unpublished data.

>> We did change the sentences, citing works of Dolo and al.:

"Three species of Plasmodium are present: P. falciparum, P. ovale and P. malariae. P. falciparum displays strong predominance, accounting for more than 85% of the parasites found [16]."

(3) Figure 6: please label the "squares" (or dots) properly in the 4 sub-figures—are these households? It would be good to represent households with children who are smear-positive with some other color or symbol in order to better highlight the clusters identified.

>> The dots represent households (we did add this information in the figure legend). In each household several children could be positive or not. We can color the households but it seems to us that it will overload the figure. To facilitate interpretation we did add the Rate Ratio for each presented spatio-temporal cluster.

Discretionary Revisions (which the author can choose to ignore)

(1) In the Background Section, it would be clearer if the authors could list the main reasons or advantages in doing spatial-temporal cluster analysis. Is it to: "reduce high costs of monitoring?", "improve understanding of the disease and control" (specify how)? or is it to identify risk factors? or to identify populations for vaccine trials? By organizing the reasons, there would be a better flow of arguments in the Background Section.
These different reasons are connected and spatio-temporal cluster analysis can improve such studies. Concerning our study, the researcher of the Malaria Research and Training Center (Bamako, Mali), wanted to improve their understanding of the environment related to malaria (in this village), and to detect local risk factor, in order to identify populations for vaccine trial. Following the reviewers comments, we did change the end of the "Background" section and the end of the "conclusion" section.

(2) Suggest add to the title (after the colon): "a dynamic cohort study in a Mali village"--this helps readers doing literature searches to immediately determine the geographic relevance/applicability of the article.

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: Needs some language corrections before being published

We have reviewed the english.

Statistical review: Yes

Declaration of competing interests:
I declare that I have no competing interests.