Author's response to reviews

Title: Sentinel surveillance system for early outbreak detection in Madagascar

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Version: 2 Date: 18 December 2009

Author's response to reviews: see over
Reviewer's report
Title: Sentinel surveillance system for early outbreak detection in Madagascar
Version: 1 Date: 13 November 2009
Reviewer: Carl D'Arcy

Reviewer's report:
This is a straightforward but interesting description of the development of a low cost, innovative, sentinel surveillance system for infectious diseases in developing country (Madagascar). Elements of the model described could be used in other jurisdictions to develop similar sentinel surveillance system. So I feel the paper is worth publishing on those grounds. It is well written, clear and easy to follow. The only minor typos that I noticed were: an extra space before a full-stop in the 2nd line of the paragraph in the section "Overview of the data ...": Corrected
; and the 2nd line in the section "Discussion" should read "...has been weak..." rather than "... has been weakened...": Corrected

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

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

Reviewer's report
Title: Sentinel surveillance system for early outbreak detection in Madagascar
Version: 1 Date: 4 November 2009
Reviewer: Charmaine Gauci

Reviewer's report:
Paper is of publishable standard with some amendments based on comments below:

Background
1. Include a brief description of the infectious disease reporting system in Madagascar, this would be useful for the reader to understand the usual practice for notification of infectious diseases and be able to understand the added benefit sentinel surveillance has in this country.
Paragraph added page 4

2. Give a brief description of diagnostic practices in Madagascar and access to diagnosis in sentinel practices.
Paragraph page 4

3. 1st and 2nd sentences of 2nd paragraph of background should go to methods section.
Corrected - page 5
Methods
1. Describe the geographic distribution of the 13th sentinel practices. Where the practices chosen to be at random geographically? Beside geographical distribution that aims to give the most representative data regarding different bio-climate in Madagascar, sentinel site needs also to fulfill some specific criteria. As recommended by the reviewer, we explained criteria of selection on section “Sentinel primary health care centers” page 6.

2. Case definition. Please clarify if Fever was the first criterion in definition and 4 illnesses were then defined i.e. malaria, ILI, arbovirus, diarrhoeal illness since this is not clear.

Fever is indeed the first inclusion criterion. For all fever, rapid diagnostic test (RDT) for malaria infection is performed by practitioner. Other clinical signs are reported based on case definition of the four illnesses under surveillance. A more comprehensive explanation was added on page 7.

3. Was the notification made on named patient basis or anonymous. Please clarify. If on name patient basis, could links with labs be made?

Notifications are anonymous. Nevertheless for diagnostic purpose, a patient form can be addressed to the lab in order to perform tests. All epidemiological data exchanges between SGPs and IPM are based identification number allocated to each patient. Nevertheless individual results from the lab can be addressed to SGPs. In the future, with data based sharing from epidemiology unit and lab unit, only identification number will be exchanges between lab, epidemiology unit and SGPs. We added sentences in page 7 for a better understanding.

Results
1. Would have liked to see more descriptive results on the four different diseases monitored including age and gender and geographic distribution for each illness apart from frequency.

We agreed with reviewer, but we would like to explain that the aim of this first manuscript was to present the network in relation with the first objective which was to identify outbreaks. To address this objective we use only data collected by SMS. Indeed we received complete forms with at least one week delay make it difficult to early detect an outbreak. However as kindly remark by the reviewer, descriptive results will be interested but this is an ongoing work based on data collected by forms to study the trends according with age and sex but also to compare declared cases and definition cases compliancy.

2. Frequency distribution by seasonality would have been of interest for each disease.

We have the same interest on frequency distribution by seasonality for each disease as mentioned by the reviewer. It is an ongoing study but to have strong evidence of seasonality, shall there is, we need to collect at least 3 years of full data for all our sentinel sites. To date, only some sentinel centers have three years of data that could allowed us to established a forecasting time series models to study seasonality in the different climate pattern.

3. 2nd paragraph of results should be in methods.
Corrected – page 6 and information deleted page 9
Discussion

1. Would appreciate to have seen a discussion on representation of these sentinel practices in terms of
   1. No of GP’s from total GP’s in country
   It is quite difficult to have the exact total number of GPs in Madagascar since the majority of them are not registered in the National council of practitioners. To give an idea of the representation of GPs belonging to sentinel sites we can say that there are 1500 health care centers and to date the sentinel network include only 13 centers. We added this information in the 2nd paragraph of the discussion section page 12.
   2. Geographic representation
   Information in the 2nd paragraph of the discussion section page 12.

3. Population covered
   Information added page 11 and 12 (Rem JMH: information manquante. J’ai fait un début de phrase en page 12
2. Can comparison be made to outbreaks detected by sentinel system to the national surveillance system # showing the added benefit this system has.
   All outbreaks detected by this sentinel surveillance were not detected by national surveillance system. This information was added the last paragraph of the discussion page 13
3. Comment on use of sentinel surveillance for trend analysis over time.
   Comment inserted page 13 voir ma remarque

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

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

Reviewer's report
Title: Sentinel surveillance system for early outbreak detection in Madagascar
Version: 1 Date: 15 October 2009
Reviewer: Salah Mahmud

Reviewer's report:
The authors are to be commended for designing and implementing an innovative sentinel surveillance system, and for their willingness to share their experience with others. I hope the following comments are of some help to the authors.

- Major Revisions
  1. If possible, provide a brief description of any surveillance systems (syndromic or otherwise) for febrile/diarrheal illnesses that may have existed in Madagascar when the new sentinel system was being designed and implemented. This essential context could help the readers understand the full significance of the new system. If such systems existed, were they replaced by the new system? If not, how does the new system complement the older systems?
  A paragraph has been added on page 4.
  The sentinel system doesn’t replaced anterior surveillance system. It is a complement and its objective is to detect earlier outbreak situation. Data are collected and analysed daily. Likewise with traditional surveillance system data are...
collected weekly and more often monthly. In fact, healthcare information is used to report annually aggregate statistics for Ministry of Health

2. The criteria for selecting a sentinel site are mentioned briefly (e.g., care level, no of GPs). It will be helpful if the authors could expand on this important element of the system design (e.g., what is meant by care level? What is the cutoff point for no of GPs used to institute a sentinel center in particular area?)

A more comprehensive explanation has been added on section “Sentinel primary health care centers” page 6

3. The case definition for suspected malaria cases (fever) seems very non-specific and overlaps with other case definitions (e.g., ILI, arbovirus). Please clarify whether a more specific presentation for malaria was used (e.g., periodic or recurring fever patterns).

At the beginning of the network, we have defined malaria suspected case because we thought that SGPs didn’t systematically used malaria rapid diagnosis for each fever syndrome. In fact, we have a good compliance for this practice. Thus, suspected malaria cases was erased in the corrected manuscript because we don’t use anymore this syndromic data and we never analyzed this data. In this surveillance system, only confirmed cases were analyzed (i.e RDT positive). Also, please specify the name (and give reference if possible) for the rapid diagnostic test used to diagnose malaria in the clinics. The reference of the RDT was added on page 7

4. The arbovirus case definition could overlap significantly with ILI. Was that a concern when the system was designed?

We agree with the reviewer that arbovirus case definition somehow overlap ILI but taken into account WHO case definition for these two illnesses, we felt that respiratory symptoms is more likely to be specific of ILI than arbovirus. Thus fever with respiratory symptoms and any other signs will be referred as ILI while fever without respiratory symptom and at least two other symptoms among headache, arthralgia, myalgia-like backache, skin rash, retro-orbital pain, haemorrhagic manifestations will be referred as Arbovirus-like infection. At the same time, we are aware that using only clinical signs to a diagnosis an illness could induce some bias due to the solely interpretation of GPs. Nevertheless, we tried to reduce at the maximum these bias using most likely case definitions.

5. Please, clarify how “aberrations” and “signals” of potential outbreaks were detected. Signals were detected by daily medical epidemiologist analysis

Was that based on comparisons with seasonally-adjusted averages or other baseline measures of syndrome incidence?

Unfortunately, because of the lack of daily historical data and due to low years of observation, we only detected aberration, in a first time, by a closer empirical examination of surveillance data collected daily.

How much deviation from baseline was required for 10 suspected outbreaks to be reported to the district health authority?

Baselines were unknown currently because since the set up of this sentinel sites, no daily historical data are available.

This is important because the interpretation of syndromic surveillance data is usually a significant challenge. Achieving the right balance between sensitivity and specificity is not easy.

The reviewer is totally right and indeed, this will be our future challenge
6. Since the implementation of this system, were there any outbreaks that were not detected by the sentinel system? In other words, what was the sensitivity of the system for outbreak detection?

All the outbreak occurred in the sentinel network have been detected. However, without historical data it was difficult to give a threshold. All recent signals are focused on increasing syndrom in relation with human permanent analysis. Actually the system must now identify the threshold for each center and for each syndrome. So, alert will be included in the data base forms. However the thresholds will not be fixed and varied according with the season if a seasonality trend was found. We are working to forecasting model able to calculate the threshold day after day.

7. Not sure what the authors mean by “selection bias” in reference to the fact that GPs were self-selected. Certain areas may have lacked GP volunteers, but that would not be considered selection bias. It will simply mean that the system is not sensitive enough for the purpose of detection of outbreaks from those areas (i.e., the system is not representative of the whole country, which is different from being “biased”).

We agree with the reviewer and we have corrected this page 11

8. When evaluating a surveillance system, there are other important considerations that the authors did not discuss. The authors discuss in detail the system costs and certain operational aspects (e.g., data transmission). However, there is little discussion of other important aspects of the system including the validity of outbreak detection (e.g., the positive predictive value of the detected signals) and timeliness of the detection (e.g., was the new system able to detect outbreaks early on? and if so by how much? Could these outbreaks have been detected in a reasonable time even in the absence of this system?).

Determining the optimal sensitivity and PPV of sentinel network is a challenge. A judgment must be made between timeliness and quality. Concerning the ability to detect outbreaks, which is the main reason sentinel network was implemented for; significant events may be missed if the system is not sensitive enough. Conversely, a system too sensitive will trigger multiple false alarms. In addition, because the true incidence of a disease in an outbreak is unknown, it is difficult to estimate the PPV of sentinel network, although across time the PPV is most likely to be very low. During an outbreak as the incidence of disease rises, the PPV should also rise. Determining the cut-off for sensitivity and PPV is an ongoing analytical problem that should continue to be refined as more historic data are collected. Outbreaks detected by this implemented sentinel surveillance system were not detected by traditional system. We are intimately persuade that in the absence of this sentinel network, outbreaks are more likely not to be detected in a reasonable time for an rapid response. We added sentences on page 11 (1st sentence in “outbreak investigation”) and 13 (last sentence). Other important considerations include acceptability of the system to its users (e.g., GP adherence rate).

To estimate acceptability of the system we use an indirect indicator : the daily data transfer rate estimated à 89% (e.g; page 9).

System costs should also include the time cost to the volunteer GPs.

We added the time cost on page 12
9. In the absence of some of these important details, it is difficult to assess whether the authors’ conclusion re the benefits of implementing this system were justified. We thank the reviewer for his pertinent remarks. We hoped that we have addressed all inquiries and improved the quality of this manuscript.

- Minor Revisions
1. Please clarify the meaning of the following statement “In general, virological indicators do not allow normal viral circulation to be distinguished from a potential epidemic situation. Actually, the essential elements needed to plan for the prevention and control of epidemics cannot be obtained from a system based on virus surveillance alone, but requires a system based on combined epidemic criteria.” It is not obvious to me what the authors mean by “virological indicators” and “combined epidemic criteria.”

Biological surveillance alone can only detect circulation of virus in the population but cannot quantify its importance. Virological indicators are positive virological results. Combined epidemic criteria are a system based on both virological and clinical surveillance.

To clarify this statement, we changed “virological indicators” with “virological surveillance” on page 4.

2. The WHO ILI case definition is fever and cough OR sore throat. The authors’ case definition is more specific (cough AND sore throat). What is the rationale for using the less sensitive case definition? The reviewer is right but we used the French translation of WHO case definition for ILI. After the remark of the reviewer we looked after the English version and found this discrepancy. To date we are aware of this difference and we will correct this case definition in the future. Since this difference was however, using more specific definition is interesting for biological surveillance when the laboratory capacities are limited. We have more chance to analyse positive samples and find viral circulation in relation with an exceed of fever. We would like to point out that the trend analysis of the network is not only focused on ILI cases but in first on increasing fever cases.

3. I am curious why axillary temp was used to define fever instead of more accurate methods (oral temp in adults and rectal temp in children). Was this decision based on the preferences of the participating clinicians? In fact in Madagascar SGPs used axillary method to measure the temperature because it doesn’t required necessarily a full disinfection after use.

4. The section labelled “supervision” is more of commentary rather than a description of the methods. It should be moved to the discussion section.

The paragraph was moved to discussion section page 12

5. Figure 2 is not described in the text. It is not clear what was the purpose of including this figure, as it mostly duplicates the information presented in figure 5.

We fell that information in figure 2 is different than information in figure 5. We demonstrated the interest for time–series analysis to transform data with as a first step the average moving smoothing.
The information presented in Figure 4 is not interesting and the figure could therefore be deleted. **We decided indeed to delete Figure 4.**

6. The following section labelled “ability to detect outbreaks” belongs to the results rather than the methods section. **With all respect due, we considered disputable to move this paragraph in the results section because we found important to describe in the Method the processes of outbreak detection.**

7. Please spell out MoH when first mentioned. **Corrected page 4**

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