Author's response to reviews

Title: Perceived morbidity and community burden after a Chikungunya outbreak: the TELECHIK survey, a population-based cohort study

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Author's response to reviews: see over
Perceived morbidity and community burden after a Chikungunya outbreak:

Reviewer's report (Jean-Paul Boutin):

1- Major Compulsory Revision.

The main outbreak took place between November 2005 and June 2006. The initial investigation "SEROCHIK survey" was conducted between August and October 2006. The "TELECHIK survey" reported here, was conducted between November 2007 and May 2008. So the authors can claim (line 175) that the average time between SEROCHIK and TELECHIK is 16 months (range 13-20 months). However, data collected, analysed and presented in this paper does say that this study has been done "two years after infection (Abstract, line 48) or that the study was done" two years after the fall of the epidemic "(Abstract, line 34) or "nearly two years after the onset of infection" (Discussion, line 230; or Conclusion, line 335) because no data presented here does not specify the expected date of infection by CHIKV, nor that this data was collected for CHIKV + patients, and TELECHIK began 16 months after the fall of the epidemic.

Authors should be wary of this approximation, although it is tempting to say that this study has been made "about" two years after the health catastrophe suffered by the islanders. In practice TELECHIK was probably conducted at the earliest, 17 months after the suspected infection of last patients (if infected in June 2006 and interviewed in November 2007) and later, 30 months after the suspected infection of first patients (if contaminated in November 2005 and questioned in May 2008). However, it is risky to say that the average time between 17 and 30 months is just 24 months!

Authors should revise these statements, or provide additional data.

Precisions concerning the time between onset of infection and the telephone survey (only available for the true positives) have been given for symptomatic CHIK+ subjects (see lines 183-184). Symptomatic CHIK+ subjects were interviewed in average 23.8 months after the acute infection (Q_1-Q_3: 21.9-24.9 mo, mediane: 23.7 mo, mode: 25 mo, range: 15-34 mo), 90% of whom beyond 20 mo. It would therefore be cautious and reasonable to keep an average decline of two years, nevertheless to fulfill the reviewer recommendation, we have replaced two years in the text by in average two years. For further details see the curve depicting the distribution of time between onset of infection and the telephone survey, the table of delay percentiles.

2- Minor Compulsory Revisions.

In Methods:

A more explicit definition of subjects “NKP” and “NKN” is desirable. An example would be useful.

Precisions have been given in lines 99 and 101 in order to better ascertain those who did not remind their symptoms or their serostatus.

In Results:

The age distribution of participants (line 170) and their sex ratio (line 172) does seem, a priori, not representative of islanders’ population when comparing the distributions of Table 1. What is it really?

The population sampled in TELECHIK was a little skewed towards older participants and women. This may have a little overestimated the clinical burden of CHIK-V, the elderly being more sensitive to musculoskeletal pains, fatigue, sensorineural impairments, the women more sensitive to fatigue and cerebral disorders (mood disturbance). However, we took into account
the case-mix representativeness to minimize the selection of people more present at home in home surveys or telephone surveys. Nevertheless, this participation bias is not specific of the TELECHIK survey. It has been encountered in all household surveys conducted in La Réunion and depicts the imbalance of persons present/absent at home at the time of interview. Though, it is difficult to quantify, we believe this bias is unlikely to affect significantly the burden of Chikungunya in La Réunion.

In Discussion:
Line 326; reference 17 does not seem good. Is this not rather reference 16?
Reference 17 was replaced by reference 16
In References:
Line 462; correct the year of publication in reference 28.
The year 2008 has been specified

In Tables: All tables have the same layout problem. The right column is always truncated.
The arrow was shifted to the left to not truncate the right column

3- Discretionary Revisions
None

Reviewer's report (Manmohan Parida):
The MS entitled “Perceived morbidity and community burden after a Chikungunya outbreak: the TELECHIK survey, a population based cohort study” by Patrick et. al. described a systematic retrospective survey on clinicoepidemiological pictures of Chikungunya outbreak. As the title indicates, this is a simple telecheck survey and thus neither having any science nor adding any new information to the Chikungunya disease. Hence I personally feel the MS is not suitable for publication in BMC Medicine.

Reviewer's report (Scott C Weaver):
This paper by Gérardin et al. describes a retrospective telephone survey of a large cohort of La Reunion residents sampled after the apparent end of the chikungunya epidemic. Chikungunya antibody-positive and –negative people were compared for a number of chronic manifestations, and statistical analyses indicated that 33% of joint pains, 10% of cerebral disorders and 7.5% of sensorineural impairments could be attributed to chikungunya virus infection. This is an important study documenting more rigorously than ever before the persistent symptoms due to an important, re-emerging arboviral disease. Although I am not an expert on the epidemiological statistics, the analyses appear to be thorough and the results robust.

Major Compulsory Revisions
1. An important topic that deserves some discussion is whether the 2004-present CHIK outbreak shows any evidence for a change in virulence over Asian outbreaks from the 1950s until 2004.
This important remark has been addressed in the discussion in the paragraph ranging from line 313 to line 317.

2. Line 112: The phrase “adaptive property to the human host” suggests that the vector had recently adapted to feed on humans, but the reference describes virus adaptation to the vector. If the latter is intended, then Tsetsarkin et al., who demonstrated more conclusively through reverse genetics this adaptation, should also be cited.
The sentence has been changed to address the important remark of Dr Weaver. In fact, the anthropization of Aedes albopictus was known for a while in La Réunion (see new reference 31). As stressed by the referee, it was mainly the virus adaptation to the vector which triggered the outbreak at the end of 2006. The adaptive property of *Ae albopictus* to the human host and its strong ecological plasticity contributed rather to sustain the transmission over time than to initiate the outbreak. Tsetsarkin et al. have been cited as recommended.

3. Line 175: A recent recrudescence in chikungunya infections has been reported in La Réunion. If there any possibility that infections occurred between the serosurveys and this telephone survey?

The ongoing recrudescence observed in La Réunion (153 cases) started in March to October 4, 2010, long after the survey was conducted (November 2007 to May 2008). Recent case-investigation demonstrates that infections occur on naïve subjects (positive RT-PCR or positive IgM but not IgM-/IgG+). After being silent for three years (June 2006 to August 2009), the CHIK has reemerged a first time from Madagascar leading to five sporadic cases in the commune of Saint-Paul (D’Ortenzio E et al., Euro Surveill. 2009), then in March 2010, from Madagascar, Bali or Indonesia leading to endemic low-noise transmission (112 confirmed, 41 suspected cases on October 4, 2010 further details available on monthly CIRE bulletin: [http://www.invs.sante.fr/regions/reunion_mayotte/pe_rm_chik_66_051010.pdf](http://www.invs.sante.fr/regions/reunion_mayotte/pe_rm_chik_66_051010.pdf)).

Minor Essential Revisions

4. Throughout: chikungunya should not be capitalized

   Throughout has been replaced by over

5. The manuscript should be read carefully by a person with strong English skills to correct minor grammatical errors and occasional, subtle inappropriate word selections.

   The manuscript has been read by two English native speakers

6. Line 172: What accounts for the unequal distribution of subjects by sex?

   The population sampled in TELECHIK was a little skewed towards older participants and women but though it may have a little overestimated the clinical burden of CHIKV, the bias is unlikely to be significant because we took into account the case-mix representativeness to minimize the selection of people more present at home at time of interview. This participation bias is not specific of the TELECHIK survey, it has been encountered in every home surveys conducted in La Réunion (see also above the response to JP Boutin)

7. Discussion: How do the levels of the symptoms surveyed compare between La Réunion and other communities of similar socioeconomic conditions that did not suffer a chikungunya outbreak? Are there any comparable data from other locations?

   To the best of our knowledge, we are not aware of the levels of symptoms in other communities of similar socio-economic conditions not exposed to chikungunya. For instance, the UK gives us valuable information on the baseline rate of musculoskeletal pains but the source of information uses QoL questionnaires (SF36, SF12), not a merely symptom elicitation by telephone interview, as done in the TELECHIK survey. Currently, there are many ongoing cohorts (NUTRINET, SUVIMAX, GAZEL, etc…) in Europe encompassing health perceptions modules, but their findings are still pending. Studies on health perception of dengue have focused on the determinants of infection. Thereby, no comparable data from other locations free of Chikungunya exists to date.