Author's response to reviews

Title: No evidence of decline in malaria burden from 2006 to 2013 in a rural province of Gabon: implications for public health policy

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Author's response to reviews:

Reviewer 1

1. This reviewer identifies apparent errors in the monthly number of cases reported, and in the deduced estimates of annual incidence. We have checked our calculations and found no error in our estimates. We therefore cannot “correct” the errors identified by the reviewer. Our calculation was carried out as follows, and I think that the reviewer will agree that it is correct: the period reviewed (January 2006 to March 2013, omitting 2010) was 75 months long (and not 63 months, as incorrectly stated by the reviewer). In total, 11,600 malaria cases were analyzed, giving 11,600/75 = 154.7 confirmed malaria cases per month (and not 110.5, as calculated by the reviewer). The monthly number of malaria cases reported in the initial version of the manuscript has therefore not been modified in the revised version. However, concerning the point raised (see our response to point 2 below) about the population of Ogooué-Ivindo used as denominator, we have adjusted the annual incidence to 72.30/00 (154.7x3x12/77) in the revised version (as opposed to 92.80/00 in the initial version of the manuscript). See lines 172 to 174.

2. As suggested, our estimates of the size of the population served by the health facilities of Ogooué-Ivindo province have been recalculated based on the most recent data from the "Direction Générale des Statistiques du Gabon". The Ogooué-Ivindo province had 48,862 inhabitants in the early 1990s (1993 census) and 64163 inhabitants 10 years later (2003 census) indicating a mean annual population increase of 3.13 % over the decade concerned. Based on the data reported in the 2003 census, this would give population estimates for 2006, 2007, 2008, 2009, 2011 and 2012 of 70 378, 72 581, 74 853, 77 195, 82 104 and 84 673, respectively, with an overall population of the province of about 77 000, on average, for this period. The average incidence calculated over the study period and the annual incidences have been adjusted accordingly on the basis of these demographic data. These changes have been introduced into the revised manuscript (lines 108-116 and 174-181).
3. According to the population pyramid of Gabon, children between the ages of 0 and 4 years accounted for 14.6% of the population in 2010, with 24% of the population aged 5-14 years, 47.2% aged 15-50 years and 13.2% over the age of 50 years. Thus, in the Makokou region, almost 50% of malaria cases occur in children under the age of five years, but this age group accounts for only 14.7% of the total population of Gabon. As suggested by the reviewer, the population denominators for the various age groups used to estimate the age-related risk of malaria in the Ogooué-Ivindo were deduced from the age-structure of the Gabon population. The age-specific incidence rates were calculated and now provides in the table I in the revised version. (Table I and lines 537-541).

4. As requested, the symbol 0/00 has been inserted, where appropriate, in the revised version.

5. We agree with the reviewer that it is difficult to determine the level of endemicity of malaria in the Makokou region accurately, because malaria cases were recorded during the passive screening of febrile outpatients. However, the high rate of positive slides (53.6%) is consistent with a high level of transmission in the region and with the work of Hay et al., (A world malaria map: Plasmodium falciparum endemicity in 2007), classifying Gabon, including its northern regions in particular, as hyperendemic for malaria (PfPR2-10>50%). However, we have taken the reviewer’s comment into account, by removing the term "hyperendemic" from the revised version (line 186).

6. As suggested, we have included the putative incidence of malaria in the study area in the revised version of the manuscript “suggesting that the real incidence of falciparum malaria is likely to be currently about 2000/00 in the rural area of Makokou” (lines 314-315).

7. The reviewer raised concerns about quality assurance and the standard operating procedures for malaria diagnosis. He asked whether the laboratory responsible for the diagnosis of malaria cases was accredited by an external quality system. We have confidence in the data for malaria cases reported, because the CIRMF has a long-standing collaboration with the Ogooué-Ivindo health district and we know how the laboratory staff work. In addition, comparative surveys conducted since our study at the Makokou health facilities revealed the concordance rate between microscopic examinations and RDT readings to be high, at about 76%. However, in Makokou, as in the vast majority of the health facilities (public or private) devoted to malaria diagnosis in Gabon (and in Africa, in general) there is no systematic quality control of slide readings. This is indicated in the revised version (lines 268-272).

Reviewer 2

1. This reviewer was concerned about the replacement of microscopy methods with RDTs in remote areas of Gabon. We agree that RDTs are a possible alternative to microscopy for malaria diagnosis, particularly in rural settings. Studies of the possible systematic use of RDTs for malaria at health facilities at
Makokou are currently underway, and the comprehensive results of these surveys will be released as soon as they become available. However, our preliminary data show a fair degree of concordance (76%) between microscopy and RDT results. These findings have yet to be published, but are reported in the revised version (line 272) to provide the reader with as complete a set of information as possible.

2. The other issue raised by the reviewer relates to the increase in the number of malaria cases observed over the study period. The reviewer argues that this increase may be due to improvements in screening conditions or an increase in the frequentation of Makokou health facilities. We agree with the reviewer that this factor may have made some contribution to the malaria trends observed, but this was clearly not a major issue, as the number of cases increased from 1173 in 2006 to 3157 in 2012, corresponding to an increase by a factor of 5.3 over the period, whereas the population increased by a factor of only 1.2 over this period. This is now stated in the revised version (lines 288-290).