

Yellow fever burden estimation: Summary

Tini Garske¹, Maria D Van Kerkhove¹, Sergio Yactayo², Olivier Ronveaux³, Rosamund F Lewis⁴, J Erin Staples⁵, William Perea², Neil M Ferguson¹ with the YF Expert Committee*

¹ MRC Centre for Outbreak Analysis, Imperial College London, UK, ² WHO, Geneva, Switzerland, ³ Immunization and Vaccine Development, WHO/AFRO, Ouagadougou, Burkina Faso, ⁴ Ottawa Public Health, Ottawa, ON, Canada, ⁵ Arboviral Disease Branch, CDC, Fort Collins, CO, United States

*Expert Committee members: Donald Burke, Fernando De La Hoz, Bryan Grenfell, Peter M Hansen, Raymond Hutubessy, Rosamund Lewis, William Perea, Olivier Ronveaux, Erin Staples, Sergio Yactayo

Scope of the project

Yellow Fever (YF) is an acute, haemorrhagic viral disease transmitted to people of all ages by infected mosquitoes. YF infection can vary in intensity, from asymptomatic disease to a severe illness that leads to death in 20–50% of patients. There is no specific treatment however the most effective measure to prevent and control YF is through vaccination. In fact, a single dose of the YF vaccine has been shown to protect individuals from contracting the disease for as long as 35 years and the protection may be life-long.

In recent years, there have been attempts to quantify the burden of YF both in geographic extent and burden, for the purposes of advising travellers regarding the necessity of vaccination¹ as well as for the purposes of targeting vaccination campaigns within endemic countries to the most affected areas and evaluating their potential impact^{2,3}. However, the most recent global estimates of the yellow fever burden stem from the 1990s and estimate that there are approximately 200,000 cases and 30,000 YF deaths each year, 90% of which occur in Africa.

During the October 2011 Quantitative Immunization and Vaccine Related Research (QUIVER) meeting held at WHO headquarters in Geneva, however, QUIVER's Advisory Committee recommended WHO to establish a working group to explore modelling techniques and review data from surveillance systems to measure the YF disease burden in Africa. Following discussions with the QUIVER Secretariat, it was suggested that an expert committee be convened by WHO to meet and agree on objectives, processes and timelines to make such estimates.

The first meeting of the Yellow Fever Disease Burden expert committee⁴ was held in Geneva in January 2012. Participants discussed past YF burden work, YF data availability, and agreed on a work plan to estimate YF disease burden in Africa. In this brief summary, we provide an overview of the methods used to estimate burden and our main findings.

Methods to estimate Yellow Fever Burden in Africa

The work plan was implemented in two stages. Stage 1 focused efforts in searching for and collating all published and unpublished data on YF. In addition to data available in published literature and reports,

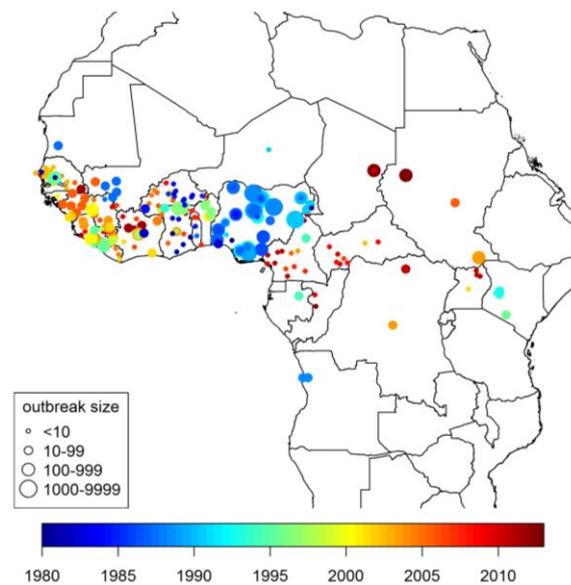


Figure 1: Outbreaks of yellow fever between 1980 and 2012.
Legend: Colours indicate the year of the outbreak, symbol sizes the approximate number of reported cases.

¹ Jentes ES, et al. The revised global yellow fever risk map and recommendations for vaccination, 2010: consensus of the Informal WHO Working Group on Geographic Risk for Yellow Fever. *The Lancet Infectious Diseases* 2011;11(8):622-32

² Briand S, et al. Assessment of Yellow Fever Epidemic Risk: An Original Multi-criteria Modeling Approach. *PLoS Negl Trop Dis* 2009;3(7):e483.

³ Yellow Fever Task Force. Yellow Fever Stockpile Investment Case: World Health Organisation, Unicef, 2005.

members of the expert committee shared data on ongoing epidemiologic surveys for YF, past outbreak reports, surveillance data bases in the African Region and other WHO publications.

Stage 2 used available published and unpublished sources of data on reported YF outbreaks by province in 32 African countries from 1987 to 2011 (Figure 1), surveillance data from the African Regional Office of WHO, YF serological studies, data on vaccination campaigns and coverage in human populations, population demographics, and environmental data including temperature, rainfall and land cover; these datasets were used to develop generalized linear regression models to estimate the burden, that is the number of infections, severe disease and fatalities, due to YF in Africa. An indicator of surveillance quality by country was also included in the models. The model was consistent with reported case data across Africa as well as the available serological datasets.

From the model predictions, the annual risk of an individual becoming infected was estimated and converted into the expected burden across the endemic African countries, taking into account the probability that a case would be detected in each country. Then the impact of the recent GAVI funded YF mass vaccination campaigns since 2006 in 12 countries was estimated. Input on these methods from the Yellow Fever Burden Expert Committee was sought via periodic teleconferences.

Results

We estimate that YF currently infects between 840,000 and 1.7 million individuals in Africa each year, resulting in approximately 84,000 – 170,000 cases and 29,000 – 60,000 deaths (Table 1). This assumes that approximately 10% of infections will develop severe symptoms including jaundice and 35% of severe cases will die (Staples personal communication). The risk of infection varies by country, with highest rates of infection found in West Africa. Our estimates evaluated for the year 1995 are very similar to the previous estimates. The estimates for 2013 are lower due to the substantial mass vaccination activities implemented since 2006. Indeed, the GAVI vaccination investment was estimated to have reduced the YF burden in the 12 investment countries by 56% (95% CI 54 – 60%) (Figure 2).

This work is currently undergoing peer-review and is due to be published in its entirety later this year.

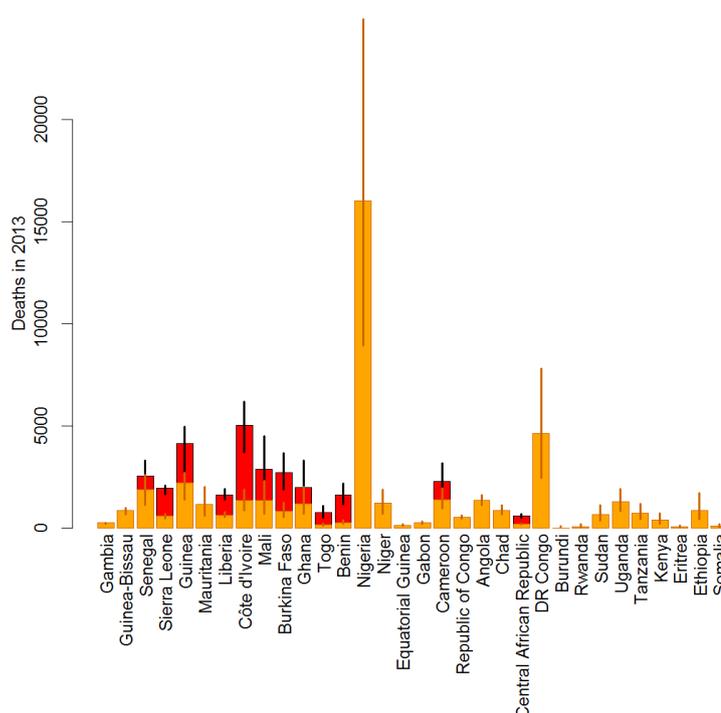


Figure 2. Impact of preventive mass vaccination campaigns between 2006 and 2012 on the estimated number of deaths due to yellow fever in 2013 by country. Orange bars: number of deaths estimated for 2013, red bars: number of deaths averted by the preventive mass vaccination campaigns. Countries are ordered west to east.

Table 1. Estimated number of yellow fever infections, cases and deaths in the 32 YF endemic African Countries. The numbers of infections, cases and deaths predicted to be averted by the GAVI programme in 2013 are also shown.

Year	Estimated Number in thousands (95% Confidence Intervals)		
	Infections	Cases*	Deaths
1995	1600 (1100 - 2100)	160 (110 - 210)	54 (38 - 72)
2005	1800 (1200 - 2400)	180 (120 - 240)	62 (43 - 83)
2013	1300 (840 - 1700)	130 (84 - 170)	44 (29 - 60)
averted by GAVI vaccination estimated for 2013	460 (350 - 560)	46 (35 - 56)	16 (12 - 20)

*Cases = matches YF case definition based on jaundice