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Research Letter

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What is the reproductive number of yellow fever?

Ying Liu[1] **and Joacim Rocklöv**[2,3]

[1]School of International Business, Xiamen University Tan Kah Kee College, Zhangzhou 363105, China, [2]Department of Public Health and Clinical Medicine, Section of Sustainable Health, Umeå University, Umeå, Sweden and [3]Heidelberg Institute of Global Health, University of Heidelberg, Heidelberg, Germany

*To whom correspondence should be addressed. Tel.: +46706361635; Email: joacim.rocklov@umu.se

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Yellow fever is a viral vector-borne disease caused by the yellow fever virus with its geographic distribution currently limited to sub-Saharan Africa and South America. The case fatality rate of hospitalized severe yellow fever is above 40%.[1]

The basic reproductive number, R_0, can be used to characterize the epidemic potential of a pathogen by assessing the number of secondary cases that would be generated by one infectious case if it was to be introduced into an immunologically naïve population. R_0 values that are larger than 1 indicate epidemic growth; values around 1 represent endemicity and for values below 1, the outbreak is declining and the number of new infections will be decreasing in subsequent generations. We conducted a review of published peer-reviewed literature on the estimates of the basic reproductive number of yellow fever and discuss the implications for herd immunity in relation to the critical vaccination levels.

We conducted searches on PubMed and Web of Science with the following search terms 'yellow fever AND (R_0 OR basic reproductive number)'. The restriction on published article language was English. We included all publications from 1950 until August 2020. Our review excluded the estimates of the effective reproductive number that depends on the background level of immunity.

A total of 31 studies were identified through the literature search based on these search terms. We excluded 23 studies because of ineligible or incomplete outcome data. Eight studies were included in the final analysis. Overall, 11 data points were collated from the included studies. R_0 estimates were derived for a variety of countries, study years and methods as provided in Table 1. The estimates range from 1.35 to 11. The average R_0 was 4.81 with a median of 4.21 and an interquartile range of 2.19.

The R_0 estimates appear to vary between studies. Partly, this can be related to methodological differences, but also different local susceptibility and exposure to vectors, i.e. which could be emphasized during due El Nino period and in warmer climate. A relationship between R_0 and climate has been observed for other viruses transmitted by the same vector (Liu *et al.*, 2020 in Supplementary data).

The R_0 is an important number for elimination and it should be considered at a high average/aggregation level over time and space as it is the long-term elimination that is being considered.

With increasing global travel patterns (at least before the COVID-19 pandemic), the risk of importation of yellow fever to vulnerable countries where the vector is present but no adequate vaccination coverage exists is high.[10] The critical vaccination level corresponds to the proportion of population that need to be vaccinated to achieve herd immunity assuming the population is vaccinated at random and that the population is mixing homogenously. Therefore, in the hypothetical situation when a vaccine is 100% effective (i.e. $E = 1$), the critical vaccination level equals the herd immunity level, $V_c = 1 - \frac{1}{R0}$; otherwise it is $V_c = \frac{1-\frac{1}{R0}}{E}$. Assuming a vaccine efficacy of 99% [30 days after vaccination (WHO, 2019 in Supplementary data)], we calculated that the critical vaccine coverage levels need to be between 26.2, 77.0 and 91.8% according to the minimum, median and maximum R_0 values, respectively. Reaching very high V_c levels, such as 91.8%, for herd immunity is logistically not feasible in many current settings.

We conclude that vaccine coverage thresholds may vary between areas and countries as the basic reproductive number can vary substantially in different localities.

Supplementary data

Supplementary data are available at *JTM* online.

Table 1. Published estimates of R_0 for yellow fever

Study	Location	Study year	R_0 estimates	Method
Zhao *et al.*[2]	Luanda, Angola	2015–2016	6(range 4–8)	Estimated from mathematical compartmental based model
Kraemer *et al.*[3]	Angola	2015–2016	4.8 (95% CI: 4.0–5.6)	Formula linking to the exponential growth rate and the generation time distribution
Wu *et al.*[4]	Angola	2016	5.2 (95% CI: 4.3–6.1)	Wallinga and Teunis method, assuming mean mosquito lifespan = 7 days
Wu *et al.*[4]	Angola	2016	7·1 (95% CI 5.5–8.7)	Wallinga and Teunis method, assuming mean mosquito lifespan = 14 days
Kennedy *et al.*[5]	Memphis, Tennessee, USA	1878	11	Estimated from mathematical compartmental-based model
Johansson *et al.*[6]	Asuncio'n, Paraguay	2008	4.1	Using moderate literature estimates of the parameters for the human infectious period, R_0 = average number of infectious mosquitoes produced per infectious human ∗ the average number of infectious humans produced per infectious mosquito
Curtis *et al.*[7]	New Orleans, USA	1878	2.38	R_0 was calculated at the neighbourhood level applying a mathematical equation; Constrained
Curtis *et al.*[7]	New Orleans, USA	1878	3.59	R_0 was calculated at the neighbourhood level applying a mathematical equation; Unconstrained
Massad *et al.*[8]	Sao Paulo State, Brazil	2001	3.23 (range 1.62–6.61)	Calculate R_0 for yellow fever for every city that R_0 of dengue>1, using a mathematical function of R_0 for dengue with dengue cases
Massad *et al.*[9]	Sao Paulo State, Brazil	2000	4.21(range 2.39–8.59)	Estimate R_0 of yellow fever using a mathematical function of R_0 for dengue with the annual outbreaks of dengue in 2000
Massad *et al.*[9]	Sao Paulo State, Brazil	1991	1.35(range 1.07–1.66)	Estimate R_0 of yellow fever using a mathematical function of R_0 for dengue with the annual outbreaks of dengue in 1991

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Conflict of interest

None declared.

Author contributions

J.R. had the idea, and Y.L. did the literature search and created the table. Y.L. wrote the first draft; Y.L. and J.R. drafted the final manuscript. All authors contributed to the final manuscript.

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