ESTIMATING CASE FATALITY RISK FOR SEVERE YELLOW FEVER CASES: A SYSTEMATIZED REVIEW AND META-ANALYSIS

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INTRODUCTION

- Case fatality risk (CFR) is the probability of a disease case being fatal. It is sometimes called the case fatality ratio or case fatality rate synonymously[1].
- CFR for diseases has been estimated by case reports[2] or through systematic review[3].
- Yellow Fever, a flavivirus spread by mosquitoes, is endemic to sub-Saharan Africa and Latin America. Cases can be asymptomatic, mild, or severe[4].
- The WHO estimates that approximately 50% of Yellow Fever cases are fatal[4,5], but this estimate has not been systematically verified.
- This study aims to estimate the case fatality risk for severe Yellow Fever cases through a systematized literature review and meta-analysis.

METHODS

- Systematized literature review[6], with search strategy run in PubMed and Ovid Medline on June 11, 2019
- Aimed to collect proportions of severe Yellow Fever cases that were fatal with a numerator and denominator.
- Cases in literature determined to be severe based on WHO criteria: fever accompanied by at least one of jaundice or hemorrhaging[4].

Search strategy:

("Yellow Fever" in the title, abstract, or MeSH term)

AND

(fatal*, severe, severit*, mortality, asymptomatic, symptomatic, diagnosis, misdiagnosis, outbreak, or cases in multiple places)

AND NOT

("Vaccine" in title or abstract)

- Data analyzed using meta-analysis: logistic intercept-only meta-regression, with random effects for study.
- Inputs for meta.prop() function[7] in R included proportions and their estimated standard errors.

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Case fatality risk is estimated to be 39%, which is lower than the current WHO estimate

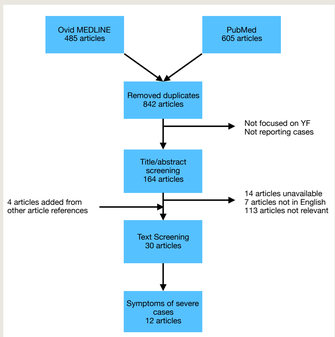

Figure 1. Overview of search strategy and inclusion/exclusion of articles

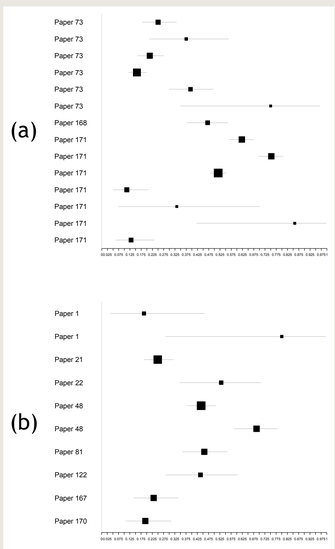

Figure 2. Forest plots of fatality proportions of (a) suspected and (b) confirmed severe Yellow Fever cases.

Table 1. Numbers of articles and proportions for confirmed and suspected YF case data.

Confirmed cases	8 articles 10 proportions
Suspected cases	3 articles 14 proportions
Combined	11 articles 24 proportions

Table 2. Case fatality risk estimates for severe Yellow Fever.

Confirmed	Suspected	Combined
0.39	**0.39**	**0.39**
[0.28, 0.51]	[0.26, 0.53]	[0.30, 0.48]
I^2 = 0.89	I^2 = 0.97	I^2 = 0.96

Table 3. Stratified case fatality risks, by continent and study type.

	Africa	South America
Split by continent	**0.36** [0.27, 0.47] n = 21	**0.55** [0.42, 0.68] n = 3
Split by study type	Investigative **0.31** [0.27, 0.49] n = 18	Reporting **0.44** [0.28, 0.61] n = 6

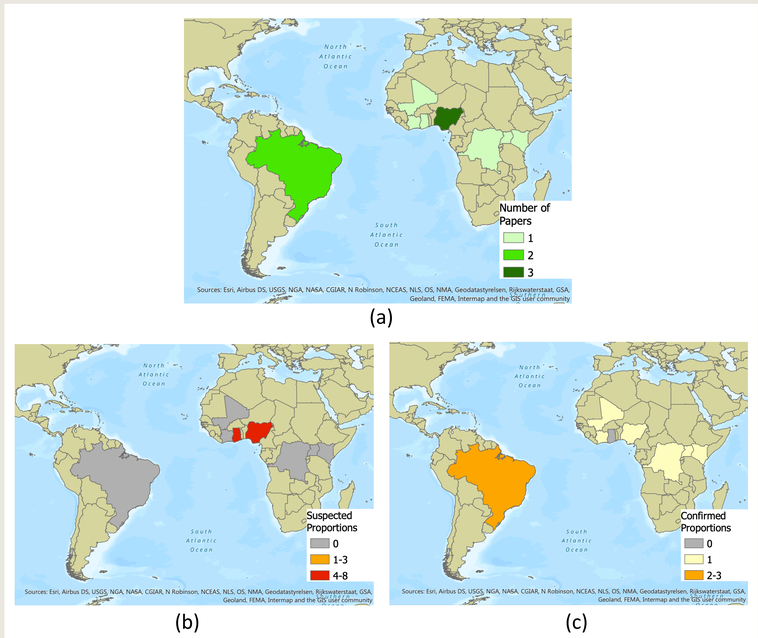

Figure 3. Locations represented in final analyses. (a) Number of papers per country. (b) Number of proportions for suspected severe Yellow Fever per country. (c) Number of proportions for confirmed severe Yellow Fever per country.

RESULTS

- Search strategy yielded 842 articles. After title/abstract screening, 164 remained. After full text screening and data extraction, 11 remained, providing 24 proportions of fatality among severe Yellow Fever cases (Figure 1, Table 1).
- Among all studies, the estimated CFR among suspected, confirmed, and total severe Yellow Fever cases was 39% (Table 2).
- Stratifying all severe cases by continent showed a largely higher CFR in South America compared to Africa
- Stratifying all severe cases by study type showed that articles with researchers involved in investigation and patient assessment had lower CFR than articles reporting cases from passive surveillance (Table 3)

DISCUSSION

- Difference between continents could be related to surveillance activities
- Difference between study types likely due to more diligent monitoring of cases. Most of these studies were conducted during outbreaks.
- This study offers an estimate of Yellow Fever CFR using a comprehensive search strategy and highlights potential effects of study design on such estimates.
- Data limitations: estimating CFR was not the purpose of the studies used, Yellow Fever cases likely underreported[5,8], and timing of fatal cases may impact fatality estimates[9].
- Results of this study can be used in estimating underreporting of cases as well as for preparedness during future outbreaks.

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