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Review

The health economics of cholera: A systematic review

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ABSTRACT

Background: *Vibrio cholera* is a major contributor of diarrheal illness that causes significant morbidity and mortality globally. While there is literature on the health economics of diarrheal illnesses more generally, few studies have quantified the cost-of-illness and cost-effectiveness of cholera-specific prevention and control interventions. The present systematic review provides a comprehensive overview of the literature specific to cholera as it pertains to key health economic measures.

Methods: A systematic review was performed with no date restrictions up through February 2017 in PubMed, Econlit, Embase, Web of Science, and Cochrane Review to identify relevant health economics of cholera literature. After removing duplicates, a total of 1993 studies were screened and coded independently by two reviewers, resulting in 22 relevant studies. Data on population, methods, and results (cost-of-illness and cost-effectiveness of vaccination) were compared by country/region. All costs were adjusted to 2017 USD for comparability.

Results: Costs per cholera case were found to be rather low: <\$100 per case in most settings, even when costs incurred by patients/families and lost productivity are considered. When wider socioeconomic costs are included, estimated costs are >\$1000/case. There is adequate evidence to support the economic value of vaccination for the prevention and control of cholera when vaccination is targeted at high-incidence populations and/or areas with high case fatality rates due to cholera. When herd immunity is considered, vaccination also becomes a cost-effective option for the general population and is comparable in cost-effectiveness to other routine immunizations.

Conclusions: Cholera vaccination is a viable short-to-medium term option, especially as the upfront costs of building water, sanitation, and hygiene (WASH) infrastructure are considerably higher for countries that face a significant burden of cholera. While WASH may be the more cost-effective solution in the long-term when implemented properly, cholera vaccination can still be a feasible, cost-effective strategy.

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1. Introduction

Vibrio cholera is a major contributor of diarrheal illness globally, particularly in developing countries. As an acute, rapidly-dehydrating diarrheal disease that is transmitted through water or contaminated food, the *V. cholerae* bacterium primarily exists in areas with poor water, sanitation, and hygiene (WASH) conditions [1]. In 2015, there were 172,454 cases of cholera reported by 42 countries, 1304 of which resulted in death [2]. The actual number of cases are likely to be higher than yearly reports because many countries lack surveillance systems to properly track cases, and others may fail to report cases altogether due to fear of trade and travel sanctions [1,3]. As a result, the World Health Organization (WHO) estimates that official reports only capture 5–10% of actual cases [3]. Recent estimates suggest that after adjusting for underreporting, there were 2.9 million cases of cholera annually between 2008 and 2012. Sub-Saharan Africa accounted for the majority of cholera cases (60%), while South East Asia accounted for 29% [3].

Apart from case management, improvements to water and sanitation have been the preferred choice for cholera control and prevention for the long term, with the added value of having benefits beyond averting cholera. However, these improvements are costly for countries that face cholera; many lack the financial resources to provide access to drinking water through pipes or protected dug wells [4]. Building basic sanitation infrastructure, such as latrines or flush toilets, and sanitation facilities that can process excreta are also a significant cost burden [5]. In spite of recent progress toward improving access to both water and sanitation, worldwide there are 663 million people who do not use improved drinking water sources, and 950 million people who practice open defecation [4,5].

As a short- and medium-term solution, cholera vaccination has been shown to be effective. The WHO recommends the use of oral cholera vaccines (OCV) in cholera-endemic areas, outbreak settings, and humanitarian emergencies at high risk for a cholera outbreak, but always in conjunction with other complementary measures (e.g., WASH, case management, and surveillance) [6]. There are currently five OCVs licensed worldwide [7], though use and cost vary. Shanchol™ (Sanofi Pasteur India, Mumbai, India) is the first low-cost, two-dose inactivated OCV with WHO prequalification, which means that the vaccine may be procured by United Nations agencies. Currently, the two-dose Shanchol™ regimen costs \$3.70, with efficacy of >65% over 5 years [8,9]. Gavi-eligible countries receive the vaccine free of charge, in addition to financial support of up to \$0.65/dose for operational costs associated with vaccine delivery.

Country investments in either WASH or cholera vaccination are clearly significant cost burdens for countries where cholera is endemic or where cholera outbreaks occur [7,10]. Few studies have quantified the cost-of-illness of cholera or the cost-effectiveness of interventions targeting cholera specifically. The majority of health economics studies focus more broadly on diarrheal diseases [11,12]. In their review of the economics and financing of vaccines for diarrheal diseases (not exclusive to cholera), Bartsch and Lee [11] found two studies specific to cholera that quantify all relevant costs-of-illness associated with cholera [13,14]. Another five studies specific to cholera described only the private cost of cholera illness in Bangladesh [15] and assessed the cost-effectiveness of

vaccination [16–19]. The authors found that while methodologies for cost collection vary, as well as the data sources for ascertaining incidence, mortality, and morbidity, the data still show that there is a substantial burden caused by cholera illness, particularly in cholera-endemic settings.

Similarly, Rheingans et al. included 11 studies published between 2000 to early 2014 on the cost-effectiveness or cost-benefit of cholera vaccinations [12,16,19–28] (two of the studies overlap with the Bartsch and Lee review [16,19]). The authors found that there is inadequate evidence of the economic value of cholera vaccination, especially when compared to rotavirus vaccination.

This review aims to provide a more comprehensive overview of the available literature on the economic burden of cholera and on the cost-effectiveness of interventions to avert cholera. The review updates earlier reviews, but is the first to specifically focus on cholera—and not on diarrheal diseases in general. In addition, and in contrast to previous reviews, this review includes both WASH and vaccination interventions against cholera, which may allow for greater comparability of investments to avert cholera.

2. Material and methods

2.1. Literature search and selection criteria

A preliminary search of existing systematic reviews was first performed on MEDLINE (PubMed) to develop and refine key search terms based on previous reviews [11,29]. A systematic search was then performed between March 2016 and July 2016 (and updated in February 2017) in PubMed, Econlit, Embase, Web of Science, and Cochrane Review with no date restrictions. The following search terms were used to identify relevant studies: ["cost*" or "economic*" or "willingness to pay" or "DALY"/"disability adjusted life year" or "QALY"/"quality adjusted life year" or "net benefit" or "value" or "investment"] AND "cholera". For PubMed and Embase, MeSH and Emtree terms were crosschecked, respectively. Animal studies and molecular/biological studies were excluded. There were no restrictions on populations.

Studies were excluded if they were: (1) not specific to cholera (e.g., cholera disease outcomes were aggregated with other diarrheal diseases); (2) did not quantify in monetary terms the resources used for the treatment of cholera; or (3) focused solely on vaccine delivery costs or willingness to pay for vaccination.

2.2. Analysis of included studies

Two reviewers independently screened titles, abstracts, and full texts for relevant key words and outcomes. Data was then extracted independently for selected studies for inclusion. Discordances between the two reviewers were resolved through discussions. For each full text review, the following characteristics were recorded to facilitate comparison: country, year, data sources, context, population, costs, and perspective. For cost-effectiveness and cost-utility studies, additional characteristics were collected: intervention specifications, comparator, time horizon, and key results (cost per case, death, and/or DALY averted). All costs reported by original studies (majority reported in USD of study year) were inflated to 2017 US dollars using the US Bureau of Labor Statistics' inflation calculator [30]. The methodological quality of studies was

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