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# Cholera

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## Abstract

**Purpose of Review—**This review describes the basic epidemiologic, clinical, and microbiologic aspects of cholera, highlights new developments within these areas, and presents strategies for applying currently available tools and knowledge more effectively.

**Recent Findings—**From 1990 to 2016, the reported global burden of cholera fluctuated between 74,000 and 595,000 cases per year; however, modeling estimates suggest the real burden is between 1.3 and 4.0 million cases and 95,000 deaths yearly. In 2018, the World Health Assembly endorsed a new initiative to reduce cholera deaths by 90% and eliminate local cholera transmission in 20 countries by 2030. New tools, including localized GIS mapping, climate modeling, whole genome sequencing, oral vaccines, rapid diagnostic tests, and new applications of water, sanitation, and hygiene interventions, could support this goal. Challenges include a high proportion of fragile states among cholera-endemic countries, urbanization, climate change, and the need for cholera treatment guidelines for pregnant women and malnourished children.

**Summary—**Reducing cholera morbidity and mortality depends on real-time surveillance, outbreak detection and response; timely access to appropriate case management and cholera vaccines; and provision of safe water, sanitation, and hygiene.

### Keywords

Cholera; *Vibrio cholerae*; Epidemiology

## Introduction

Epidemic cholera is caused by fecal-oral transmission of the toxigenic bacterium *Vibrio cholerae*, serogroup O1 or O139. In individual patients, cholera presents with the sudden onset of profuse watery diarrhea that can lead rapidly to dehydration and death. Its public health presentation is no less dramatic, as it spreads rapidly within vulnerable populations, often causing multiple outbreaks or, in severe cases, a rapid epidemic surge capable of crossing national borders and engulfing whole regions. Although its primary route of

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transmission has been known for over 150 years, and the means to prevent infection and control outbreaks have become increasingly evident since then, cholera remains a major public health concern in countries in Africa, Asia, and the Americas where coverage with safe drinking water and sanitation is low. Promising new tools for cholera prevention, diagnosis, and treatment, and a new initiative for reducing global cholera deaths by 90% and eliminating local cholera transmission in 20 countries by 2030, may mark a turning point in public health control of this persistent plague.

## Epidemiology

### History

Although references to a cholera-like illness occur in Greek and Sanskrit writings from before the Common Era, the first of seven great cholera pandemics only began when populations became more mobile in the early nineteenth century [1]. Despite extensive knowledge of cholera biology, pathology, prevention, and treatment gained since that time, the current and ongoing seventh pandemic, which began in 1961, has lasted longer, traveled further, and caused far more cases than any of its predecessors.

Cholera causes an estimated 2.9 million cases and 95,000 deaths each year [2•]. The cholera burden disproportionately affects marginalized, poor populations, including those affected by conflict or natural disasters, who live in areas with unsafe water, sanitation, and hygiene conditions, and limited access to healthcare. As countries have invested in expanding coverage with safe water, sanitation, and hygiene (WASH) infrastructure—in the early twentieth century in Europe and the USA, and in the late twentieth century in Thailand, other parts of Asia, and much of Latin America—local cholera transmission has ceased.

To address remaining gaps in cholera prevention and control, the Global Task Force on Cholera Control (GTFCC) recently released “Ending Cholera: A Global Roadmap to 2030” [3••]. This new initiative outlines a strategy to reduce the number of global cholera deaths by 90% and eliminate cholera transmission in 20 countries by 2030. The strategy relies on an integrated multi-sectoral approach to (1) improve timeliness and effectiveness of cholera responses by building capacity for surveillance, laboratory diagnosis, and treatment, and by prepositioning clinical and WASH resources; (2) ensure longer-term prevention through investments in WASH infrastructure; and (3) prevent and control endemic and epidemic cholera in the short-term through appropriate use of oral cholera vaccines. The strategy also depends on identifying cholera “hotspots”—areas and populations with the highest cholera incidence or mortality—and targeting these for intensive, focused efforts. To support implementation, it recommends a governance structure in which national governments are responsible for coordinating internal mechanisms and technical and financial support from external institutions within a structured monitoring and evaluation framework. Urbanization in developing countries, climate change, and the high number of fragile states with endemic cholera will present challenges for achieving GTFCC goals.

## Burden of Disease

From 1990 to 2016, the global burden of cholera cases and deaths reported annually to WHO has ranged from 74,000 to 595,000 cases, with the greatest variation attributable to epidemic surges associated with the introduction of cholera to Peru in 1991 and to Haiti in 2010–2011 (Figs. 1 and 2a) [4, 5]. In 2017, a surge in epidemic cholera in war-torn Yemen reportedly exceeded 1 million cases [6•]. Reported cholera deaths over the same period have ranged from 1304 to 19,302 per year, with a global case fatality rate (CFR) between 0.8 and 4.4% (Figs. 1 and 2b).

Because many cholera cases and deaths do not present to healthcare facilities, and are therefore not captured by passive surveillance systems, and because political and economic concerns may favor under-reporting,[1] estimates of cholera burden by public health researchers exceed reported totals severalfold [10, 11]. The most commonly cited estimates, which are based on incidence rates and CFRs from population-based studies, and on estimates of the population without access to sanitation, are that 2.86 million (1.3–4.0 million) cholera cases, including 95,000 (21,000–143,000) cholera deaths, occurred each year from 2008 to 2012 [2•]. Reported cases and deaths during this 5-year period account for only 11.6 and 6.6%, respectively, of the estimated numbers of cases and deaths, which is consistent with WHO estimations that only 5–10% of cholera cases are reported [12, 13]. Other recent estimates of global cholera burden also suggest that reported cholera cases and deaths significantly underestimate the true extent of cholera morbidity and mortality [14, 15].

Sub-Saharan Africa has consistently reported the largest proportion of cholera cases and deaths each year, except during 1991–1993 and 2010–2013 when epidemics in cholera-naïve populations in Latin America and the Caribbean were predominant (Fig. 2a, b). The cholera case-fatality ratio has also been consistently higher in sub-Saharan Africa than in other regions. Although it has gradually decreased, in 2016, it was 2.5%, compared with 1.1% in the Americas and 1.0% in Asia [16]. In recent years, large outbreaks of cholera in Afghanistan, Iraq, and, in 2016–2017, Yemen suggest that cholera has established a firm foothold in the Middle East [6•, 17, 18].

## Risk Factors for Cholera Infection, Severity, and Death

Although sporadic cholera cases may arise from consumption of raw or inadequately cooked seafood contaminated by free-living toxigenic *Vibrio cholerae* O1, cholera epidemics are spread primarily through fecal contamination of drinking water, and occasionally food, by infected persons [19]. A recent review and meta-analysis of the role of water, sanitation, and hygiene exposures in 51 case-control studies of cholera found that cases were significantly more likely than controls to report use of an unimproved water source, contact with surface water, unsafe water transport and storage, untreated drinking water, open defecation, unimproved sanitation, shared sanitation, and poor hand hygiene [20]. Several recent studies found that household contacts of cholera patients had high risk of infection, which could

[1]Bangladesh and Ethiopia, countries where outbreaks of cholera (sometimes referred to as outbreaks of “acute watery diarrhea”) are known to have occurred, do not typically report cases to WHO, despite publications and reports that attest to patients with culture-confirmed cholera at the time [7–9].

occur through contaminated fomites, food, or drinking water [21–23]. Another study found that proximity to a case's home increased risk of cholera in neighbors [24].

Infection with certain strains of *Vibrio cholerae*, including the recently described El Tor variant, that produces more cholera toxin of a more potent form, increases the likelihood of severe disease, as does a larger inoculum of *Vibrio cholerae* ingested [25, 26]. Host factors, such as achlorhydria or blood group O also increase the risk of severe illness [27].

Risk factors for cholera mortality have been studied in outbreaks in rural and urban settings, but can be challenging to investigate due to underreporting and limitations in surveillance [2•, 10, 11]. People at the extremes of age, and those with certain co-morbidities, are more susceptible to the effects of dehydration [28]. However, limited access to healthcare, poor health-seeking behavior, and inadequate rehydration are the salient preventable risk factors for cholera deaths [29–32]. Despite challenges, simple strategies such as improving access to oral rehydration have been proven to lower mortality rates from dehydrating diarrheal diseases [33].

## Cholera Hotspots

Besides the presence of toxigenic *V. cholerae* O1 or O139, the primary determinant of cholera outbreaks and endemicity is a failure to protect drinking water, food, and the environment from fecal contamination. Many other factors influence cholera risk, including environmental and meteorological conditions, population density, mobility, and immunity, and social customs, such as those associated with burials [34]. A core component of *The Global Roadmap to 2030* is the identification of cholera hotspots for intensive prevention and preparedness efforts. A 2017 paper suggests three key types of hotspots: "burden hotspots," where disease prevalence or incidence is high; "risk hotspots," where transmission efficacy or risk of disease acquisition and amplification is high; and "emergence hotspots," where there is increased likelihood of disease emergence [35].

Identifying these hotspots is critical to cost-effective cholera prevention and control. Initial efforts have relied on historical cholera data, enhanced by more granular mapping of GIS data on cholera cases, population density, and drinking water and sanitation services [36•]. Improvements in climate and environmental models that predict conditions where *V. cholerae* might thrive [37•], the use of migration and cell phone data to predict areas with high transmission risk [38•, 39], and more accurate estimates of cases and fatalities through improved surveillance [40] have helped enable more accurate and timely hotspot identification.

## Predicting Disease Emergence: Climate Modeling

The association between cholera outbreaks and environmental drivers has been recognized for decades [41]. *V. cholerae* are free-living organisms commonly found in brackish waters in close conjunction with zooplankton, shellfish, and other flora and fauna [42–44]. Conditions of temperature and salinity that promote growth of these organisms may also promote growth of *V. cholerae*. These conditions, and algal blooms and other proxy indicators, are measurable by satellite imagery and may help predict cholera outbreak risk in vulnerable nearby populations [45, 46]. The El Niño Southern Oscillation (ENSO), a

periodic warming of a section of the Pacific Ocean, was associated with cholera outbreaks in Bangladesh and Peru [47], though its effects are modified by local climate and other variables, complicating accurate outbreak prediction [48, 49]. ENSO also affects inland temperature and rainfall [6•, 45, 50–53]. A study of cholera incidence in Africa over a 15-year period found decreases in Madagascar and parts of Western, Central, and Southern Africa, and increases in Eastern Africa during El Niño years [37].

Several papers have noted a relationship between cholera incidence and rainfall [6•, 45, 50–52, 54]. Proposed pathways include fecal contamination of drinking water sources due to excessive precipitation and flooding; increased use of unsafe water sources due to reduced rainfall and drought; and the effects on other factors related to Vibrio survival and growth in water sources, including zooplankton, bacteriophage, and iron content [55–57].

## Identifying Transmission Risks: Population Migration

Population mobility can facilitate the spread of cholera, and tracking population movements can help predict areas of increased transmission risk. Bengtsson et al. used mobile phone data in Haiti to retrospectively track the movements of 2.9 million people during the cholera outbreak in 2010. They combined this with surveillance data to create a model that could predict new areas of transmission based on population movements from high incidence areas [39]. Mobile phone and rainfall data were used by Finger et al. to retrospectively model a 2005 cholera outbreak in Sierra Leone. They found that a religious pilgrimage had significant impact on the spread of cholera, likely due to a sudden increase in population that strained water and sanitation services. Following the event, infected individuals disseminated cholera across the country when they returned to their homes [38•].

## Identifying Areas of High Incidence and Prevalence: Urbanization

On a larger and longer scale, decades of population migration from rural to urban areas across the developing world has outstripped the capacity of municipal water and sanitation infrastructure in many cities, and led to densely populated, underserved informal settlements, where cholera and other infectious diseases find fertile ground [58–60]. In recent years, cholera outbreaks have occurred in the capital cities of Benin, Ghana, Guinea, Guinea Bissau, Haiti, Ivory Coast, Kenya, Sierra Leone, Tanzania, Togo, Uganda, Zambia, and Zimbabwe, while cholera is considered endemic in Dhaka, Bangladesh, and Kolkata, India.

According to data from the Joint Monitoring Programme (JMP), improved sanitation coverage decreased from 2010 to 2015 among urban populations in 36 (67%) of 54 African countries, a net increase of 24 million city-dwellers without access [59, 61]. Crowded urban environments with poor sanitation conditions in Europe and the USA were frequent foci of cholera epidemics in the nineteenth century; similar unsanitary conditions prevail in parts of many cities today [27•, 62–64].

## Identifying Areas of High Incidence and Prevalence: GIS Methods

A recent paper used spatial analysis and case count data in India to identify areas with high cholera burden and to examine associations with socioeconomic characteristics. The study

found that 25% of districts in India, representing 31% of the population, reported cholera and 90 (14%) of these were “hotspots,” defined as areas where clustering of cases was unlikely due to chance. Districts with higher rates of literacy, mobile phone ownership, and households using tap water from a treated source had lower risk of reporting cholera, and districts with higher proportions of households using latrines without a slab or using open drainage for sanitation had higher risk [65].

## Identifying Areas of High Incidence and Prevalence: Conflict Areas and Fragile States

The *Global Roadmap to 2030* calls for countries and donors to support cholera control efforts, and specifies that countries should coordinate efforts within their own boundaries. Cholera may persist in states with weak governments that under-prioritize healthcare, and in conflict areas where interventions are difficult to implement.

Conflict can damage water and sanitation infrastructure directly, as in Yemen [66], and it weakens economies and health systems, which can limit people from accessing healthcare, safe drinking water, or proper sanitation and hygiene facilities [67, 68]. Conflict can also limit the potential for outside support from NGOs, UN agencies, or bilateral donors. The World Bank’s list of fragile situations includes countries and territories with ongoing conflict or risk of conflict, and those with low performance on indicators of governance [69]. Among people living in fragile states, the proportion without access to safe drinking water is twice, and the proportion who lack basic sanitation is fourfold, that among people living in non-fragile states [70].

Of the 34 countries on the World Bank list of fragile situations for FY 2018, 22 have endemic cholera and 3 more share a border with countries identified by GTFCC as cholera-endemic (Fig. 3) [69, 71]. Fragile states that border states with endemic cholera are at higher than average risk for cholera, and need prevention, detection, and response protocols. Most countries with endemic cholera share a border with at least one other country with endemic cholera, making cross-border coordination essential.

## Diagnosis

Isolation and identification of *Vibrio cholerae* serogroup O1 or O139 by stool culture is the gold standard for confirming a cholera outbreak. Ideally, a stool sample or rectal swab is preserved in Cary-Blair media and transported at room temperature to the nearest diagnostic lab within several days; fresh stool transported without media must arrive at the lab within 2 h [72•, 73, 74].

Identification of the serogroup (O1 or O139), serotype (Inaba or Ogawa), and biotype (El Tor or classical) can be useful for epidemiologic purposes, while antimicrobial susceptibility testing is essential for validating treatment recommendations [72•, 73]. Toxigenic *V. cholerae* O1 can also be identified in stool by PCR testing, but further subtyping and antimicrobial susceptibility testing require culture.

Antimicrobial-resistant strains of *V. cholerae* O1 caused major outbreaks in the 1970s [75]. Since then, resistance to over a dozen antimicrobials, including fluoroquinolones, tetracycline/doxycycline, and multidrug resistance, has often been reported [76–82]. Whole

genome sequencing can identify epidemiologically relevant patterns, antimicrobial resistance genes, and virulence factors; however, resources for this are not usually available during outbreak responses [83, 84].

A variety of rapid diagnostic tests (RDTs) are available or under development for point-of-care diagnosis. Most are lateral-flow immune-chromatographic antigen detection tests that use monoclonal antibodies to surface lipopolysaccharide antigens of *V. cholerae* O1; some also include antibodies to O139 antigens [85, 86]. Because of the varying sensitivity and specificity of available tests, and the lack of standardization and external quality control, WHO recommends they be used for confirming diagnoses, prioritizing samples to be sent for lab confirmation, rapid pre-confirmation screening of suspected new outbreaks, and monitoring outbreak dynamics [85–91]. Despite clear WHO guidelines, RDTs are often misused for individual diagnosis, which is unnecessary and may lead to inappropriate treatment decisions.

*V. cholerae* O1 can be identified in water and food samples by culture or PCR. Membrane filtration or ultrafiltration may be used to process water samples; other methods are available for processing food samples [92]. During outbreak responses, these efforts require lab capacity that may be needed for more critical tasks, such as testing clinical samples and monitoring antimicrobial susceptibility [93]. In some situations, data on Vibrio contamination of water or food may strengthen public communication messages about cholera prevention and motivate policy makers to dedicate more resources to the response. However, negative results from environmental samples, even by PCR, do not necessarily mean a total absence of *V. cholerae* from the water or food source. *Escherichia coli* is a simpler, more practical, and less expensive proxy indicator of fecal contamination, and therefore of cholera risk.

## Treatment

### Clinical Presentation and Case Management

The hallmark symptom of cholera is the sudden onset of painless watery diarrhea, often profuse, described as “rice-water” stools. The diarrhea may be accompanied by vomiting and muscle cramps, but is neither bloody nor accompanied by fever. When *V. cholerae* bacteria are ingested, they attach to intestinal cells and produce a toxin that disrupts normal absorption and secretion of fluid and electrolytes [94]. Cholera infection manifests in a wide range of presentations from asymptomatic, to mild or moderate symptoms that mimic common enteric diseases, to massive outpouring of watery diarrhea that can lead to hypotensive shock and circulatory collapse within hours [95, 96]. Disease severity depends on the virulence of the agent, the dose ingested, and host factors including age, gastric acidity, blood type, and acquired immunity [97–99]. In endemic settings, asymptomatic cases may represent nearly half of all cholera cases [99]. Timely rehydration with the proper mix of fluids and electrolytes is the cornerstone of cholera treatment, and can reduce mortality rates from > 50% to less than 1% [100].

Case management begins at home, with administration of oral rehydration solution (ORS) and continued feeding before and while seeking medical care. If a patient can drink

sufficient fluids, the preferred treatment is oral rehydration with ORS, prepared by mixing a prepackaged sachet of glucose and electrolytes with 1 l of safe drinking water. Treatment of severe dehydration, and of patents who cannot drink sufficient volumes of ORS, requires intravenous rehydration. Ringer's lactate is preferred since its electrolyte composition is comparable to that of cholera stools. Cholera patients require replacement for baseline fluid losses and for ongoing losses from vomiting and diarrhea.

### Antimicrobial Treatment

Antibiotics are not recommended for mild or moderately ill patients, but when used in conjunction with rehydration treatment of severely ill patients, they can reduce the volume of stool, duration of diarrhea, and duration of *V. cholerae* carriage [100–104]. By reducing rehydration needs and the duration of hospitalization, this may help conserve resources in busy cholera treatment centers [100]. Because *V. cholerae* O1 and O139 have demonstrated resistance to several antibiotics, antimicrobial susceptibility testing is essential for informing treatment guidelines [77, 79, 105–107].

### Zinc

Zinc supplementation significantly reduces the duration and severity of cholera in children < 15 years old [108]. Zinc is administered once a day for 10 to 14 days; dosage is age-dependent [108].

## Special Populations

### Children

Children with cholera are at higher risk of hypoglycemia than adults [109]. This can lead to lethargy, coma, seizures, and even death. Cholera-affected children also lose more potassium in stool than adults making them more susceptible to hypokalemia [110, 111]. Therefore, ORS, which contains more glucose and a higher concentration of potassium than Ringer's lactate, is particularly important for rehydration of children. Additionally, to restore stable glucose levels, children should be fed/breastfed as soon as they are able to tolerate oral intake.

### Children with Severe Acute Malnutrition

Children suffering from severe acute malnutrition (SAM) are a fragile patient population with a ninefold increased risk of mortality compared with well-nourished children [112]. Several factors, including propensity for hypothermia, hypoglycemia, and a decreased immune response, render these patients extremely vulnerable to infection and death [113]. Moreover, SAM patients require specialized treatment, feedings, and close monitoring when ill. Cholera is difficult to detect and manage in children with SAM because the signs used to determine the level of dehydration are not reliable in these patients. The delicate balance of fluid and electrolytes makes clinical management extremely difficult, especially in low-resource settings. At present, consensus on cholera treatment and evidence on best practices in this vulnerable population are lacking [114].

### Pregnancy

Cholera during pregnancy has been associated with higher rates of fetal death, particularly among mothers who are vomiting, severely dehydrated, and in their third trimester [115]. Assessing the level of dehydration in pregnancy can be challenging due to increased plasma volume [116]. Poor fetal outcomes are a result of physiologic changes in the cholera-infected mother [117]. Fetal death may result from electrolyte changes in amniotic fluid following severe vomiting and/or resultant fetal acidosis and hypoxia following severe maternal dehydration and shock [115].

## Prevention and Control

### Water, Sanitation, and Hygiene Interventions

From the mid-1800s through the early twentieth century, cholera helped drive the “sanitary revolution” that led to its elimination from Europe and North America [118]. Key interventions included improved access to safe drinking water, safe collection and disposal of fecal waste, and hygiene promotion. More recently, water, sanitation, and hygiene (WASH) investments a century later helped eliminate cholera from Central and South America. In each case, cholera elimination was accompanied by dramatic reductions in infant and child mortality, and in the incidence of other enteric diseases [119, 120]. In other countries, such as Thailand and South Africa, cholera has also lost force as population coverage with water and sanitation increased. Between 1991 and 2010, countries in which less than 71% of the population had access to improved water sources, or less than 39% had access to improved sanitation, were more likely to have endemic cholera than countries with higher coverage rates [121].

In addition to the longer-term benefit of cholera elimination, WASH interventions have short-term, but dramatic benefits in response to cholera outbreaks as shown in recent reviews and a meta-analysis (Table 1) [20, 122].

A recent and novel intervention in Tanzania during a cholera outbreak in 2015 attempted to bypass challenges with household-level chlorination by chlorinating water in large tanks operated by private vendors [123]. A similar approach, using emergency public water storage tanks, was recently successfully used in Zambia [124].

The CHOBI-7 randomized controlled-trial in Bangladesh evaluated handwashing and water treatment promotion in the homes of index cholera patients for 1 week after their release from a cholera treatment center. Households that received the intervention had 41% fewer secondary cholera infections than households that did not [125–127].

Disinfecting households of cholera patients by spraying them with a chlorine solution is a popular intervention, without evidence of impact. In 2011, UNICEF, CDC, and MSF recommended against spraying chlorine in homes and vehicles and suggested resources should instead be focused on providing water chlorination and improving hygiene [128].

### Vaccines

Oral cholera vaccines (OCVs) can be a useful complementary tool for cholera prevention and control when used in conjunction with mainstay measures such as surveillance, appropriate medical treatment, WASH interventions, and community mobilization [129]. OCV campaigns can be considered in endemic settings, pre-emptive or reactive epidemic settings, or during humanitarian emergencies, but must not disrupt other critical cholera control measures [130•, 131]. Currently, three oral cholera vaccines are WHO pre-qualified: Dukoral® (SBL Vaccines), Shanchol® (Shanta Biotec), and Euvichol-Plus®/Euvichol (Eubiologics). All three are killed whole cell vaccines that contain a mix of different *Vibrio cholerae* biotypes and serotypes. Dukoral is monovalent and contains only *V. cholerae* serogroup O1 with the recombinant B subunit of cholera toxin. It requires a buffer and is licensed for children ≥ 2 years old. Shanchol and Euvichol are bivalent and contain both O1 and O139 *V. cholerae* without the toxin subunit, do not require a buffer, and are licensed for children ≥ 1 year old [132–134]. All three vaccines are licensed as a two-dose regimen with doses given 14 days apart for Shanchol and Euvichol, and between 1 and 6 weeks apart for Dukoral. OCVs have been found safe in pregnant women. Shanchol has demonstrated protection for 5 years among adults and children 5–15 years old, but not in children ≤ 5 years old [135, 136]. Recent studies have shown that single-dose regimens can be useful in special circumstances and provide short-term effectiveness [137–140]. In 2013, a global OCV stockpile was established to ensure rapid access to cholera vaccine in endemic and emergency settings. As of April 2017, over 7 million doses of OCV had been deployed for more than 40 mass vaccination campaigns in 14 countries [130•, 131].

### Chemoprophylaxis

Antimicrobial chemoprophylaxis or mass treatment may be useful in helping contain and control outbreaks in institutional settings, including prisons and mental hospitals [141–143]. In these settings, which are at high-risk for cholera introduction and dissemination, antimicrobial agents can quickly be delivered to the entire population, minimizing the risk of antimicrobial resistance. Institutional WASH assessments and interventions should accompany or precede antibiotic chemoprophylaxis. In some instances, community OCV campaigns have included prison populations with little extra cost or effort [144]. Antibiotic chemoprophylaxis is not recommended for the general population, because its effectiveness is uncertain, it is time- and resource-intensive, and it has been associated with the emergence of antibiotic resistance [145–147].

## Conclusions

Reducing cholera morbidity and mortality depends on effective, real-time surveillance, detection and response; timely access to appropriate case management; and the provision of safe water, sanitation, and hygiene. More recently, newer oral cholera vaccines (OCVs) that are between 60 and 85% effective for up to 5 years have been used in combination with WASH for cholera prevention and control in high-incidence and high-transmission areas [139, 148, 149]. During the 2018 World Health Assembly, recognizing the unique opportunity for progress toward cholera control offered by new tools and by the Ending Cholera strategy, UN member nations approved a resolution to prioritize cholera and support

integrated efforts for its control. If their efforts succeed, the global burden of cholera will be considerably less by 2030.

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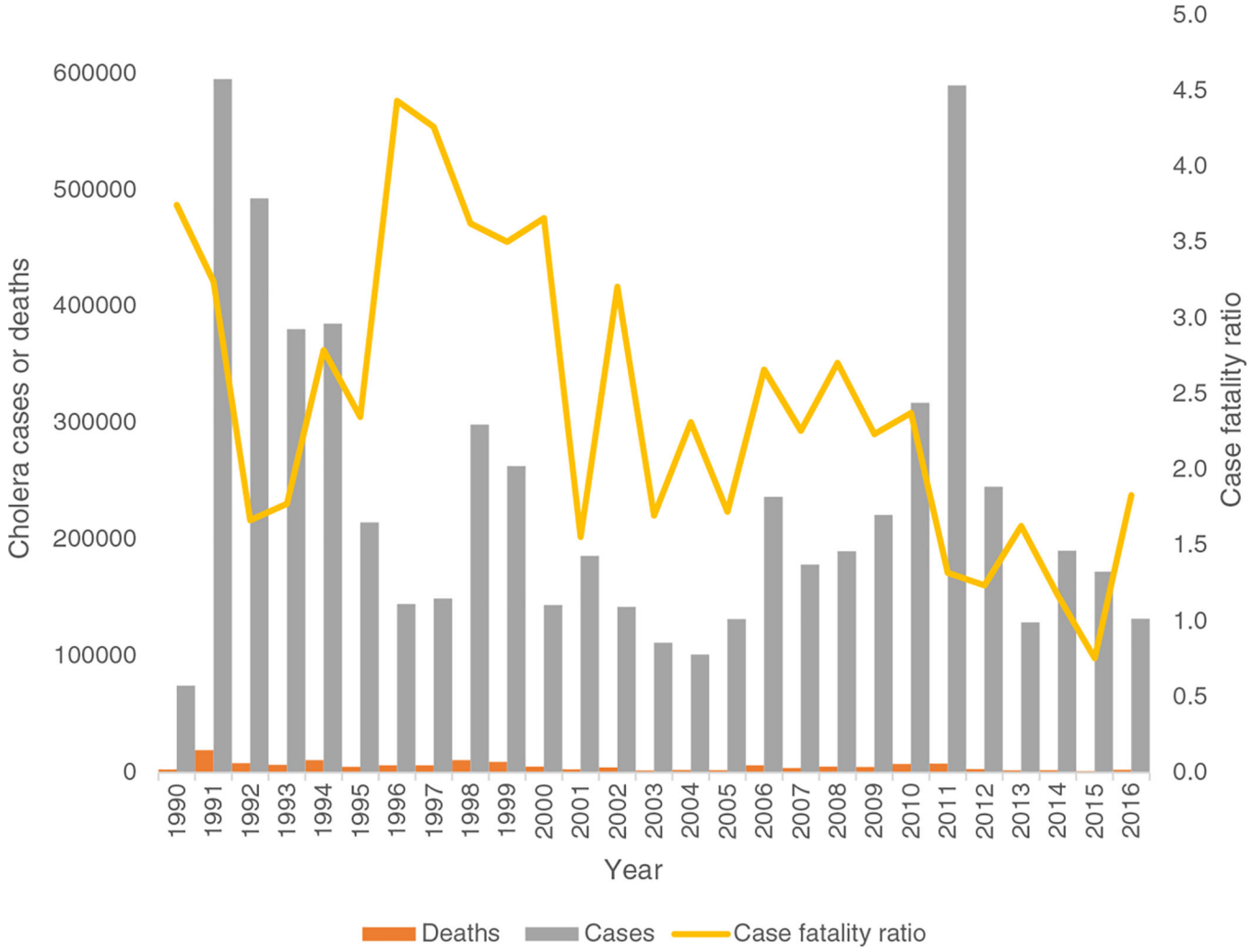


**Fig. 1.**
Reported global cholera cases, deaths and case fatality ratios by year, 1990–2016

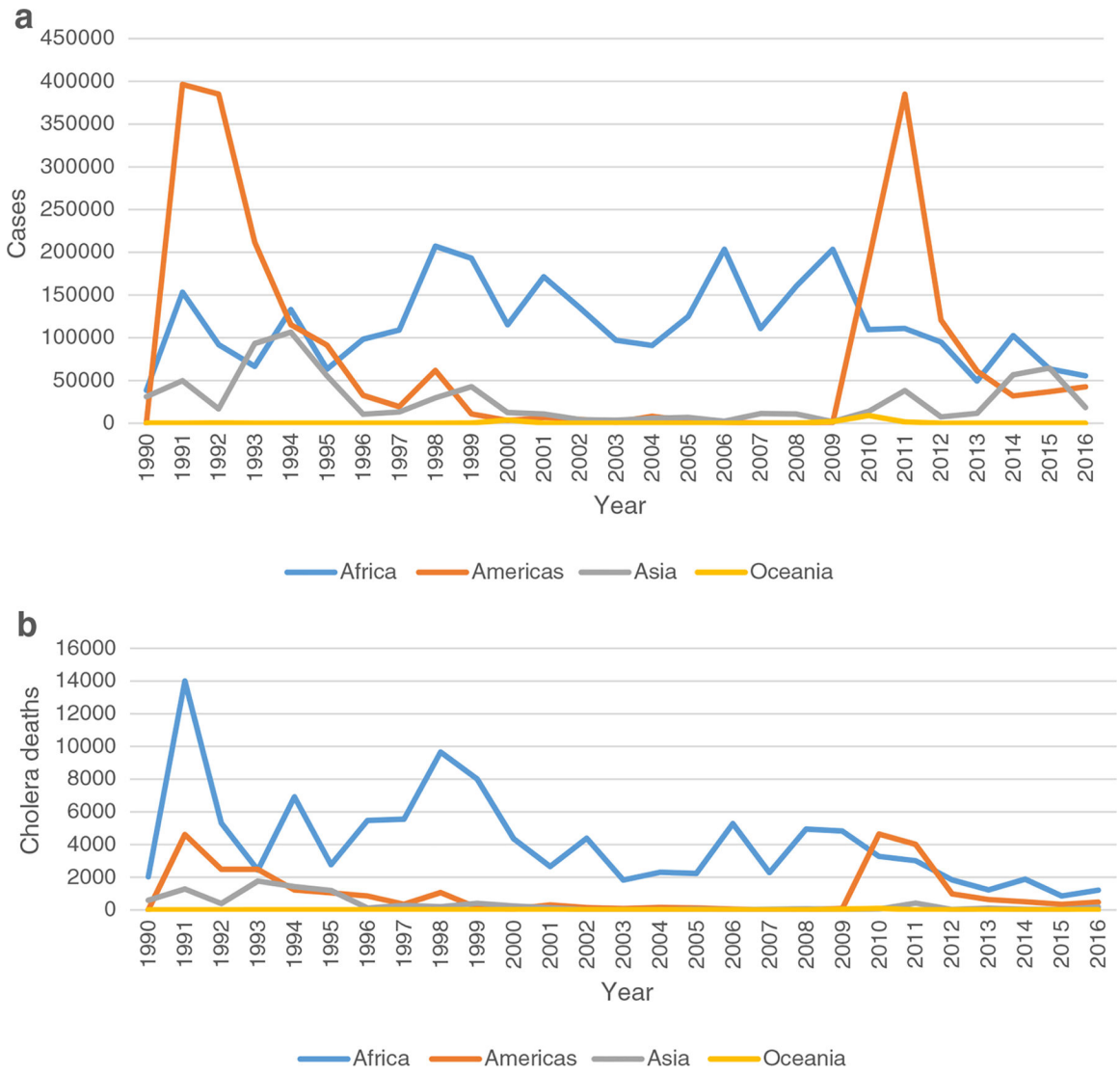


**Fig. 2.**

**a** Reported cholera cases by continent, 1990–2016. **b** Reported cholera deaths by continent, 1990–2016


**Fig. 3.**
Cholera-endemic countries and fragile situations

## Table 1

Reviews of the effects of WASH interventions on risk of cholera

| Risk/protective factor | Taylor 2015[a] | Wolfe 2018[b] |
|---|---|---|
| Household water treatment (chlorine) | Protective | Protective |
| Improved communal water supply | Protective | Not protective |
| Bottled water source | N/A | Protective |
| Safe water storage | Protective | Protective |
| Sanitation | Protective | Neither protective nor risk |
| Hygiene | N/A | Protective |
| Household water filtration | Protective | N/A |
| Household solar disinfection | Protective < 5 years old | N/A |
| Well disinfection | Varies | N/A |
| Unimproved water source | N/A | Risk |
| Unsafe storage and transport | N/A | Risk |
| Open defecation, unimproved sanitation and shared sanitation | N/A | Risk |
| Lack of hygiene | N/A | Risk |

Results of interventions depend on setting, sample size, quality of intervention implementation, and study design. Both papers noted that the quality of the intervention and of the study designs tended to be highly variable

[a] Reference number [122]

[b] Reference number [20]