

A PUBLIC HEALTH EMERGENCY

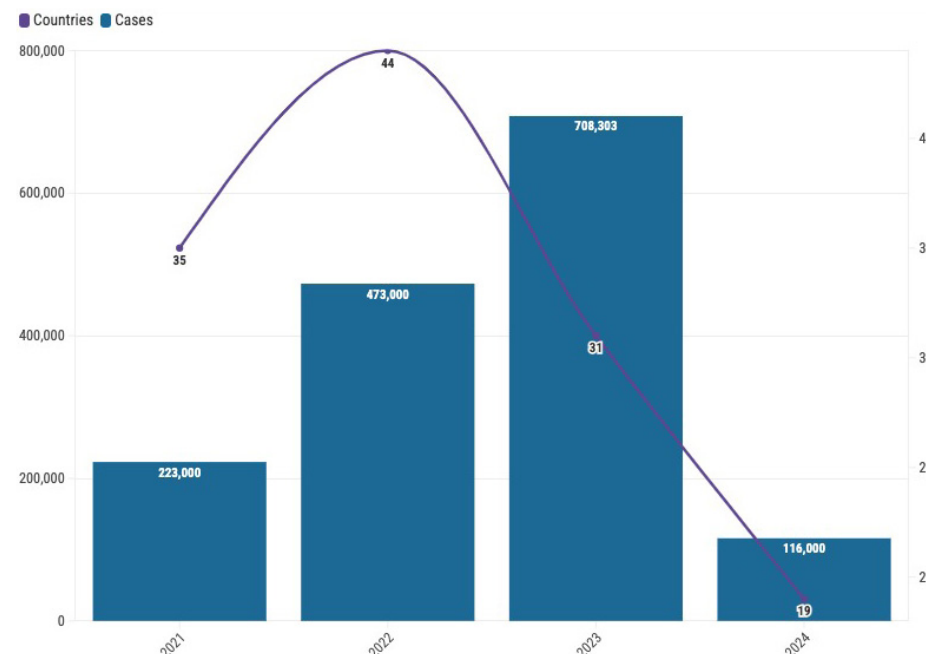
The global resurgence of cholera aggravated by vaccine shortage and El Niño

CRISIS OVERVIEW

In recent years, there has been a concerning global increase in cholera cases, with outbreaks reported in multiple countries since 2021. In 2015, around 1.3 billion people in endemic countries were estimated to be at risk of cholera, with roughly 2.86 million cases occurring annually (with an uncertainty range between 1.3–4 million) and 95,000 deaths (with an uncertainty range between 21,000–143,000) (Ali et al. 04/06/2015). The average case fatality ratio has risen to 1.9% worldwide currently, reaching 2.9% in Africa, marking the highest case fatality ratio in over ten years. By 2022, the number of reported global cholera cases had more than doubled compared to 2021, exceeding 473,000 cases across 29 countries (Cholera Alliance 23/01/2023; WHO 20/03/2024). So far in 2024, until April, the African region had recorded the highest number of cases followed by the Eastern Mediterranean, the Americas, South East Asia, and the Western Pacific (WHO 17/04/2024).

Cholera case and death figures vary across sources. Between 1 January and 30 March 2024, the WHO recorded a cumulative total of 116,000 cases and 1,470 deaths across 19 countries, and the European Centre for Disease Prevention and Control reported more than 97,330 cases and 1,240 deaths (WHO 17/04/2024; ECDC accessed 24/05/2024). By comparison, the European Centre for Disease Prevention and Control reported 169,971 cholera cases and 1,562 deaths globally between January–March 2023 (ECDC accessed 24/05/2024). The decline in cholera case numbers for the same period between 2023–2024 may be a result of underreporting and are not conclusive.

Figure 1. Number of countries and cholera cases reported (by 17 April 2024) between 2021–2024



Source: Cholera Alliance (23/01/2023); WHO (17/04/2024)

About this report

Aim: this report highlights the key contributing factors and aggravating conditions that can increase the global prevalence of cholera, focusing particularly on the impact of the global OCV shortage that is heightening humanitarian needs among affected populations and those vulnerable to spread. This report also examines the impact of the continuing El Niño phenomenon and impending La Niña on precipitation patterns, as well as the influence of these patterns on cholera incidences.

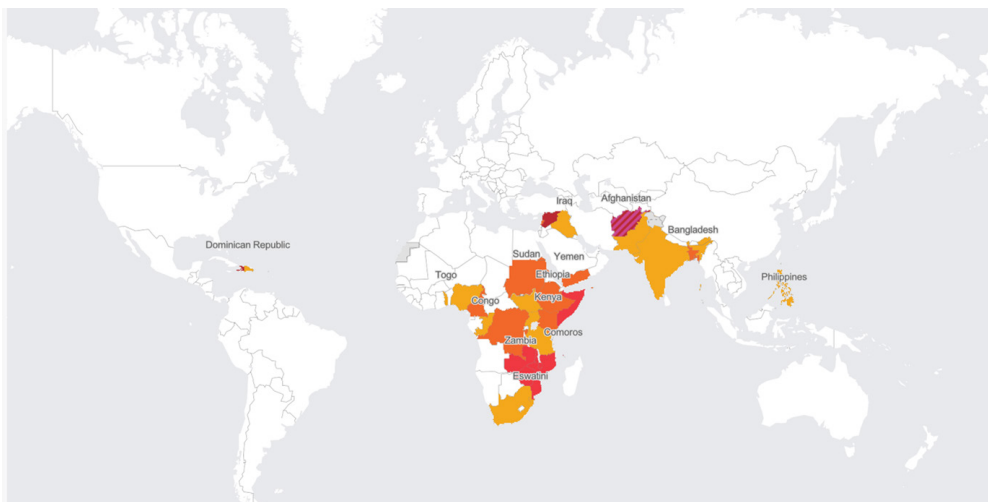
Methodology: the report is based on a review of secondary data sources.

Limitations: globally, aggravating factors limiting the local and national capacity of disease surveillance systems and health response in endemic countries mean that cholera cases are often underreported. Information on International Coordinating Group (ICG) processes, prioritisation of countries in the allocation of OCVs, and OCV campaign strategies for administering the vaccine are either unavailable or very limited.

Terminology: 'OCV' refers, in this report, to the killed whole-cell oral cholera vaccine that is stockpiled and widely used for cholera prevention in lower-income countries.

At the beginning of 2023, as a result of the shortage in vaccines, increasing number of outbreaks, and geographical spread, the WHO elevated the global cholera resurgence to a grade 3 emergency, its highest internal emergency level (WHO 07/12/2023).

Figure 2. Reported cholera cases by 8 April 2024



Source: WHO (accessed 24/04/2024)

Vulnerability to the spread of cholera arises from a complex interplay of factors, not least of which are fragile healthcare systems in many cholera-prone regions (WHO 11/02/2023). Globally, cholera is endemic (meaning areas where confirmed cholera cases have been detected in the last three years with evidence of local transmission) in approximately 47 countries. Being in an endemic area means the population is exposed to a higher risk of infection because the bacteria is persistent in the environment and the healthcare system is strained by constant cases (GTFCC 10/2019). Although the Oral Cholera Vaccine (OCV) has been recommended as a public health tool since 2022 – alongside WASH interventions – in cholera endemic countries and areas at risk of outbreak, the global cholera response remains hampered by severe OCV shortages, undermining response efforts (Reuters 14/02/2024; WHO 02/2012). Depending on the dose regimen, the OCV has between six months (one dose) and three years (two doses) (GTFCC accessed 03/05/2024). As one of the two vaccine manufacturers exited the market in 2023, reducing vaccine availability, cholera cases may rise even further (Georgetown 16/04/2024).

The continued effects of El Niño, and the anticipated onset of La Niña in late 2024, are also likely to result in an increase in cases because of the above and below-average rainfall associated with these phenomena. According to a 2008 study, cholera cases rose by as

much as 24% with every 10mm increase or decrease in average rainfall levels (IRI accessed 22/04/2024; C3S accessed 22/04/2024; Hashizume et al. 01/2008).

DRIVERS OF THE SPREAD OF CHOLERA

Impact of El Niño and Southern Oscillation

El Niño and Southern Oscillation (ENSO) pertains, as it relates to El Niño, to the periodic fluctuation in sea surface temperatures and, as it relates to Southern Oscillation, to the changes in air pressure of the overlying atmosphere across the equatorial Pacific Ocean (NCEI accessed 12/04/2023). The ENSO cycle is a natural climate phenomenon, active for thousands of years, resulting from complex interactions between the atmosphere and ocean. Although many processes are involved in the global climate system, ENSO is one of the main drivers of interannual climate variability (Met Office accessed 13/04/2023).

The two extreme ENSO phases, El Niño and La Niña, both trigger precipitation and temperature anomalies, contributing to increased incidence of disease outbreaks in several of the world's regions, such as sub-Saharan Africa (Met Office accessed 23/04/2024). Reduced rainfall leads to depleted water sources, forcing communities to use contaminated water, while heavy rainfall leads to flooding and sewage overflows, creating environmental factors favourable to an increase in cholera bacteria (Makuntima et al. 04/12/2023; Global Dispatches Youtube 03/11/2022). El Niño, in particular, has been associated with an increase in cholera outbreaks in Bangladesh, East Africa, Latin America, South India, and Yemen (Carbon Brief 10/04/2017; EOS 03/09/2019; WT 08/11/2023; Makuntima et al. 04/12/2023). As a result of climate change, El Niño and La Niña events have become stronger, and more frequent swings from a strong El Niño to a strong La Niña can be expected in the future (Cai et al. 18/05/2023).

Following an exceptionally long La Niña (2020–2023), El Niño was announced in June 2023 (The Conversation 09/06/2023). According to recent forecasts, El Niño is expected to end between April–June 2024, with 60% chance of La Niña developing by June–August 2024 (NOAA 20/05/2024). In 2023, El Niño aggravated cholera outbreaks in both endemic and non-endemic countries, as associated above and below-average rainfall resulted in outbreaks in countries that had not reported cases in years, such as Comoros (Makuntima et al. 04/12/2023). This has worsened the effects of the vaccine shortage, as some non-endemic countries had not established the cholera outbreak control systems found in endemic countries.

Historical observations typically indicate above-average temperatures during El Niño years in tropical and subequatorial regions (Climate Central 08/02/2023). The combination of El Niño and climate change meant that 2023 was the hottest year on record, with heatwaves reported in several regions across the world (Copernicus 09/01/2024). Until at least June 2024, temperature

anomalies are expected to persist in the regions currently affected by cholera epidemics (IRI accessed 23/04/2024). Warmer temperatures are likely to result in the faster growth of cholera bacteria, leading to higher incidence of the disease (Asadgol et al. 06/11/2019).

Climate change

The countries facing cholera epidemics are among those most vulnerable to climate change, primarily because of weak adaptation and response capacities and lack of access to basic services (ND-GAIN 05/2023). The combination of extreme rainfall events and above-average temperatures are associated with an increase in incidence of cholera, as such conditions create a favourable environment for breeding and transmission (Olago et al. 06/2007; Climate Centre 14/02/2023). In countries where climate change is causing more frequent and intense droughts, such as in Southern Africa, water scarcity is challenging access to safe drinking water, hygiene, and sanitation, enhancing the risk of cholera spread (UNICEF 2021). By triggering more frequent and intense hazards such as storms and flooding, climate change also adds considerable pressure on healthcare systems, which manifests in both heightened demand for health services and hindered capacity for effective response within the system as a result of infrastructure damage (WB 05/04/2024). Between 2030–2050, projections suggest that climate change will result in 250,000 more deaths from infectious diseases, malnutrition, diarrhoea, and heat stress annually, with the majority occurring in low-income countries (Africa CDC 09/03/2024).

Inadequate WASH services

Inadequate WASH services aggravate cholera transmission. In the absence of reliable access to treated water, individuals are forced to use potentially contaminated surface water sources. Without proper sanitation facilities, such as toilets and latrines, human waste is released directly into the environment, contaminating drinking water sources (Giroto et al. 20/05/2024; Bocha et al. 13/06/2023; Taylor et al. 18/08/2015). As a result, countries experiencing prolonged cholera outbreaks, particularly in Southern Africa, have turned to alternative response strategies, such as improving WASH services, as a measure to mitigate the spread of the disease (WHO 14/03/2024 and 20/03/2024; Gavi 05/2023).

Depleted cholera response capacities

Critically depleted cholera response capacities mean many low and middle-income countries face significant challenges addressing cholera outbreaks. Cholera has resurged on a global scale in recent 2021, exposing healthcare systems' fragility to managing prolonged

outbreaks. Depleted cholera response resources have cascading consequences, hindering early detection, undermining healthcare infrastructure, impeding access to clean water and sanitation, and lowering vaccination rates (WHO 17/04/2024; Buliva et al. 21/04/2023).

Disease surveillance and case detection: in countries facing humanitarian crises, disease surveillance systems are frequently underdeveloped, making detection and prompt response to outbreaks difficult. Cholera, categorised as 'acute watery diarrhoea', shares symptoms with numerous other diseases, complicating diagnosis. Confirming cholera cases typically requires access to a laboratory, which may not be locally available in some countries. The time required for confirmation can delay response efforts, allowing outbreaks to spread unchecked (GTFCC accessed 06/05/2024).

Overwhelmed healthcare systems: limited response capacity can strain healthcare facilities during outbreaks. Shortages of trained personnel, beds, or essential supplies – such as the Oral Rehydration Solution and antibiotics – can impede effective treatment, resulting in higher case fatality rates. These deficiencies may also deter individuals from seeking medical assistance (GTFCC accessed 06/05/2024).

Risk communication and community engagement: insufficient resources for community engagement can result in a lack of public awareness of cholera symptoms, prevention methods, and the importance of seeking treatment. Delays in seeking help can impede the adoption of essential hygiene practices that prevent the further spread of the disease (GTFCC accessed 06/05/2024; IFRC 10/01/2024).

Shortage of cholera vaccines compared to global demand

Since 2013, the ICG – a group that includes Médecins Sans Frontières, UNICEF, the International Federation of Red Cross and Red Crescent Societies, and the WHO – has overseen the management of the OCV global stockpile. The ICG functions as the main entity responsible for procuring and distributing vaccines to areas affected by cholera outbreaks or at high risk of one (Shaikh et al. 29/02/2020). The primary goal of the OCV stockpile – composed of Shanchol and Euvichol, two essentially identical vaccines produced by different manufacturers – is to distribute vaccines during outbreaks to aid effective response (WHO accessed 23/04/2024).

The surge in the number of countries reporting cholera outbreaks has created high demand for cholera prevention and control commodities, including skyrocketing demand for the OCV, with stockouts at the country level becoming a reality (Wierzbza 12/10/2018). The severe gap between the number of available vaccine doses and the level of need puts unprecedented pressure on the global vaccine stockpile. Between 2021–2023, more doses were requested for outbreak response than in the whole of the previous decade (CVEP 23/03/2024). As a result

of the vaccine shortage, humanitarian responders have begun using the OCV vaccination strategy of case-area targeted intervention, which focuses on proactively containing the first clusters instead of relying on the community-wide vaccination approaches previously used (GTFCC accessed 06/05/2024).

In October 2022, in response to the vaccine shortage, the ICG announced a temporary shift from the standard two-dose regimen to a single-dose regimen in cholera outbreak-response campaigns. This adjustment aimed to enhance the impact of vaccination efforts in regions affected by outbreaks (WHO 19/10/2022; Johns Hopkins 19/01/2024). This directive affected response programming, as a single vaccine dose provides protection against cholera for six months to one year, while the two-dose vaccine provides protection for two–three years. As a result, between January 2023 and February 2024, there was a significant increase in OCV demand, with 14 countries requesting 79 million doses, double the available supply of 40 million doses (WHO 07/12/2023; WHO accessed 09/04/2024). There were also no vaccines available for prevention in locations where the conditions contributing to significant outbreaks were present or where cholera was endemic (NYT 11/04/2024).

As of December 2023, there were three OCVs prequalified by the WHO for use in cholera prevention: Dukoral (mainly used by travellers and produced by SBL Vaccines in Sweden), Shanchol (manufactured by Shantha Biotech in India), and Euvichol (manufactured by EuBiologics in South Korea) (WHO 11/12/2023; WHO accessed 03/05/2024; CDC accessed 03/05/2024). A study conducted between 2018–2020 revealed that the two-dose Euvichol vaccine, like the Shanchol vaccine, was over 60% effective over two years (Matias et al. 22/11/2023). Since January 2024, only EuBiologics has continued to manufacture the vaccine, as Shantha Biotechnics halted production at the end of 2023 citing the small volumes produced (The Guardian 14/10/2022; WHO 20/03/2024).

On 18 April 2024, the WHO approved a new EuBiologics vaccine with a simplified formulation but the same efficacy, which can be produced rapidly (WHO 18/04/2024). This is anticipated to increase annual production up to 46 million doses. It is not clear, however, if this will be sufficient to meet global OCV demand (IVI 26/12/2023; NYT 11/04/2024). The existing vaccine shortage is expected to continue until 2025, when a new manufacturer is expected to enter the market (Reuters 22/05/2023).

Insufficient investment in medicine and vaccines for neglected diseases, such as cholera

As cholera mainly affects people in lower-income countries, insufficient investment in medicine and vaccines is a persistent issue, as pharmaceutical companies view such as unprofitable, resulting in significant gaps in research and development. From 2007–2022,

while USD 23.7 billion was invested in HIV/AIDS research and development, only USD 564 million went towards cholera. In 2022, only USD 37 million was allocated to cholera research and development, with most funding coming from public and philanthropic sources; industry contributions were minimal, at around USD 200,000 (Georgetown 16/04/2024).

To encourage companies to invest in cholera vaccine production, Gavi, the Vaccine Alliance – a public-private global health partnership aiming to increase access to immunisation in countries vulnerable to cholera – has suggested the use of advanced market commitments involving promised future orders to incentivise drugmakers' investment in producing the cholera vaccine (Gavi accessed 24/05/2024; NYT 31/10/2022). In Africa, where up to 80 million people reside in cholera hotspots, the vaccine shortage has underscored the necessity for a manufacturer on the continent. This initiative is facilitated by Gavi's African Vaccine Manufacturing Accelerator, which has made USD one billion available over the next ten years to enhance Africa's capacity to produce essential medicines and vaccines locally, reducing dependence on imports and ensuring timely access to critical medications (Health Policy Watch 20/02/2024; GTFCC 10/2019). In South Africa, the vaccine manufacturer Biovac has initiated clinical trials for a potential vaccine, which, if successful, would mark the first vaccine fully developed in sub-Saharan Africa, with trials anticipated to conclude by 2027 and subsequent steps expected to take at least a year before WHO prequalification is obtained (NYT 31/10/2022).

AGGRAVATING FACTORS

Food insecurity

Research has found a relationship between the annual incidence of cholera and national food security, availability, and affordability, suggesting that food insecurity may affect the scale of cholera outbreaks (Elnaiem et al. 06/02/2023). A 2019 analysis of 30 countries between 2012–2015 revealed a direct relationship between food security and cholera incidences (Richterman et al. 18/09/2019). Reduced food availability can affect a household's food-related behaviour, potentially resulting in poor food hygiene practices. Individuals may reassess the choices of what they eat, where they acquire food, or how they prepare it when the focus shifts to meeting immediate food needs (Elnaiem et al. 06/02/2023).

Conflict

Conflict can aggravate the spread of cholera and impede efforts to control outbreaks. During conflict, essential services, disease control programmes, and healthcare systems may be disrupted, and critical health infrastructure potentially destroyed. Security concerns may

lead response and healthcare workers to leave affected areas. Conflict can also increase populations' humanitarian needs and displacement, further limiting access to healthcare and basic services, such as WASH (GAAC 27/03/2023).

A 2022 study investigated the link between conflict and cholera in Nigeria and the Democratic Republic of Congo (DRC) from January 1997 to May 2020. Historically, both countries have experienced high cholera burdens and continued conflict, such as the Boko Haram insurgency in northeastern Nigeria and armed conflict in eastern DRC. The study revealed that conflict significantly heightened the frequency of cholera outbreaks in both countries. In Nigeria, conflict increased the risk of cholera by 3.6 times, while in the DRC, the risk was 2.6 times higher. 19.7% of cholera outbreaks in Nigeria and 12.3% in the DRC were attributed to conflict (Charnley et al. 12/2022; Agbiboa 10/10/2013; WHO accessed 24/04/2024).