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Chapter

An Update on Cholera Studies in Mozambique

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Abstract

Cholera is endemic in Mozambique and, together with other diarrheic diseases, is a major cause of infant death. There are yearly outbreaks in the northern provinces. The last major review of cholera in the country was published in 2013, but there have been major events since then, such as the 2015 outbreak in central and northern Mozambique and others in the following years. Plenty of related information were shared during the XVI National Health Journeys, 17–20 September 2018, in Maputo City. This chapter aims to summarize and discuss the most relevant information on cholera from the journeys, and other recent publications, in order to update the information from the latest major review. Regarding etiology, new strains of *V. cholerae* irradiating from several areas have been replacing the original from the Indian subcontinent. Water and sanitation are major challenges but, in some instances, sociocultural features play a significant role in people's reluctance to use untreated water, even when they have access to potable sources, and mistrust toward government interventions. Vaccination campaigns seemed effective but there is a need to promote more adherence and collaboration from people at risk, perhaps by involving more the local government and religious and traditional authorities.

Keywords: cholera, diarrhea, Mozambique, update, epidemiology

1. Introduction

Diarrheic diseases are a serious public health issue in the entire world [1, 2]. Cholera is among the deadliest gastrointestinal diarrheic maladies in tropical areas [3–5], resulting almost exclusively from ingestion of water contaminated with *Vibrio cholerae*, but any fecal-oral pathway can potentially transmit the disease [6]. When untreated, the disease rapidly results in death, and transmission is quick within the community [2]. It is a problem because many developing countries lack resources and time necessary for confirmation and management of cholera outbreaks [7].

In the African continent, cholera has been a significant cause of morbidity and mortality [3, 6]. The disease was introduced in Mozambique from the Indian subcontinent in 1970 and became a major cause of infectious diarrhea [4, 8, 9]. Since then, the country has been facing outbreaks, particularly in Nampula Province [6]. The most severe happened during the 1990s, resulting in one third of all cases in Africa [5]. All diarrheic diseases together are the fourth major cause of death

of <5-year-old children, causing in average 13,105 demises per annum. Cholera's epidemiological profile is changed from epidemic to endemic due to the frequent outbreaks [6]. In general, there is a virtually countrywide epidemics every 5 years, but Nampula and Cuamba cities register annual cases [1], usually during the rainy season (December to June) [8]. According to Chissaque et al. [10], the last major outbreak was in 2015. Furthermore, some issues have been worsening the situation and raising increased concern. For instance, diarrhea-causing enteric bacteria are developing resistance to antibiotics [11], possibly because of overprescription.

Cholera is endemic in Mozambique, but there is very limited research on the matter. There is little information on transmission patterns and how risk factors such as non-potable water, improper sanitation, and hygiene affect the incidence, prevalence, and severity of the disease [4, 9]; there is no local protocol for treating acute diarrhea in children, the only reference being from the World Health Organization (WHO) [4, 12, 13]; little is known about the challenges, success cases, and the extent of the impact of the struggle against cholera in Mozambique [2] and the operational cost to implement a vaccination campaign against cholera [14]. If such information gaps are filled, it will be possible to substantially improve the strategy to mitigate the disease.

Gujral et al. [15] wrote an important contribution to the overall understanding of cholera epidemiology in Mozambique up to 2013, based on the national surveillance data. Though it is a good reference for researchers and scholars, there were some updates published in at least three journal articles [9, 10, 16], reports from the United Nations [17] or other organizations, and 17 presentations [1–8, 11, 14, 18–24] at the XVI Scientific Journeys organized by the Mozambican National Institute of Health [25]. This chapter aims to summarize the contributions of such publications for the current knowledge of cholera in Mozambique.

2. Sources and reviewing process

The current analysis is based on updates presented during the XVI National Health Journeys, 17–20 September 2018, in Maputo City, in Mozambique. National Health Institute organized the event under the motto "Promovendo a intersectorialidade e a participação comunitária para o alcance dos Objectivos de Desenvolvimento Sustentável" [Promoting the multi-sectoral collaboration and community participation to meet the Sustainable Development Goals]. Since the beginning, in 1976, the journeys have been arguably the country's most relevant event on the matter, hosting presentations from leading health researchers in Mozambique [26].

Summaries of all presentations were then compiled to Revista Moçambicana de Ciências de Saúde [Mozambican Journal of Health Sciences]. There were 19 presentations directly or indirectly related to cholera. Some content was a follow-up of other previously published international journals, and it facilitated their interpretation. ATLAS.ti 8.1 (ATLAS.ti Scientific Software Development GmbH, Berlin, Germany) was used to analyze most information and Jamovi 0.9 (The Jamovi Project, Amsterdam, Netherlands) for meta-analysis when necessary.

Most studies on cholera in Mozambique conducted during the last decade were complementary, connected as part of a multidisciplinary approach for accompanying control campaigns led by the Ministry of Health, targeted to susceptible groups in areas where annual outbreaks occur during the rainy season [16]. At least half of the studies used data from Nampula City [23], but there were also studies in Tete, Moatize, Quelimane, Mocuba, Guruè, Metangula, Cuamba, and the country in general [1, 2, 5, 19–21]. Chissaque and Deus [20] presented, in the journeys, content directly related to a journal article published the same year [10].

It is perhaps important to mention the group that contributed the most with presentations about cholera during the Scientific Journeys. It was the team of Baltazar and Baloi [23], from the National Institute of Health, mostly reporting on different aspects of the immunization campaign in Nampula City, 2016. Their particular presentation was focused on the vaccine coverage and acceptability, but the same group also analyzed local media coverage and people's reaction [21], evaluated environmental determinants [4] and post-campaign adverse effects [18], validated a rapid test to monitor the efficacy of the vaccine [7], and evaluated the economic cost of the vaccine [14].

3. The current situation of cholera in Mozambique

Since most publications are interconnected, based on the same campaigns and projects, they shared some constraints and limitations. They might not be explored in full depth in the following subsections. Section 5.7.3 presents more details and respective analyses on the limitations and constraints.

3.1 Etiology

The main causes of diarrhea in Mozambique, especially in children, are *V. cholerae,* rotavirus, *Shigella* spp., *Escherichia coli*, *Cryptosporidium* spp., and *Aeromonas* spp. [20]. At this stage, *V. cholerae* is well-known as the cholera-causing microorganism, even outside scholarly or scientific circles. Etiological studies are now focused on peculiarities or diversity of endemic strains in Mozambique, and how to rapidly distinguish cases of cholera from other forms of diarrhea, especially during emergency situations. The more accurate the diagnostic, the more appropriate the treatment.

According to Langa et al. [16], Mozambican *V. cholerae* O1 isolates from 2012 to 2014 outbreaks are genetically closely related to strains of pandemic worldwide, unlike the Indian-born found 20 years ago. Garrine et al. [9] went one step forward by analyzing how related 75 isolated were from patients in Manhiça District Hospital from the start of the millennium up to 2012 and 3 from the Komati River. They were able to reveal four unrelated genotypes and two clonal complexes with 22 genotypes by using a multilocus variable-number tandem-repeat analysis (MLVA), and through whole genome sequencing (WGS), they detected recombination and four isolates genetically unable to produce cholera toxin. The investigators were also able to deduct that Wave 3 of the seventh pandemic [27–29] remained in the area for at least 8 years, originating 67 of the isolates analyzed.

It is worth mentioning *Aeromonas* spp., as Chitio and Langa [24] demonstrated that these microorganisms cause symptoms easy to confuse with cholera's, particularly during outbreaks. They detected *Aeromonas* spp. in 30 (10.4%) of 289 samples of rectal swabs from patients with suspicion of cholera during outbreaks in 2014 and 2015. The species were *Aeromonas sobria* (57%), *Aeromonas hydrophila* (20%), *Aeromonas caviae* (13%), *Aeromonas veronii* (7%), and *Aeromonas salmonicida* ssp. *salmonicida* (3%).

3.2 Risk factors and health determinants

Environmental sanitation is important to control disease for the benefit of public health [19]. For several natural, sociopolitical, cultural, and economic reasons, Mozambique is spatially heterogeneous in terms of distribution of resources, including water, housing, their conditions [30], and certainly other features potentially affecting the transmission of cholera. Thus, one shall expect to see substantial differences in terms of risk factors and health determinants in different

areas throughout the country. Yet, it is possible to draw some comparisons on how one or another factor affects the dynamics of cholera transmissibility, from different authors' points of view.

Marrufo et al. [4] evaluated water, sanitation, and hygiene in the area with more cases of cholera in Nampula City and found that 42% had improved latrines and 90% of the inhabitants had access to at least one improved water source, as defined by the World Health Organization and the United Nations Children's Fund (UNICEF) [31]: with potential to deliver safe water by nature of its design and construction. The authors did not specify their sample size (n) in the summary for the presentation, but their sample was certainly representative because they followed the guidelines of the United Nations High Commissioner for Refugees, and they were the same research team as Baltazar et al. [23] (n = 636), besides the fact that they covered a very wide area and used a statistical treatment of the data. A major health determinant is likely the lack of drainage and sewage through the entire suburban area covering six neighborhoods, particularly when it rains [4, 8, 20]. According to Ramos et al. [19], residents of Bairro Novo [New Neighborhood], Quelimane City, claimed to frequently observe human stool and trash floating when it rains and water accumulates through the streets. This area also lacks a sewage system and has a shortage of latrines.

A different research team [22] interviewed 59 patients with suspicion of cholera in the rural community of Casacone and found the same percentage as Marrufo et al. [4] of households with latrines (42%), but there were differences: 64% used well water, and none treated it before consuming. Besides the differences in the settings (suburban and rural), the study groups were fundamentally different, as Paulo et al. [22] worked with people having acute diarrhea, while Marrufo et al. [4] worked with populations from a risky area. The former group was by definition people who had contact with contaminated water; thus it is not surprising that all used untreated water, unlike the latter group.

Borges et al. [5] found that people in Metangula District (Niassa Province) prefer using untreated water from the lake, even when they have access to potable water, and they could not find any explanation, particularly because most (98%) were aware of cholera and the associated risks. Adding to that fact, Francisco and Chindia [3] stated that in this particular area, temperature and precipitation do not seem to be major health determinants, and it reinforces the idea that the issue is led by behavior. There are perhaps sociocultural or religious reasons. For instance, the Zion Christian Church is well-known in Mozambique, and it is the third largest (17.5% of the population), only surpassed by Catholicism (23.8%) and Islam (17.8%) [32]. One notable ritual of this church is the "Jordan" baptism, performed in rivers, lakes, and sometimes the sea. Such level of exposition to waterborne pathogens is highly concerning, particularly in hotspots of cholera endemism. Furthermore, virtually all over Mozambique, there are people who believe that malicious individuals intentionally created cholera to harm others [2, 6, 33]. Thus, it is important to debunk such self-destructive mentality and the resulting attitudes.

3.3 Epidemiology

3.3.1 Geographical distribution

The World Health Organization [34] identifies Mozambique among the African countries most affected by cholera epidemics. In the first decade of the millennium, cholera had an incidence of 12 to 127 per 100,000 inhabitants, especially in the rainy season [20]. The variant of *V. cholerae* O1 (El Tor strains) active in the country then came from the Indian subcontinent, and it can be found, for instance, in Bangladesh

[16, 35]. Between 25 December 2014 and 22 March 2015, there was a sequence of outbreaks through 5 provinces and 18 districts, resulting in 7073 cases reported and 53 deaths (fatality rate was 0.7%) [17]. Genetic analyses suggest that strains found in Mozambique since 2012 are also common in several other parts of the world [16], indicating the existence of different waves of contamination converging in the country.

Chitio and Langa [24] and several other presenters in the XVI National Health Journeys seemed to agree that cholera has been more widespread throughout the central and northern provinces (**Figure 1**), particularly Niassa and Nampula in the north, where outbreaks occur annually, in contrast to the rest of the country, where it occurs every 5 years [1, 4, 22].

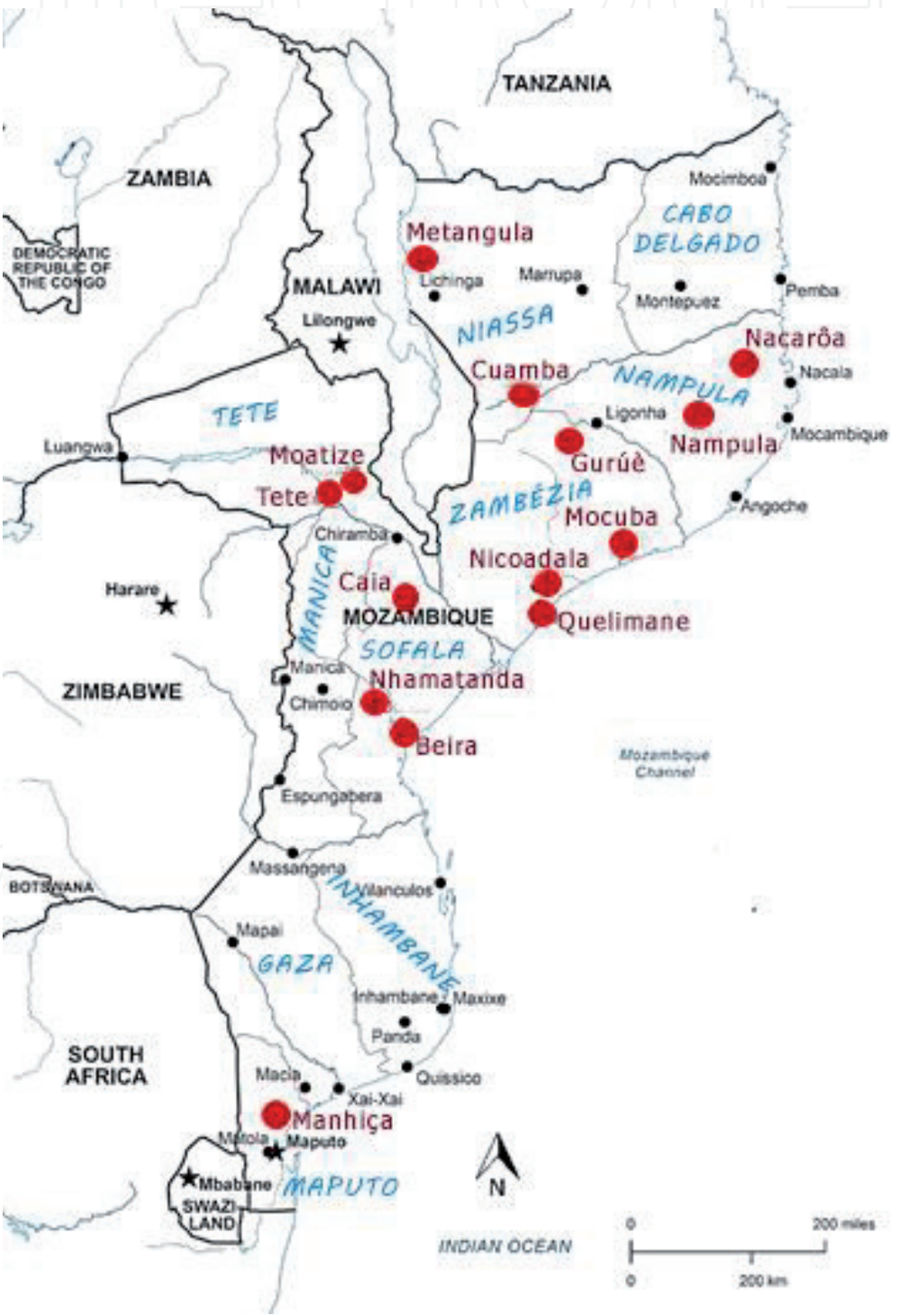

Figure 1.
Draft of Mozambican map showing the areas where research and interventions related to cholera occurred since 2013. Image adapted from Wikimedia Commons [36] under public domain. Data was compiled from the XVI National Health Journeys [1–8, 11, 14, 18–24], Chissaque et al. [10], and Vanormelingen et al. [17].

Vanormelingen et al. [17] included Sofala in the list of affected provinces, and Chissaque et al. [20] mentioned *V. cholerae* among the causes of diarrhea in the country's south. The main cause is the lack of potable water and proper sanitation such as improved latrines [4], though behavioral factors also contribute to the incidence and prevalence of cholera [6, 8, 21].

In Niassa Province, the most frequent reports have arisen from in two municipalities: Metangula, where the majority of the cases occur [5], and Cuamba [1]. Besides similar causes as in Nampula City, a major risk factor for cholera contamination in Niassa is the insistence on using untreated fresh water to wash dishes, take a bath, and drink, especially the population of Metangula who live at the Niassa lakeshore [5]. In their presentation, Borges et al. [5] stated that choice of fresh water is not necessarily related to the access to potable water, as there were sufficient wells for the community.

In Nampula, the six most severely affected neighborhood cities are Carrupeia, Muatala, Murrapaniua, Mutauanha, Napipine, and Natiquiri, with 193.403 inhabitants [1, 4, 18]. Other neighborhoods under risk are Namicopo, Namutequeliua, and Belenenses, especially considering a recent observation that some residents showed very low awareness on how cholera is transmitted [6]. In this decade, the city had annual outbreaks recorded at least from 2013 to 2018 [4], and it is confirmed that an outbreak is happening as this article is being written [37], but this topic will be briefly discussed in the post-conclusion note (Section 7). There was another outbreak notified 17 November 2017 in Nampula Province, Nacarôa District [22]. The most affected areas were Munana and Casaconde neighborhoods, in the administrative area also called Nacarôa, within the district.

Zambezia was another province studied, and there were studies from cities of Quelimane, Mocuba, and Gurúè [1, 2, 19]. Vanormelingen et al. [17] added Nicoadala District. First, regarding "Bairro Novo" [New Neighborhood] in Quelimane City, Ramos et al. [19] mentioned the rapid expansion of the city, hardly complying with proper urbanization planning, thus resulting in improper sanitation and hygiene. The authors decided to investigate the frequency of waterborne diseases, including diarrheic maladies, by interviewing members of 21 households, and analyzing records from the Healthcare Center from 24 July 2014 to 2017. Cholera was mentioned among the most frequent diseases, although the authors did not specify the prevalence. In general, they included the disease among the diarrheic, with 564 cases (47.3%) in 1193 recorded in the healthcare center's registry. In Mocuba, Mesa et al. [1] analyzed 128 processes of patients carrying diarrheic diseases. Although the authors did not specify the diseases, they suspected that most had cholera considering the symptoms recorded, the fatality rate of 4% (plausible, according to the World Health Organization [38]), and the fact that there was an outbreak as they were conducting their investigation. The most affected neighborhoods were Samora Machel (33%), Marmanelo (15%), CFM (11%), carreira de tiros (10%), and Tomba de Água (8%). Carlos [2] said that various minor towns of Gurúè District have been registering outbreaks of diarrheic diseases and cholera, but in 2015 there was an outbreak in its main city, also called Gurúè.

There are other areas where cholera is endemic, but the scholarly publications from the last decade did not explore in depth the epidemiologic point of view, but they are worth mentioning. For instance, the 2015 outbreaks in the country's north and center seemed interconnected and occurred during the same period, and they reached areas including the cities of Tete, Moatize, and Sofala Province [17]. There are also studies from the south, though in different time and context. Salomão et al. [21] presented results of a 2-year study (2017–2018) related to immunization campaigns in the cities of Tete and Moatize, after an outbreak in 2017. As the outbreaks were stabilizing in the provinces mentioned so far, in Sofala it was spreading, with

reports from Beira City, Caia, and Nhamatanda. Manhiça District Hospital keeps isolates of cholera [9], and it reflects the history of the disease there and in the areas nearby. Garrine et al. [9] worked with these isolates in their research and added three from the Komati River.

3.3.2 Prevalence, impact, and susceptible groups

Since most studies presented at the XVI Health Journeys were follow-ups of ongoing studies, they all tended to miss some details, and some were complementary to each other. For instance, the studies after the 2015 outbreak of cholera in Nampula explored different perspectives on the problematics [4, 6–8, 14, 18, 22, 23]. **Table 1** shows some epidemiological data recorded after 2013. These are just some examples because it would be redundant to include some papers, particularly the studies conducted in Nampula. Still, there is plenty of information worth sharing.

The studies did not explain the dynamics of how the disease is spread during non-epidemic periods because virtually all were conducted during outbreaks, or at least based on them, though it might not differ much from times of outbreak, especially because the area is endemic. Phenomena such as heavy rain and natural catastrophes certainly work as amplifiers of the disease severity by increasing people's exposition to untreated water [3, 20, 39–42]. Yet, it would be a good idea to study the risk factors and disease determinants during times of low prevalence because it would, for instance, minimize the need for researchers to work under pressure or "under budget" because of non-research-driven priorities [43], avoid panic or undesirable reactions from study subjects, and perhaps be easy to prevent outbreaks or lower considerably their impact on public health. On the other hand, outbreak investigations are crucial to ensure proper intervention. Thus, the information below represents outbreak-related scenarios but somehow the best lead so far of the country's reality with or without an outbreak.

According to **Table 1**, the country's cholera fatality rate (CFR) in 2015 was 0.7%. This value is low, within the range 0–15.8% of the Global Health Observatory (GHO) in 2016, published by the World Health Organization [38]. According to the GHO, 22 countries had CFR > 1%, and only Niger, Zimbabwe, and Congo had CFR > 5%. Even the global (1.8%) was higher than Mozambique the previous year during the outbreak. Such low fatality rate was likely due to a very fast and effective response in terms of vaccination, treatment [11, 23], and other measures such as health education and support in sanitation [8, 17]. Cholera is highly virulent but also easy to treat and there is vaccine [44]. The fatality rate observed in Nacarôa (2%) was not far from the global, and it seems reasonable to expect such kind of fluctuations in a considerably small sample. It should be also reasonable to expect a value slightly higher than average in endemic areas.

Author	Year	Area	Cases of cholera	Deaths
Vanormelingen et al. [17]	2015	Countrywide	7073	53
Salência et al. [11]	2014–2017	Countrywide (6 hospitals)	19/784*	ns
Dengo-Baloi et al. [18]	2016	Nampula City	44/171*	ns
Paulo et al. [22]	2017	Nacarôa	135	3

**Confirmed cases/suspected cases in children recorded in healthcare institutions; ns, non-specified.*

Table 1.
Cases of cholera recorded in the decade so far.

It is general knowledge that cholera is spread through water and improper sanitation is a major risk factor for transmission. Thus, the disease deeply related to poverty in several ways including obviously the lack of resources for prevention or treatment and limitations in education or information. It is intuitive that the most susceptible are people living in highly crowded suburban areas when people have little access to clean water, or in rural settings, when people directly consume water from lakes or rivers without any treatment. People living around Lake Niassa use it for domestic purposes [5]. This is the reality in several areas of Mozambique. This must be understood on top of any specificity of the studies explained or discussed in this subsection. It must be implicit that all the studies' target populations were susceptible to cholera.

The research team of Baltazar et al. [23] belongs to the National Institute of Health, and they conducted most studies related to the vaccination campaign in Nampula City, 2016. In the particular study cited, they focused on inhabitants over 1 year old living in the city's six most susceptible neighborhoods, mentioned in Section 5.4.1 (Geographical distribution). People from surrounding areas are also at risk [4] because of mobility and interaction with residents of the endemic neighborhoods or exchange of food or drinks coming from such zones.

Children are the most susceptible to diarrheic diseases in general [11, 20] perhaps because of their immunity still under development, their unawareness of the bacterial load in the untreated water, and their behavior. In reality, they have always been the priority and focus of the vaccination campaigns [10, 45]. Among 1910 children hospitalized with acute diarrhea from May 2014 to December 2017, Salência et al. [11] found that <1-year-olds were the most affected and 19 infants (2.4%) had *V. cholerae*. The majority (58%) were male, but it seems that the proportion male/female always gravitates around 1:1 [1, 11, 22]. Mesa et al. [1] analyzed 128 processes of patients with acute diarrhea in Mocuba District Hospital, admitted during June and July 2015 in the local hospital. According to the authors, all patients presented symptoms consistent with cholera, but, despite their convictions, there was no confirmation, and they based their conclusions on clinical data (aqueous stool, vomit, and fever). In any case, all were below 16 years old in which 41% were below 5 years and 4% of the cases ended in decease. Differently, Paulo et al. [22] found 68% of individuals over 15 years old among 135 cases of cholera in the Center for Treatment of Diarrheic Diseases in Nacarôa District, recorded from 12 to 28 November 2017. The difference is likely due to a fact mentioned by the authors that none treated the water before consuming and the majority (64%) used well water. One has to imagine that the entire household uses the same water source and all the members have nearly the same level of exposition if it is contaminated, independently of the age and behavior of each individual. The age or sex differences might be a reflection of the actual sociodemographic profile of the community.

3.4 Diagnosis

There is little novelty on diagnosis in Mozambique since the beginning of the decade. It is perhaps worth mentioning that during the 2016 massive vaccination campaign in Nampula, Dengo-Baloi et al. [18] performed a rapid test to verify if it could be an alternative to the culture-based standard, as the latter takes 48 to 72 hours and the rapid test would take approximately 6 hours. They used an alkaline peptone water (APW) enrichment method, but they did not specify the origin of the kit. It was likely Crystal VC RDT (Span Divergent, Mumbai, India), previously used by George et al. [46] in Bangladesh and Ontweka et al. [47] in South Sudan. According to the latter, it is also considerably inexpensive. Dengo-Baloi et al. [18]

observed exactly the same results using the standard method and the rapid test for 75 samples, demonstrating its efficacy as a good alternative for the standard in areas with limited resources.

3.5 Control strategies

3.5.1 Overview, prophylaxis, and awareness

Cholera control strategies in Mozambique have been changing over time, perhaps due to governmental priorities, an increasing knowledge, or resources available. Regarding Mozambique, it is important to keep in mind that Mozambique has undergone major political changes, there have been conflicts, including armed, natural calamities such as drought, floods, typhoons, economic crises, and fluctuations. All these phenomena resulted in mobility or affected people's livelihoods, changing the dynamics of access to resources, including potable water, ultimately impacting public health. This ever-changing environment has been determining, at a certain extent, the way the government deals with the epidemics of infectious diseases, including cholera. Chissaque et al. [20] mentioned some key actions of the government's strategy: vaccination, health education, introduction of zinc and salts for oral hydration, improvement of basic sanitation (construction of latrines and access to potable water), and organization of national health weeks. Dengo-Baloi et al. [18] added vigilance among the measures, and Vanormelingen et al. [17] said that the government coordinated a real-time mapping of the epidemic and supported social mobilization with the assistance of the United Nations Children's Fund, World Health Organization, and Médecins Sans Frontières (MSF).

The most relevant actions in the last decade are perhaps related to the Ministry of Health's implementation of vaccination campaigns using Shanchol™ (BivWC, Shantha [48], Ranga Reddy District, Telangana, India) in Nampula City's six most vulnerable neighborhoods, in October 2016 and also the subsequent years [4, 10, 21]. It was in response to the outbreak in 2015, and the strategy was to deliver the vaccine door to door in two rounds [23]. Paulo et al. [22] mentioned another outbreak in November 2017, but it did not seem as severe. The 2016 campaign was strategically set to cover 193,403 individuals and prevent the expansion of cholera to less affected areas [4, 18]. Though the first round only covered 69.5% of the target population, and the second covered 51.2%, Baltazar et al. [23] considered the experience as a success and shared the belief that similar strategies can have more adherence in urban settings when there is no emergency. Considerably low adherence was mostly because many people were not at home during the campaign, and 17.3% of 636 people enquired said that they were unaware of the campaign. The situation was similar in the following 2 years [21]. Thus, it is important to improve or use more effectively the channels to communicate with the residents.

After vaccination, there were adverse effects such as abdominal pain, nausea, and diarrhea, but none seemed severe enough to require any medical assistance [18]. The National Institute of Health organized a vigilance of postimmunization adverse effects in nine healthcare units, and, according to Dengo-Baloi et al. [18], there were eight cases reported after the first round of vaccination, three during the second, and one case during both rounds. Yet, there were certainly more cases because Baltazar et al. [23] reported adverse effects in 47 people of 451 interviewed after receiving vaccination. A possible explanation for the discrepancy between both studies is the fact that PIAE vigilance recorded mostly cases that occurred 24 h after vaccination, and it was based on records from healthcare units, while the other study was based on inquiries directly to randomly chosen individuals from the community from 2 to 9 November 2016 [18, 23].

Among the 428 interviewees of Borges et al. [5] in Metangula, the level of awareness on cholera was very high (98%), and they said that radio (35%) and lectures at the healthcare center (28%) were the main sources of information about the disease. If the population in general is aware of the disease and still Metangula is the town most affected with cholera in Niassa Province, perhaps most inhabitants lack essential knowledge on how to prevent the disease or have very few alternatives as source of water or means to properly treat it. Yet, the investigators claim that most people from Metangula have access to potable water, but they prefer the untreated from the Lake Niassa and proposed further studies to understand their motivation. They also believe that it is necessary to intensify awareness campaigns on how to prevent cholera. However, such campaigns might not be very effective if people mistrust the authorities, as Victorino et al. [6] said. The latter authors interviewed 30 residents throughout three neighborhoods of Nampula City (the same region of the country), and they unanimously claimed that the government was responsible for the outbreak of cholera. Furthermore, the majority (18 people) did not really understand the concept of cholera (bacterial disease transmitted through water), and 12 did not know how to prevent the disease. In this case, it would be more prudent to approach the residents through authorities they might be more prone to trust, such as teachers at schools, traditional leaders and religious entities.

3.5.2 Constraints and limitations

At a first glance, the main constraints seem related to vaccination, improper treatment and potential misdiagnosis of diarrheic diseases, unclear notion on the impact of risk factors, shortage of resources for interventions, and government mistrust. Some constraints might be related, and for this reason they will not be necessarily presented in the same order as mentioned. This subsection might seem redundant in the sense that it recapitulates some limitations from the previous subsections. However, it seems important to discuss them in more detail, as they are likely to be the starting point for future researchers aiming to study the dynamics of cholera epidemiology and control strategies in Mozambique. Furthermore, some ideas are consolidated, and some relationships are explored more critically in this subsection.

According to Baltazar et al. [23], during the 2016 vaccination campaign in Nampula, more than one third missed the vaccine because they were not at home or did not receive any information prior to the campaign, and in the second round, there were less people available, though dropout rates from the first to the second dose up to 13% is not uncommon due to factors such as migration or other reasons leading people to be absent [49, 50]. Salomão et al. [21] stated that it happened again the following year, and, according to them, the main reasons were lack of time, absence, and lack of information. The overall vaccine wastage rate was 10%, and it seems high if compared with the experience in Bangladesh between February and April 2011, where it was 1.2% [49]. Such wastage might be partially related to reasons to be discussed in the following paragraph.

It seems important to discuss the most likely motivation for the vaccination campaign's suboptimal adherence. Since the strategy was door to door, it seems difficult to suddenly receive someone claiming to be from the government and offering substances to all family members including children. Even if the visitors show credentials, many inhabitants mistrust the government and blame it for the disease [6, 8]. In contrast, Botão et al. [8] interviewed 145 individuals from the target population, and 92% said they were willing to receive the vaccine. It is hard to clarify why they showed interest, but the actions were different, but a possible explanation would be that they just manifested agreement for the convenience of the interview or because

they fear the authorities. Such attitude toward the government is not new or exclusive to Nampula or northern Mozambique. For instance, Pool et al. [33] reported a similar behavior during a campaign for immunization against malaria 10 years before in Manhiça District, southern Mozambique. Similarly, rumors stated that the local clinic was trying to poison the children. In Gurúè City, people believe that cholera is sent as spells by evil individuals [2]. It would be an asset to investigate what religious leaders or traditional healers think of cholera and government interventions, because it is common for people in Mozambique to rely on them in matters of health, in some cases even for immunization. The fact that conventional practitioners are a direct competition for their source of income cannot be underestimated, and if people, including their leaders and traditional healers, regard outbreaks of diarrhea as a spiritual matter, they might not understand the governments' true motivations, and "conspiracy theories" will keep spreading. Botão et al. [8] reported emerging conflicts related to previous cholera interventions between health professionals, community leaders, and health activists, sometimes escalating to episodes of violence. Interventions seem to become more difficult over time as the locals create barriers for the professionals, and both Botão et al. [8] and Salomão et al. [21] believe only the notion that cholera is life-threatening can motivate the population to accept the vaccine. In any case, prior to vaccination, there should be a strong campaign targeting traditional authorities in order to promote their collaboration and influence the adults, and likewise directed to teachers, to influence the children. It would also include, in the strategy, ways to make sure that people are not absent during the campaigns.

Baltazar et al. [23] also stated that 10% of the individuals experienced side effects after vaccination, and it seems a plausible explanation for the decline of 18.3% in adherence between the two rounds. It is possible that such individuals and their families or relatives preferred not to receive the second dose, and it can still be confirmed if the interview records are available. Minor side effects to this vaccine (Shanchol™) should have been expected in some people [48, 51], and it has been observed in Bangladesh [52]. The vaccination campaign in Nampula was certainly carried with informed consent and following the WHO [53] recommendations, but if the side effects in fact led people to withdraw from the second round, it is important to reevaluate the communication with the target population. The Centers for Disease Control and Prevention [54] recommend competent authorities to explain the people to be vaccinated about the "benefits of and risks from vaccines in language that is culturally sensitive and at an appropriate educational level."

Misdiagnoses should also not be underestimated, especially because it has impact on the choice of treatment. Chissaque et al. [20] reported lack of consistent protocols to directly relate a pathogen with a particular diarrheic profile and also the respective risk factors. Outbreak of a disease can be misleading when there are people carrying diseases with similar symptoms. For instance, Chitio et al. [24] detected *Aeromonas spp.* in 10.4% of 289 samples of rectal swabs from individuals with symptoms consistent with cholera during outbreaks of the latter. Sometimes even conventional culture methods can fail to detect *V. cholerae* [55]. Furthermore, Gupta et al. [56] found that clinical conditions of a coinfection cholera-rotavirus and cholera alone can easily be confused. There should be efforts to ensure rigorous differential diagnoses when it is possible.

Salência et al. [11] reported the abusive use of antibiotics to treat acute diarrhea in children, including confirmed cases of cholera (2.4%), between May 2014 and December 2017 in major hospitals from all regions of Mozambique. According to the authors, antibiotics were used to treat 94% of the patients, and this represents a violation of the WHO's protocol that recommends the use of these compounds when there is cholera, dysentery, and other "recognizable severe cases" [57].

Antibiotic misuse is frequent in developing countries but such level was extreme. For instance, Runesson et al. [58] reported the use of antibiotics in 70% of cases of children with diarrhea, randomly examined in a children's hospital, from which at least 35% did not really need antibiotics. According to Rogawski et al. [59], antibiotics have the potential to modify the gastrointestinal microbiota and increase the risk of a reduced time to a subsequent diarrhea episode. It is also known that antibiotic abuse frequently results in resistance. In 2007, Mandomando et al. [60] reported a high incidence of resistance to chloramphenicol (57.9%), co-trimoxazole (96.6%), and tetracycline (97.3%), and low for quinolone (4.2%). Salência et al. [11] mentioned the use of ampicillin (45%), gentamicin (39%) combined with therapy, and gentamicin (10%). Thus, there should be efforts to discourage physicians to prescribe antibiotics when it is not necessary. When appropriate, they can use quinolone or third-generation cephalosporins [60].

4. Conclusions

The presentations in the XVI National Health Journeys and the recent articles on cholera offered an invaluable contribution to the current knowledge on the disease in Mozambique, particularly regarding the risk factors, health determinants, and immunization process. Such contributions showed how important the journeys were. The Ministry of Health and related institutions have been active in research and interventions to control cholera in Mozambique. The immunization campaign in 2016 certainly had high impact in reducing the incidence of cholera, as no outbreak has been as wide and severe as 2015's (the ones this year are not considered because their extent is still to be assessed). Yet, governmental effort cannot achieve the desired results if there is no collaboration from the civil society. The etiology, risk factors, and epidemiology of the disease are fairly known, and, although the government lacks resources to provide proper sanitation, access to clean water, or vaccine coverage for all people at risk, it is now a matter of designing a strategy to tackle each the issue, and if the plan is solid, funds can be acquired and well used.

5. Recommendations

The following recommendations are not simply observations based on findings shared during the XVI Health Journeys. They are supplemental observations on their actual recommendations, in a broader context if necessary. It seemed unnecessary to bring to light ideas of improvements if the authors have already done so, this being a mere enhancement if they seem incomplete.

Environmental determinants such as water, sanitation, and hygiene synergistically impact the extent of severity of cholera. Thus, Marrufo et al. [4] strongly recommended their evaluation during outbreak-related emergencies. It is true, but such evaluation should not solely occur during outbreaks. Proper management of the way people use water is crucial to prevent outbreaks in the first place, although factors such as heavy rainfall, warm air temperature, or low river flows cannot be controlled, and they increase the exposition of humans to *V. cholerae* [61, 62]. Ramos et al. [19] and Chissaque et al. [20] agreed, but they proposed a more practical approach through construction of specialized improved latrines, adaptable to high levels of the water table, and improved sanitation. Paulo et al. [22] added that it could be done through multi-sectoral groups involving researchers, community leaders, and engineers. It is eventually necessary to act rather than waste plenty of time analyzing the situation, particularly when it urges to make decisions, but

Marrufo's opinion seems more prudent, and it should be the first step, and then the government could consider improvements, still after evaluating their viability. Considering the cost Dengo-Baloi et al. [7] explained the necessity to evaluate how much the Ministry of Health spends for an immunization campaign, but it applies to all forms of intervention and also research. The economic component is crucial, and it should also include how and where to obtain and channel the funds and the best way to manage it in order to prevent unnecessary losses.

Still within the context of health determinants, Borges et al. [5] manifested preoccupations with the people directly using lake water in Niassa, without any treatment, even when they have potable water available. They intended to understand why, and they recommended studies in this direction. They and other authors [6, 22] also think health education campaigns could lead people to understand the risk of such behavior and ultimately take the appropriate measures. The authors are certainly pointing to a constructive direction, but it is a delicate endeavor to convince people to abandon their values and traditions. Niassa Lake, more than a useful water source, is certainly also a source of recreation and economic activities such as fishing or *garimpo*, and the reasons why people use the lake even with water at home might be the same as why urban populations leave their homes to a swimming pool or to the sea for surfing or fishing. Maybe they are moved by the experience, not merely out of necessity. The disbelief in cholera as a bacterial worldwide pandemic in favor of theories of government conspiracy worsens the situation. In this case, particularly if the lake is a source of so many benefits, positive psychology seems to be a more effective direction to consider: showing the benefits of using alternatives (e.g., consuming only treated water) for the same ends rather than repeating how prejudicial the lake water might be. It still means that community education is necessary because people have to know how to prevent cholera.

Chitio and Langa [24] called for a clear definition of cases of *Aeromonas* spp. contaminations during cholera outbreaks to prevent improper treatment. This should not be just for the genus mentioned, but in general physicians should require differential diagnostic for suspected cases of cholera, rather than taking rushed decisions based on arbitrary probability during outbreaks, because it might worsen the problem or create new problems for the patients. If they found that 10% of the cases suspected of cholera were actually related to *Aeromonas* infection, how many might have been related to other causes than *Vibrio* or *Aeromonas*? And which were the consequences of their possible misdiagnosis?

After successfully performing the rapid test for cholera, Dengo-Baloi et al. [18] recommended it as an alternative tool, but they believe that the culture method shall remain to confirm the epidemics, to monitor antibiotic sensitivity, and to produce pure isolates for molecular characterization. Considering how critical outbreaks are, the authors provided a very prudent opinion, and, although their results were highly promising, it is perhaps better to keep testing the method and compare the results with others from authors in different settings before it becomes a standard.

Immunization is already a well-developed area because there are very well-crafted guidelines, based on logical, scientific, and empirical sources, and it has been practiced for many years. Still, healthcare professionals have to face contextual issues, and it results in every-evolving strategies. The door-to-door vaccination strategy seems very effective, and Baltazar et al. [23] said it is better to implement as a preventive measure against potential outbreaks. Having said so, they did not put emphasis on the strategy during outbreaks, possibly because it is preferable to manage the disease when it is easier to control. It is perhaps important to consider the Médecins Sans Frontières [63] recommendations for door-to-door strategies, some of which are already fulfilled. First, it is good that people already have

experience with this approach, and there is some acceptance [23]. Second, it is important to coordinate the process with the authorities at neighborhood levels or small communities, where information is easy to spread, and it is also easy to record the number of residents or households in order to keep track of individuals absent during each round and organize catch-up rounds. Baltazar et al. [23] also suggested short-term effectiveness studies, but these have been done and reported by Dengo-Baloi et al. [7] from the same research team. Perhaps the results had not yet been analyzed when Baltazar et al. [23] had already completed their report. To maximize adherence, Botão et al. [8] suggested sensibilization of the population through identification of credible leaders and other influential individualities to function as mobilizers during the entire campaign.

Salência et al. [11] discussed about the indiscriminate use of antibiotic to children with acute diarrhea as a violation of WHO guidelines, and the authors appealed for the optimization of prescription of antibiotics for diarrhea. The authors are correct, but the issue requires perhaps more attention, considering that WHO guidelines result from the international consensus and, in general, physicians are expected to be aware of the dangers of antibiotic overprescription, and this practice is often most likely an act of negligence. Thus, there should be penalties to discourage such kind of misconduct because it is a sensitive public health matter.

The National Health Institute and partners shall keep organizing the National Health Journeys and similar events because they are very constructive platforms in which researchers, scholars, and health professionals can share information and broaden their scope regarding the reality of cholera and other diseases in Mozambique. Such events should be more frequent and organized all over the country to give opportunities to people residing in other areas than the capital city. It would perhaps be a very good idea to promote conferences about the control of cholera or diarrheic diseases in areas of high incidence and engage local health professionals or potential actors who can really influence the current situation.

The final recommendation is based on the words of Chissaque et al. [10] in their summary: the key to control cholera and other diarrheic diseases is a deep understanding of the local epidemiology. Such comprehension would facilitate predictions and planning on how to prevent outbreaks and manage them if they eventually happen. Mozambique could study carefully experiences from other countries where cholera is endemic, such as India or Bangladesh, and understand how they deal with the matter or at least draw some comparisons and interact with foreign scientists. The contexts are surely different, but the problem is similar, and solutions might arise from unexpected variables.

6. Post-conclusive note

There will be soon more updates on cholera in Mozambique because there were two major outbreaks [40, 64, 65], one still ongoing as this manuscript is under preparation [66]. They are related to the intense tropical cyclones Idai and Kenneth that made landfall in Mozambique's central and northern provinces, respectively [67]. According to Miller and Adebayo [37], Kenneth it is the strongest cyclone recorded in the country, and together the tragedies certainly caused the biggest losses since the flood in 2000 [68]. Briefly, Devi [40] said that up to April 20, the Ministry of Health had declared an outbreak due to Idai, and there had been at least 4979 cases of cholera and 6 deaths. Regarding Kenneth, the United Nations Office for the Coordination of Humanitarian Affairs (OCHA) [64] declared that as of 12 May, there were 149 confirmed cases of cholera in Pemba, Metuge, and Mecufi.

Conflict of interest

The authors declare no conflict of interest.

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References

[1] Mesa F, Simbine E, Faranguana AC. Análise de casos de diarreias agudas e óbitos no Hospital Distrital de Mocuba-Junho a Julho de 2015. Revista Moçambicana de Saúde Pública. 2018;**4**:190

[2] Carlos I. Perfil sociodemográfico e cultural dos munícipes da cidade de Gurué, sua relação com a epidemiologia de cólera. Revista Moçambicana de Ciências de Saúde. 2018;**4**:256

[3] Francisco J, Chindia JA. Factores ambientais associados a eclosão e reeclosão da endemia da cólera no Niassa. Revista Moçambicana de Ciências de Saúde. 2018;**4**:134

[4] Marrufo T, Salomão C, Chicumbe S, Muianga C, Cardoso N, Baltazar C, et al. Avaliação de determinantes ambientais (água, saneamento e higiene) na cidade de Nampula em 2016. Revista Moçambicana de Ciências de Saúde. 2018;**4**:66

[5] Borges BV, Armando E, Missage E. Acesso à água, higiene, atitudes e práticas relacionadas com a prevenção da cólera em torno das comunidades do município de Metangula, província de Niassa, 2016. Revista Moçambicana de Ciências de Saúde. 2019;**4**:104

[6] Victorino J, Savaio L, António M. Mitos e boatos da cólera na província de Nampula Janeiro-Março 2018. Revista Moçambicana de Ciências de Saúde. 2018;**4**:149

[7] Dengo-Baloi L, Semá-Baltazar C, Barata A, Malaco C, Chitio J, Muloliwa A, et al. Uso do teste rápido de cólera (modificado) para detectar e monitorar surtos: Monitoria da eficácia da vacina oral contra cólera após campanha de vacinação massiva em Nampula, 2016. Revista Moçambicana de Ciências de Saúde. 2018;**4**:214

[8] Botão C, Paulo J, Chucumbe S, Sinai C, Magaço A, Matsimbe M, et al. Avaliação antropológica: barreiras e facilitadores para aceitação da vacina oral de cólera em Nampula Cidade, 2016. Revista Moçambicana de Ciências de Saúde. 2018;**4**:236

[9] Garrine M, Mandomando I, Vubil D, Nhampossa T, Acacio S, Li S, et al. Minimal genetic change in *Vibrio cholerae* in Mozambique over time: Multilocus variable number tandem repeat analysis and whole genome sequencing. PLoS Neglected Tropical Diseases. 2017;**11**(6):e0005671

[10] Chissaque A, de Deus N, Vubil D, Mandomando I. The epidemiology of diarrhea in children under 5 years of age in Mozambique. Current Tropical Medicine Reports. 2018;**5**(3):115-124

[11] Salência J, Chissaque A, Chilaúle J, Anapakala E, Guimarães E, Manique L, et al. Aderência ao protocolo no uso de antibióticos para tratamento de diarreia aguda em crianças. Revista Moçambicana de Ciências de Saúde. 2018;**4**:86

[12] World Health Organization. The Treatment of Diarrhoea: A Manual for Physicians and Other Senior Health Workers. Geneva, Switzerland: WHO Library; 2005. 44p

[13] World Health Organization, UNICEF. Clinical Management of Acute Diarrhoea: WHO/UNICEF Joint Statement. Geneva, Switzerland: WHO Library; 2004. 8p

[14] Capitine I, Chicumbe S, Chitio J, Langa JP. Avaliação económica da campanha de vacinação com a vacina oral contra cólera em Nampula, Moçambique. Revista Moçambicana de Ciências de Saúde. 2018;**4**:290

[15] Gujral L, Sema C, Rebaudet S, Taibo CLA, Manjate AA, Piarroux R, et al. Cholera epidemiology in Mozambique using national surveillance data. The Journal of Infectious Diseases. 2013;**208**(suppl_1):S107-SS14

[16] Langa JP, Sema C, De Deus N, Colombo MM, Taviani E. Epidemic waves of cholera in the last two decades in Mozambique. Journal of Infection in Developing Countries. 2015;**9**(6):635-641

[17] Vanormelingen K, Le Pechoux M, Bonde T. Cholera Outbreaks in Tete, Sofala, Zambezia, Nampula and Niassa Provinces: UNICEF Mozambique. 2015. Available from: www.unicef.org/appeals/files/UNICEF_Mozambique_SitRep_26_March_2015.pdf

[18] Dengo-Baloi LL, Langa JP, Semá-Baltazar C, Chicumbe S. Avaliação dos eventos adversos pós campanha de vacinação oral contra cólera (EAAI-VOC) em cinco bairros da cidade de Nampula, 2016. Revista Moçambicana de Saúde Pública. 2018;**4**:213

[19] Ramos E, Jasse L, Samo T. A problemática de saúde pública no bairro novo na cidade de Quelimane. Revista Moçambicana de Saúde Pública. 2018;**4**:127

[20] Chissaque A, Deus ND, Vubil D, Mandomando I. Revisão da epidemiologia da diarreia em crianças nos últimos 20 anos em Moçambique (1997-2017). Revista Moçambicana de Ciências de Saúde. 2018;**4**:133

[21] Salomão C, Langa J, Bertil A, Baltazar C. Vacina oral contra cólera, conhecimentos atitudes e práticas, diferenças e igualdades em duas campanhas, Tete 2017-2018. Revista Moçambicana de Ciências de Saúde. 2018;**4**:282

[22] Paulo M, Gurjal L, Cardoso N. Investigação de surto de cólera, na comunidade de Casacone, na província de Nampula, Novembro 2017. Revista Moçambicana de Ciências de Saúde. 2018;**4**:134

[23] Baltazar CS, Baloi LD, Salomão C, Rafael F, Mengel MA, Gessner BD, et al. Cobertura vacinal e aceitabilidade durante a campanha de vacinação contra cólera na cidade de Nampula, 2016. Revista Moçambicana de Ciências de Saúde. 2018;**4**:53

[24] Chitio JJE, Langa JPM. Frequência e perfil de susceptibilidade de *Aeromonas* spp. isolados de surtos de cólera nas regiões centro e norte de Moçambique, 2014-2015. Revista Moçambicana de Ciências de Saúde. 2018;**4**:29

[25] Mocumbi AO. Revista Moçambicana de Ciências de Saúde. Special ed. Maputo, Mozambique: Instituto Nacional de Saúde de Moçambique; 2018

[26] Instituto Nacional da Saúde. Sobre as Jornadas Maputo. 2018. Available from: http://jornadas.insconferencias.co.mz/sobre-as-jornadas/

[27] Domman D, Chowdhury F, Khan AI, Dorman MJ, Mutreja A, Uddin MI, et al. Defining endemic cholera at three levels of spatiotemporal resolution within Bangladesh. Nature Genetics. 2018;**50**(7):951-955

[28] Mutreja A, Kim DW, Thomson NR, Connor T, Hee Lee J, Kariuki S, et al. Evidence for several waves of global transmission in the seventh cholera pandemic. Nature. 2011;**477**:462-465

[29] Hu D, Liu B, Feng L, Ding P, Guo X, Wang M, et al. Origins of the current seventh cholera pandemic. Proceedings of the National Academy of Sciences. 2016;**113**(48):E7730-E77E9

[30] Gradín C, Tarp F. Investigating growing inequality in Mozambique.

South African Journal of Economics. 2019;**87**(2):110-138

[31] World Health Organization, United Nations Children's Fund. Drinking Water | JMP: World Health Organization (WHO) and United Nations Children's Fund (UNICEF). 2019. Available from: https://washdata.org/monitoring/drinking-water

[32] Seibert G. "But the Manifestation of the Spirit Is Given to every Man to Profit Withal": Zion Churches in Mozambique since the Early 20th Century. Le Fait Missionnaire. 2005;**17**:125-150

[33] Pool R, Munguambe K, Macete E, Aide P, Juma G, Alonso P, et al. Community response to intermittent preventive treatment delivered to infants (IPTi) through the EPI system in Manhica, Mozambique. Tropical Medicine & International Health. 2006;**11**(11):1670-1678

[34] World Health Organization. WHO | Areas Affected by Cholera Epidemics: World Health Organization. 2016. Available from: https://www.who.int/gho/epidemic_diseases/cholera/epidemics_text/en/ [Updated: 26 September 2016]

[35] Ansaruzzaman M, Bhuiyan NA, Safa A, Sultana M, McUamule A, Mondlane C, et al. Genetic diversity of El Tor strains of *Vibrio cholerae* O1 with hybrid traits isolated from Bangladesh and Mozambique. International Journal of Medical Microbiology. 2007;**297**(6):443-449

[36] Wikimedia Commons. File: Mozambique sat.png. San Francisco, California, USA: The Wikimedia Foundation Inc. 2006. Available from: https://en.wikipedia.org/wiki/File:Mozambique_sat.png

[37] Miller B, Adebayo B. Cyclone Kenneth. Thousands Evacuated as Mozambique is hit with the Strongest Storm in its History. Atlanta, Georgia, USA: Cable News Network. 2019. Available from: https://edition.cnn.com/2019/04/25/africa/cyclone-kenneth-mozambique-evacuation-intl/index.html

[38] World Health Organization. WHO | Cholera Case Fatality Rate: World Health Organization. 2017. Available from: https://www.who.int/gho/epidemic_diseases/cholera/case_fatality_rate_text/en/ [Updated: 18 September 2017]

[39] Schnoering K. Mozambique Cyclone Idai Response. UN Migration; 2019. Report No.: 2

[40] Devi S. Cyclone Idai: 1 month later, devastation persists. Lancet (London, England). 2019;**393**(10181):1585

[41] Anjichi-Kodumbe T, Abreu S, van Vliet T. Southern Africa: Tropical Cyclone Kenneth Flash Update No. 8: United Nations Office for the Coordination of Humanitarian Affairs (OCHA). 2019. Available from: https://reliefweb.int/sites/reliefweb.int/files/resources/ROSEA_20190503_SouthernAfrica_TCKenneth_FlashUpdate8_DRAFT.pdf

[42] Anjichi-Kodumbe T, Abreu S, van Vliet T. Southern Africa: Tropical Cyclone Kenneth Flash Update No. 7: United Nations Office for the Coordination of Humanitarian Affairs (OCHA). 2019. Available from: https://reliefweb.int/sites/reliefweb.int/files/resources/ROSEA_20190501_SouthernAfrica_TCKenneth_FlashUpdate7_FINAL.pdf

[43] Cabral D, Balde T, Schmachtel C. Tropical Cyclone Idai, Mozambique: Donor Alert. Geneva, Switzerland: World Health Organization; 2019

[44] Chingwaru W. Letters to the Editor: How to Keep Cholera and Typhoid at Bay in the Post Cyclone Idai Period:

@ChronicleZim. 2019. Available from: https://www.chronicle.co.zw/letters-to-the-editor-how-to-keep-cholera-and-typhoid-at-bay-in-the-post-cyclone-idai-period/

[45] Jeuland M, Lucas M, Clemens J, Whittington D. A cost–benefit analysis of cholera vaccination programs in Beira, Mozambique. The World Bank Economic Review. 2009;**23**(2):235-267

[46] George CM, Rashid MU, Sack DA, Bradley Sack R, Saif-Ur-Rahman KM, Azman AS, et al. Evaluation of enrichment method for the detection of *Vibrio cholerae* O1 using a rapid dipstick test in Bangladesh. Tropical Medicine & International Health. 2014;**19**(3):301-307

[47] Ontweka LN, Deng LO, Rauzier J, Debes AK, Tadesse F, Parker LA, et al. Cholera rapid test with enrichment step has diagnostic performance equivalent to culture. PLoS One. 2016;**11**(12):e0168257

[48] Shantha. Cholera Vaccine (Inactivated, Oral) I.P. Shanchol Mahape, Navi Mumbai, India: Sanofi Pasteur India Private Limited. 2014. Available from: https://www.stopcholera.org/sites/cholera/files/shanchol_insert_3-2015.pdf

[49] Khan IA, Saha A, Chowdhury F, Khan AI, Uddin MJ, Begum YA, et al. Coverage and cost of a large oral cholera vaccination program in a high-risk cholera endemic urban population in Dhaka, Bangladesh. Vaccine. 2013;**31**(51):6058-6064

[50] Khan AI, Levin A, Chao DL, DeRoeck D, Dimitrov DT, Khan JAM, et al. The impact and cost-effectiveness of controlling cholera through the use of oral cholera vaccines in urban Bangladesh: A disease modeling and economic analysis. PLoS Neglected Tropical Diseases. 2018;**12**(10):e0006652

[51] World Health Organization. Use of Oral Cholera Vaccine in Humanitarian Emergencies. Geneva, Switzerland: World Health Organization; 2014. Available from: https://www.who.int/cholera/vaccines/OCV_in_humanitarian_emergencies_15Jan2014.pdf

[52] Saha A, Chowdhury MI, Khanam F, Bhuiyan MS, Chowdhury F, Khan AI, et al. Safety and immunogenicity study of a killed bivalent (O1 and O139) whole-cell oral cholera vaccine Shanchol, in Bangladeshi adults and children as young as 1 year of age. Vaccine. 2011;**29**(46):8285-8292

[53] World Health Organization. WHO Recommendations for Routine Immunization—Summary Tables. Geneva, Switzerland: World Health Organization; 2019. Available from: https://www.who.int/immunization/policy/immunization_tables/en/

[54] Centers for Disease Control and Prevention. Preventing and Managing Adverse Reactions. Atlanta, Georgia, United States: Centers for Disease Control and Prevention; 2017

[55] Alam M, Hasan NA, Sultana M, Nair GB, Sadique A, Faruque AS, et al. Diagnostic limitations to accurate diagnosis of cholera. Journal of Clinical Microbiology. 2010;**48**(11):3918-3922

[56] Gupta S, Jhamb U, Uppal B, Chakraverti A, Mittal SK. Diagnosing cholera in the young: A review of WHO criteria. JK Science. 2007;**9**(3):137-139

[57] Bruzzese E, Giannattasio A, Guarino A. Antibiotic treatment of acute gastroenteritis in children. F1000Res. 2018;**7**:193

[58] Runesson J, Shamansurova E, Jacobsson G. Antibiotics are being misused to treat diarrhoeal disease in children in Central Asia. Acta Paediatrica (Oslo, Norway: 1992). 2016;**105**(12):1382-1383

[59] Rogawski ET, Westreich DJ, Becker-Dreps S, Adair LS, Sandler RS, Sarkar R, et al. Antibiotic treatment of diarrhoea is associated with decreased time to the next diarrhoea episode among young children in Vellore, India. International Journal of Epidemiology. 2015;**44**(3):978-987

[60] Mandomando I, Espasa M, Valles X, Sacarlal J, Sigauque B, Ruiz J, et al. Antimicrobial resistance of *Vibrio cholerae* O1 serotype Ogawa isolated in Manhica District Hospital, Southern Mozambique. The Journal of Antimicrobial Chemotherapy. 2007;**60**(3):662-664

[61] Jutla A, Whitcombe E, Hasan N, Haley B, Akanda A, Huq A, et al. Environmental factors influencing epidemic cholera. The American Journal of Tropical Medicine and Hygiene. 2013;**89**(3):597-607

[62] Camacho A, Bouhenia M, Alyusfi R, Alkohlani A, Naji MAM, de Radiguès X, et al. Cholera epidemic in Yemen, 2016-2018: An analysis of surveillance data. The Lancet Global Health. 2018;**6**(6):e680-e690

[63] Médecins Sans Frontières. Chapter 4: Strategies for epidemic response. 2018 [cited 7 June 2019]. In: Management of a Cholera Epidemic: Practical Guide for Doctors, Nurses, Laboratory Technicians, Medical Auxiliaries, Water and Sanitation Specialists and Logisticians [Internet]. Geneva, Switzerland: Médecins Sans Frontières; 7 June 2019. Available from: https://medicalguidelines.msf.org/viewport/CHOL/english/4-7-vaccination-strategies-23448968.html#

[64] Anjichi-Kodumbe T, Abreu S, van Vliet T. Southern Africa: Tropical Cyclone Kenneth Flash Update No. 13: United Nations Office for the Coordination of Humanitarian Affairs (OCHA). 2019. Available from: https://reliefweb.int/report/mozambique/southern-africa-tropical-cyclone-kenneth-flash-update-no-13-12-may-2019

[65] Isbell T, Bhoojedhur S. Cyclones add to Mozambique's Public Health Challenges. 2019. Available from: https://www.afrobarometer.org/publications/ad297-cyclones-add-mozambiques-public-health-challenges

[66] United Nations Office for the Coordination of Humanitarian Affairs. Southern Africa: Tropical Cyclone Kenneth: United Nations Office for the Coordination of Humanitarian Affairs (OCHA). 2019. Available from: https://reliefweb.int/report/mozambique/southern-africa-tropical-cyclone-kenneth-flash-update-no-8-3-may-2019

[67] Isbell T, Bhoojedhur S. Cyclones add to Mozambique's Public Health Challenges/Ciclones aumentam os desafios de saúde pública em Moçambique South Africa: Centre for International Governance Innovation, South African Institute of International Affairs. 2019. Available from: https://www.africaportal.org/publications/cyclones-add-mozambiques-public-health-challenges-ciclones-aumentam-os-desafios-de-sa%C3%BAde-p%C3%BAblica-em-mo%C3%A7ambique/

[68] Filipe J. In: Muiambo P, editor. Moçambique 2000: As Águas da Morte. 1st ed. Maputo: Moçambique Editora Lda.; 2003. 191p