

The Revival of Cholera Vaccines

The Century-Old Making of a Global Success Story

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Abstract: Cholera vaccines have existed since the nineteenth century but were largely considered an ineffective control strategy for much of their history. However, in 2012, cholera vaccination campaigns were piloted in Haiti and Guinea using a preexisting vaccine formula. These initial efforts quickly expanded to dozens of countries. A global stockpile of millions of doses was established, positioning cholera vaccines as a cornerstone to the Global Task Force on Cholera Control's Roadmap to ending cholera by 2030. What factors contributed to this remarkable turnaround? This piece explores the epistemic, moral, and industrial reconfigurations that sustained the crafting of a global vaccine *success story* and its ramifications within a shifting global health landscape, including the potential displacement of water and sanitation interventions. The research is based on my participation in cholera vaccine introductions as a medical NGO worker and on symmetric ethnographic fieldwork conducted in African settings targeted for reactive cholera vaccination and in global North centers influencing global cholera vaccine policy.

Keywords: cholera; vaccines; global health; pharmaceuticalization; epidemic response; vaccine deployment; humanitarian medicine; Water and Sanitation (WASH)

Résumé: Les vaccins contre le choléra existent depuis le XIX^e siècle, mais ont été considérés comme une stratégie de contrôle inefficace pendant la majeure partie de leur histoire. Cependant, en 2012, des campagnes de vaccination contre le choléra ont été menées à titre expérimental en Haïti et en Guinée en utilisant une formule vaccinale préexistante. Ces efforts initiaux se sont rapidement étendus à des dizaines de pays. Un stock mondial de millions de

doses a été constitué, faisant des vaccins anti-choléra, la pierre angulaire de la stratégie du Groupement mondial pour la lutte contre le choléra (Global Task Force on Cholera Control's Roadmap), qui vise à éradiquer le choléra d'ici 2030. Quels sont les facteurs ayant contribué à ce remarquable revirement? Cet article explore les reconfigurations épistémiques, morales et industrielles qui ont soutenu l'élaboration d'un vaccin à succès et ses ramifications dans un paysage sanitaire mondial en mutation, y compris le déplacement potentiel des interventions dans le domaine de l'eau et de l'assainissement. La recherche est basée sur ma participation à l'introduction du vaccin contre le choléra en tant que membre d'une ONG médicale et sur un travail de terrain ethnographique mené à la fois dans des environnements africains ciblés par la vaccination réactive contre le choléra et dans des centres du Nord qui influencent la politique mondiale en matière de vaccins contre le choléra.

Mots clés: choléra; vaccins; santé mondiale; pharmaceutiques; réponse aux épidémies; déploiement de vaccins; médecine humanitaire; Eau, Assainissement et Hygiène (WASH)

Introduction

Cholera vaccines have had a long and complex history, dating back to the nineteenth century. Despite their early development, they were considered an ineffective control strategy for over a century. However, a dramatic shift occurred in 2012 when oral cholera vaccine (OCV) campaigns were piloted in Haiti and Guinea using a preexisting vaccine formula. These campaigns sparked a global interest, leading to the establishment of a vaccine stockpile by the Global Vaccine Alliance (Gavi). OCVs soon became the cornerstone of cholera control strategies. This research paper examines the epistemic, moral, and industrial reconfigurations that led to the transformation of the cholera vaccine into a global success story, as well as its ramifications within the ever-evolving global health arena, including the potential sidelining of water and sanitation efforts.

This research is informed by my direct experience participating in cholera surveillance and cholera vaccine introductions as a medical NGO worker,¹ as well as symmetric ethnographic fieldwork conducted in African settings targeted for reactive cholera vaccine introductions and in global North centers that have shaped global cholera vaccine policy. By analyzing the forces that propelled the cholera vaccine into prominence, I seek to understand the driving factors behind its resurgence and the potential implications of its widespread use for cholera control efforts and global health strategies.

In 1885, one year after Robert Koch's identification of the causative agent for cholera, Jaime Ferrán Clúa developed the first cholera vaccine and used it to vaccinate 50,000 individuals in Valencia, Spain, during an outbreak (Lopez et al. 2014; Pollitzer 1959). While this injectable (parenteral) vaccine provided limited protection to its recipients, it also caused severe or even fatal reactions in some cases (Pollitzer 1959:293). In 1891, Waldemar Haffkine created another injectable cholera vaccine at Institut Pasteur, testing it first on himself before travelling to the Ganges delta in India primarily through self-funding to find voluntary participants for further trials (Lutzker, Jochowitz, and Haffkine 1980).

In 1893, two years after Haffkine's vaccine, Sawtschenko and Sabolotny introduced the first oral cholera vaccines. The inventors, along with one of their students, followed the tradition of self-experiment by ingesting the vaccine. They later also ingested a virulent cholera broth and monitored their symptoms. Noting none, they sought other volunteers for their vaccine.

Over the following decades various oral and parenteral vaccines were developed. To discover which type was more effective against cholera, field trials comparing advanced versions of both oral and parenteral vaccines were conducted in India during the 1920s and 1930s. Russell's results, as discussed by Pollitzer, indicated that the parenteral anti-cholera vaccine was more effective and caused fewer complications. Notably, the tested oral vaccine, bilivacin, occasionally triggered reactions, including diarrhea, undermining the vaccination effort and leading to accusations of spreading the disease (Russell 1928 also cited in Pollitzer 1959).

Pollitzer and Burrows concluded in the late 1950s that the adverse reactions, challenges in preparing oral solutions, and high costs likely contributed to the decline in the use of oral vaccines. Parenteral vaccines would soon experience a similar fate. Studies from the 1960s reported unstable and short-lived protection, as well as frequent side effects (Benenson, Joseph, and Oseasohn 1968; Berger and Shapiro 1997; Clemens et al. 2018). A 1973 *Lancet* article dealt the final blow, asserting that in an epidemic context, parenteral vaccination could prevent only one in 20 cholera cases with one staff member per health unit, or one in four cases with an "unlimited" number of human resources for the campaign (Sommer and Mosley 1973). That same year, the World Health Organization (WHO) removed cholera vaccine certifications from the International Health Regulations. Although the WHO had never recommended cholera vaccines, some countries had required them for travelers during epidemics. This marked the end of 80 years of uncertain cholera vaccination efforts.

The Unexpected Resurgence of Oral Cholera Vaccines

In the 1970s and 1980s, the treatment of cholera and other diarrheal diseases underwent a revolution with the development of new intravenous and Oral Rehydration Therapies (ORT). This led to a reduction in mortality from enteric diseases, including cholera, with mortality rates dropping from 30%–50% to 1%–5% with ORT, with one million lives saved each year among children under five (Hirschhorn et al. 1968). The era also resolutely focused on integrated approaches to preventing waterborne diseases. These efforts aimed to address multiple waterborne pathogens by broadening access to safe water and sanitation. A key example is the establishment of the “International Decade for Drinking Water Supply and Sanitation” (WHO 1983).

Despite this seemingly unfavourable context to cholera vaccines, which were unreliable and only protected against one waterborne disease, interest was revived by a new generation of researchers who believed that oral vaccines developed with modern tools could offer better intestinal immune response than their predecessors, including parenteral vaccines. Initial oral cholera vaccine experiments were conducted on volunteers in Sweden and the United States of America (US) followed by a clinical trial involving 65,000 people in Bangladesh in the 1980s (Clemens et al. 1986). The vaccine was found to confer 85% protection at six months but declined to 62% at one year and 58% at two years (Sanchez et al. 1994). From this candidate vaccine emerged Dukoral[®], a commercial vaccine produced and sold by Crucell in Sweden. Dukoral[®] was expensive² and required a glass of water (water buffer) during administration; it was intended for wealthy travellers but was also used by the US Army for Gulf War operations. The vaccine formula was later transferred from Gothenburg University to a Vietnamese public biomedical institution and modified to include a newer *Vibrio Cholera* strain (0139). The Vietnamese modified formula was licensed under the commercial product ORC-Vax in 1997 by Vabiotech, a company contracted by the Vietnamese Ministry of Health (Odevall et al. 2018). ORC-Vax provided 66% protection against cholera at 8 to 10 months, comparable to Dukoral[®] (Trach et al. 1997).

Throughout these developments, however, WHO maintained its position not to recommend cholera vaccines. The WHO 1993 Guidelines for Cholera Control stressed the importance of investing resources in water, sanitation, and rehydration therapy and emphasized that there is no substitute for drinking safe water, practicing good personal hygiene, and preparing food safely (WHO 1993). The authors listed vaccination under the section “Ineffective control measures,”

claiming that cholera vaccines were not efficacious, losing their efficacy rapidly, while not specifying which vaccine they were referring to or citing sources. Their claims mirrored the 1973 *Lancet* arguments against parenteral vaccines and did not discuss the new generation oral cholera vaccines. The authors further explained that vaccination could give a false sense of security to vaccinated individuals, an argument that had already undermined the classical cholera vaccines. Second, the authors underlined that cholera vaccines could divert resources from control activities deemed more useful, such as Water and Sanitation and ORT. These negative arguments dominated the debate on cholera vaccines for the following two decades.

Overcoming Stagnation: Publicizing the Vaccine Debate

The sticky negative perception of parenteral vaccines compelled the proponents of new oral cholera vaccines to distinguish their vaccines from the former. For instance, Clemens and colleagues (Clemens, Spriggs, and Sack 1994) highlighted the harms of parenteral cholera vaccines at length before presenting their own oral cholera vaccine trial results conducted eight years prior.

The same year, Sack (1994) wrote about the cholera epidemic that affected Rwandan genocide refugees in Zaire (now the Democratic Republic of Congo). Sack had worked on cholera prevention and response in India and Bangladesh and participated in vaccine studies as well as new formulations of oral rehydration treatments. Noting that “there can be no dispute about clean water,” he wonders: why have the new treatments and oral cholera vaccines not been used to control the epidemic in Zaire (DRC)? He deplored what he perceived as a reluctance to consider research “of the last ten years” and, while not pointing at the WHO directly, called for an urgent update on recommended tools to control cholera epidemics, arguing that the fight against cholera should not be limited to “strategies of the 1970s” (Sack 1994).

Still in 1994, the WHO faced another, more publicized attack in a CBS TV report accusing the WHO of impeding the use of vaccines during epidemics in Rwanda and Latin America. An American military officer lamented not being allowed to donate leftover doses of Dukoral® from the Gulf War to control the outbreak. Featuring images of impoverished neighbourhoods in Lima and refugee camps in Rwanda, it did not interview local officials or potential beneficiaries. The WHO was accused of being «stuck in some sort of time warp» and «pushing a political agenda» that prioritized bringing water to populations at all costs over using available biomedical tools. The controversy quickly

gained momentum, leading to fears of budget cuts among WHO representatives in Geneva (Briggs 2003, 272–75).

The WHO held a meeting six weeks later to discuss the potential role of novel cholera vaccines in the context of humanitarian emergencies linked to natural disasters or outbreaks affecting refugee camps. The organizers estimated that 20 of the last 28 refugee crises had been affected by cholera epidemics. The authors argued that OCVs would have been ineffective against the Rwandan refugee outbreak, as it would have subsided before the necessary two doses had time to confer immunity. However, the authors conceded that for other, less disastrous, weeks-long outbreaks in “established” camps, the vaccine could have prevented some cases. Unlike the 1993 guidelines, an explicit distinction was made between traditional parenteral and new-generation oral vaccines, with a value assigned to the latter. “The traditional whole cell parenteral cholera vaccine has long been abandoned as a public health tool. In the past 15 years, however, substantial progress has been made in developing oral cholera vaccines” (WHO 1995).

The report, which remained internal to the WHO,³ concluded that the vaccine could be used reactively at the start of outbreaks in the context of established refugee camps (WHO 1995). In the field, things began to move: using Dukoral® doses donated by the US army, a small-scale campaign targeting a refugee camp was organized in Uganda in 1997 and was deemed successful.

Four years later, in 1999, WHO organized a second meeting on the use of the vaccine in emergencies, and this time its report was made public. The justification for the potential use of vaccines came in the form of an admission of weakness. Drawing on the 1998 epidemiological data—a particularly deadly year for cholera—the report stated that deaths occurred “despite continued efforts to provide safe drinking water and basic sanitation.” Recalling the importance of traditional WASH⁴ control measures, the authors added that “it must also be recognized that they are difficult to fully implement” (WHO 1999). While the WHO finally recommended cholera vaccines publicly, it did so only in limited settings as an additional tool that could not replace other classical cholera control interventions. The recommendation was expanded beyond epidemics to use the vaccine as a prevention tool in established refugee camps. Importantly, the report also called for the creation of a renewable vaccine stockpile of two million doses of oral vaccine monitored by WHO.

The situation seemed to be turning in favour of the vaccine proponents. In 2001, WHO formalized these recommendations in the first *position paper* on cholera vaccines⁵, and in the same year, Dukoral® obtained WHO prequalification, allowing the vaccine to be purchased and used in the United Nations system.

Despite these advances on paper, in the following years, the vaccine was only used sporadically in the field and never as a pre-emptive tool. A meeting in 2005 dampened the previous enthusiasm, and the idea of a vaccine stockpile was eventually discouraged. Vaccine promotion bogged down again. Dr. Morgane⁶, an epidemiologist who has worked for decades on cholera control, remembers somewhat bitterly these years of negotiations.

We did the first campaign (in Uganda, 1997), we made some relative progress, and then we embarked on 10, 15 years of fruitless discussions, blah blah. How many people have I heard saying that “people are not going to take it, they are afraid!”

If we tell them, “Take this and it will protect you,” of course they will take it, they are not stupid! (Morgane, interview, telephone, January 2017)

During this lull, opposition to the vaccine focused on two arguments: the cost and the anticipated public reaction. The cost-effectiveness⁷ of the vaccine compared to other interventions was questioned, as Dukoral® was priced at USD \$6 a dose and required a water buffer (implying additional operational costs), making it too expensive to be a viable option for public spending. The opportunity cost also triggered the long-lasting fear that the vaccine would compete against activities associated with access to drinking water and sanitation. Anticipated public reaction to the vaccine also sparked concerns. Experts’ fear of overconfidence among vaccinated individuals, as previously raised by WHO in 1993, persisted. However, a contradictory idea also emerged—that the public would refuse the vaccine. Interestingly, these expectations were based on expert opinions debated in meeting rooms and not data collected from potential beneficiaries.

Reshaping the Vaccine and Its Story

In the 1990s, the cholera vaccine, in its Dukoral (Sweden) or Orc Vax (Vietnam) forms, had little chance of becoming a standard control tool. It needed to evolve to function effectively in the cholera-affected regions of the Global

South. The issue lay not so much in the pharmaceutical effects of the vaccine but in its production processes, regulatory dimensions, and persuasiveness of its relevance. The Dukoral vaccine, intended by its manufacturers for affluent travellers, was too expensive for its deployment to be perceived as “cost-efficient.” Moreover, although an affordable version of the vaccine was available in Vietnam, the Vietnamese drug regulatory agency that approved it was not recognized by key international health organizations, such as the WHO. Consequently, the vaccine in its Dukoral or ORC-Vax™ forms could not be deployed internationally. Before it could become what Rottenburg calls a “travelling model” (Behrends, Park, and Rottenburg 2014) for deployment in different cholera contexts, the vaccine needed to successfully pass through the hands of other allies. Having built his career on the epidemiology and microbiology of cholera in Asia since the 1980s and been involved in the development of the new generation OCVs, Singh explains that this essential reformulation was primarily an institutional change.

In 2000 we had pretty good evidence that the Vietnam [ORC-Vax™] vaccine would work. So, in terms of cholera, there was no scientific breakthrough [...]. It was just a matter of getting that vaccine produced in a place that could scale it up and then could become available through the UN system. (Singh, interview, telephone, July 2018)

That matter was, in fact, a particularly dense chain of alliances. It was necessary to secure the cooperation of Vietnamese scientists who would provide the most advanced vaccine. The vaccine and its production protocol then had to be reformulated so that it could be replicated anywhere. Next, a “host” had to be found in a country with an internationally (WHO) recognized National Advisory Technical Advisory Group (NITAG), to ensure both the vaccine production and approval could be acknowledged on a global scale. Additional allies were required to implement the trials needed for the vaccine’s approval. Finally, partners were needed to fund this multilayered metamorphosis. Securing financial support was particularly challenging: the vaccine held limited interest for pharmaceutical companies, as the vaccine’s beneficiaries were, as Dr. Morgane described in one of our interviews, “the poorest of the poorest.”

For vaccine advocates, the early 2000s saw the emergence of a significant new player in global health, the Bill and Melinda Gates Foundation, which would become the driving force behind the financial support for vaccine development and distribution. The Gates Foundation has prioritized public-private partnerships for vaccines that do not offer sufficient market

opportunities (that is, profits) for pharmaceutical companies; these candidates are often referred to as “marketless” vaccines. One example is the meningitis A vaccine, which has 300 million potential beneficiaries in sub-Saharan Africa (SSA) (Graham 2016).

The International Vaccine Institute (IVI), founded in Korea in 1996, received an initial grant from the Bill and Melinda Gates Foundation to reformulate the cholera vaccine and address other enteric diseases under the Diseases of the Most Impoverished (DOMI) project. Led by John Clemens, who was involved in the 1985 Bangladeshi cholera vaccine trials, IVI’s work gained further support in 2006 when the Gates Foundation launched the Cholera Vaccine Initiative (ChoVI). This initiative aimed to advance the reformulation of the oral cholera vaccine and research new live attenuated vaccines. However, a manufacturer was still needed to produce the vaccine.

In 2005, IVI initiated discussions with the Indian firm Shanta Biologics for technology transfer, ensuring low production costs and the potential for approval by the Indian National Drug Regulatory Agency, recognized by the United Nations. The combination of expertise, “biological citizens” capable of testing new drugs at low costs, and legislation consistent with that of Northern countries enabled “experiments to travel” (Petryna 2009); India had become a popular destination for conducting low-cost clinical trials (Sunder Rajan 2017). Shanta Biologics was known for developing a hepatitis B vaccine with a manufacturing cost of 25 US cents, intended for WHO-sponsored vaccination campaigns in developing countries (Sunder Rajan 2017). The resulting new oral cholera vaccine, Shanchol™, contained killed bivalent (O1 and O139) whole cells. It had to be administered in two doses taken 14 days apart. Importantly, unlike Dukoral, it did not require a water buffer. During a phase III trial in Kolkata, Shanchol™ was found to be safe and confer 67% protection from infection two years after vaccination with two doses. Shanta Biologics was acquired by Sanofi Pasteur in 2006, shortly after agreeing to manufacture the reformulated cholera vaccine (Sur et al. 2009).

The Shanchol™ vaccine was introduced in 2009. The power dynamics surrounding vaccine usage shifted on three crucial aspects: the vaccine cost a third of what Dukoral cost for comparable effects, it did not require a buffer, and it was approved by a recognized drug regulation agency. Despite these advantages, global deployment of the vaccine still required winning political and technical battles within global institutions to secure the WHO’s recommendation. In this “return to the big world” (borrowing the phrase from

Callon, Lascoumes, and Barthe 2001), humanitarian medical doctors became vital allies in legitimizing cholera vaccines as public health tools.

The Contribution of Humanitarian Doctors

Shanchol™ found allies in the humanitarian sphere among medical doctors (MD) working on epidemic response within international non-governmental organizations. Calico, an MD with extensive experience in NGO response to cholera outbreaks, started to champion the vaccine when he felt traditional response strategies failed to control massive epidemics.

It was late 2008–2009, I remember, we started talking with my colleague Jo, we were sitting at the CTC (Cholera Treatment Center), “Uh, what are we going to do with this epidemic?” We were in the slum [x], and the epidemic had spread everywhere; and you know, we were trying to put control measures in place and then nothing, you see, *nothing [no effect on the epidemic]*. So we asked ourselves: “Why don’t we try [the vaccine]?” (Calico, interview, Geneva, July 2018)

Dr. Calico’s frustration with a massive epidemic was not isolated. The late 2000s coincided with a failure to control several large-scale, high-profile cholera epidemics in Haiti, Guinea, and Zimbabwe using emergency WASH methods, echoing WHO’s 1999 second cholera vaccines meeting.

The experience [of epidemic response] has been to put in place huge WASH interventions and to see epidemics continue to spread undisturbed without having a real control effect, you know? So, from a medical organization point of view, it was frustrating. You are there, you try to scale up, scale *up*, *scale up* your treatment centres, and the epidemic continues to spread undisturbed. [...] So after that experience, I know that [NGO] wanted to try the vaccine, especially in the context of the displaced. We tried to see if there was room for this tool. (Calico, interview, Geneva, July 2018)

In 2008, Calico and colleagues began to discuss the vaccine with representatives from the ministries of countries regularly affected by cholera. They quickly encountered opposition from other humanitarian actors, concerned that adopting the vaccine would sideline WASH efforts. Vaccine advocates did not dispute the idea that, ultimately, access to clean water and sanitation was the solution to cholera; they simply argued that *in the meantime*, the vaccine could be beneficial.

That's why they scare me, people who oppose [the vaccine] head-on [...] there are people who respond to the vaccine in a way that is not objective. The vaccine is not the solution to cholera, it is one of the tools you can use in the fight; every time I talked about vaccines [...] I make a reminder of *how you eliminate cholera*. In France, we don't have cholera because we have good water and sanitation and hygiene systems [...] we will not arrive at this standard in [the next few] years in many countries in Africa. (Calico, interview, Geneva, July 2018)

Vaccine proponents further argued that vaccination was a humanitarian and moral imperative:

So I put myself in the population's shoes, if I know that there is a vaccine that protects my children and myself and that I can give it as easily as putting drops in eyes, and that someone hides this information from me, it's nonsense. I would like to have this tool, plus there are people who are willing to pay for this tool. I wish the people who oppose this [those advocating against cholera vaccines] would give me one valid reason for how the vaccine would kill people or cause disease: the vaccine has no side effects, is easily administered. (Calico, interview, Geneva, July 2018)

Novel vaccines targeting the global south and spanning private-public partnerships have been criticized for being intermediate (that is, placeholder) technologies (Thiongane 2021). In the case of OCV, this transitional aspect is not a pitfall but an acclaimed feature. To those who viewed water and the vaccine as mutually exclusive, vaccine advocates worked to present them as complementary. The vaccine negotiated a place in the gap that separated the present from a future where access to safe water and sanitation would be ubiquitous in the Global South.

In 2009, a new review of oral cholera vaccine data and Shanchol™ vaccine specifications was prepared for the WHO Strategic Advisory Group of Experts (SAGE). The authors highlighted the benefits of Shanchol and included a reanalysis of the 1985 Bangladeshi clinical trial to assert herd protection of the oral vaccines, counterbalancing the limited efficacy (67%) of the vaccine. With this knowledge, and an estimated price of USD \$1 per dose, SAGE concluded that the vaccine could be a “cost-effective” tool, including for use in so-called endemic areas (Enwere et al. 2009). In 2010, after nearly a decade, the WHO published a second position paper that significantly expanded the

recommendation for use to the general population, primarily for control of epidemics but also for prevention in known at-risk areas (later referred to as “cholera hotspots”) in cholera endemic countries (WHO 2010).

Yet, despite Shanchol’s prequalification by WHO, WASH advocates maintained their concerns over the vaccines’ threat to the mid- to long-term commitment to financing water and sanitation infrastructure. When it was proposed among emergency committees where representatives of NGOs and ministries met to organize cholera control efforts, suggesting a vaccination campaign was futile.

It never works! This is normal because you have something completely innovative. Of course, there’s always that one guy who’ll say, “No way! Are you nuts? It’s access to drinking water [that is required],” and they will win the decision. (Morgane, interview, July 2018, Geneva)

Additional institutional allies were necessary to establish a vaccination campaign in a country that would serve as a pilot for other cholera settings. International institutions were considered too conservative for such novel interventions, and the ideal candidate would be:

Either an NGO or someone who’s going to carry the thing, who’s going to say, “You have to take the risk, you have to try.” And then there must be the same thing on the ministry side, of course, otherwise it will never work. (Morgane, interview, July 2018, Geneva)

Paul Farmer, a renowned medical doctor, anthropologist, and key figure in global health, emerged as a “champion of the vaccine” during the massive cholera outbreak that struck Haiti following the 2009 earthquake (Gupta et al. 2016). In a context where debates raged between WASH advocates and vaccine proponents, Farmer’s advocacy for Oral Cholera Vaccines (OCVs) may initially seem surprising, especially considering his previous work.

However, it’s important to recognize that, unlike many other actors involved in the Haitian crisis, Farmer had been deeply engaged with the island for more than two decades before the earthquake and the subsequent cholera epidemic. He co-founded Partners in Health (PIH), a non-governmental organization dedicated to providing care for the poor. Often described as a “counter-example” to the compartmentalized approach to global health, PIH focuses on community-centred initiatives and utilizes technology to strengthen health systems “from below,” while also offering long-term patient support (Biehl and

Petryna 2013). PIH's mission "to bring the benefits of modern medical science to the poor and to serve as an antidote to despair" was central to Farmer's vision of liberating oppressed populations. He drew parallels between the availability of cholera vaccines and Antiretroviral Treatments (ARTs) for people living with AIDS in the Global South (Farmer 2012, 203). The absence of accessible ARTs in HIV/AIDS-affected communities had become "intolerable" in the early 2000s (Chabrol 2012; Dozon 2005). In that context, Farmer viewed the failure to deploy the cholera vaccine as a matter of inequitable access, echoing Sack's plea from the 1994 outbreak in Zaire (DRC) (Farmer 2012, 202).

Stemming from the struggle to improve living conditions, including access to water and sanitation for all in Haiti, Farmer also shared the frustration of Calico and other humanitarian actors regarding the challenges of implementing traditional non-vaccine interventions. PIH's efforts to advocate for investment in water and sanitation infrastructure with US administrations had been thwarted when promised aid was "held hostage" due to renewed political tensions between the Bush and Duvalier administrations in the early 2000s. Hindered by stagnation in improving water infrastructure, the ability of PIH's supplementary water and sanitation programs to control epidemics was humbled: "Our own small water projects over the years had humbled us about our ability to stave off epidemics of waterborne disease" (Farmer 2012, 198). He observed that despite these efforts, "the great majority of the rural population still lived without ready access to potable water and modern sanitation" (Farmer 2012, 198).

Faced with the immediacy of the cholera crisis and the slow pace of infrastructure improvements, Farmer endorsed the cholera vaccine as a necessary intervention. He framed this support within a broader strategy, advocating for an integrated approach that included both vaccination and efforts to improve water and sanitation. Farmer argued that, in the face of an ongoing epidemic, it was essential to mobilize

all the tools for preventing its spread (from improved sanitation, including chlorine tablets, to effective and safe vaccines) and for treating those already stricken (from rehydration and replacement of electrolytes to antibiotics) needed to be promptly integrated with the more restrained public health responses. Interventions such as exhorting people to drink clean water and wash their hands or distributing chlorine tablets were necessary, but would never stop the epidemic. (Farmer 2012, 199-200)

Farmer's support for the vaccine was not merely a pragmatic concession but a reflection of his belief in using the best available tools to address urgent health crises. He stated that "an aggressive and integrated approach might lead in a decade or so to the eradication of this disease [...] An integrative approach could help in other cholera hot spots around the globe, too" (Farmer 2012, 254).

This nuanced stance positioned Farmer among those he described as "maximalists," who believed in deploying all available interventions to combat cholera. He contrasted this approach with that of the "minimalists," who favoured traditional solutions such as hygiene education and distribution of chlorine tablets (Farmer 2012, 199).

As in the past, it was by bringing the case into the public domain through "friends in the press" that the institutional unblocking took place. Dr. Ivers, who was leading PIH, advocated their OCV endorsement on National Public Radio (NPR):

The general culture around cholera vaccination in public health agencies has been that it's not a good idea. It's too complicated. It's too hard. It's costly [...]

Then there's the philosophical notion – an ideological argument that you shouldn't be trying to vaccinate against cholera when really the solution is water and sanitation. (Ivers, NPR, 2012).⁸

The portrayal of the vaccine as a transitory yet indispensable solution had now become established, as reported by the journalist:

Vaccine advocates agree, but say cholera won't wait for improvements in water and sanitation. (Ibid.)

Concomitantly, an executive of the Haitian NGO Gheskio underlined the imperative and urgent need for the vaccine in the Haitian context:

Eight million Haitians lack potable water or proper sanitation [...] So what are you going to do? [...] In the best conditions, with the best government, it's not going to be done in five years. So you *need* this vaccine. (Pape, NPR, 2012)

In early 2012, the institutional deadlock was finally broken. The Haitian government swiftly approved the reactive use of OCVs while the American Red Cross secured the necessary Shanchol™ doses (Rouzier et al. 2013). In April of that year, PIH launched the first OCV campaign in Haiti, reaching 50,000 people. Writing in the afterword of his book just days before the

campaign, Paul Farmer (2012) reflected on the hope it symbolized for Haiti and other “cholera hotspots” worldwide. Haiti indeed became a trailblazer for the global implementation of oral cholera vaccines. However, it was likely a different campaign, which began just six days after the Haitian effort, that truly demonstrated the vaccine’s potential in Africa. On April 18, 2012, the first reactive cholera vaccination campaign on the continent was launched in Guinea.

The Making Of a Success Story. Africa’s First Reactive Cholera Vaccination Campaign

The cholera epidemic in Guinea began in February 2012 among fishermen from the same family in a village located on the island of Kaback, not far from the Sierra Leonean border. On 8 February, a health team dispatched by the ministry and funded by the Africhol project reported 59 suspected cases and six deaths. Two of the five collected stool samples tested positive for cholera. Guinean authorities informed international partners by email and invited them to a crisis meeting.

In 2012, before the Ebola outbreak, Guinea had only a handful of international actors to help it respond to epidemics⁹. These partners met several times a week in a cholera response cluster led by Dr Keita Sakoba, the head of the Guinean Disease Prevention and Control Centre (Division Prévention et Lutte contre la Maladie). In Dr Sakoba, OCV advocates found another OCV champion:

We were there [in Guinea] and we talked to Dr. Sakoba, [and] he said, “I’m *very* interested in using the vaccine,” and here they went. (Calico, interview, July 2018)

Cholera epidemics can be devastating in Guinea, one of the poorest countries in West Africa, causing thousands of cases and hundreds of deaths (Rebaudet et al. 2014). The Ministry of Health immediately recognized the urgency of the situation and the potential life-saving impact of a vaccine delivered free of charge to affected areas. The lack of infrastructure in Guinea presented both advantages and disadvantages to those implementing the novel OCV campaign. As an epidemiologist colleague noted excitedly as we were flying to Conakry to support cholera surveillance and outbreak investigations in the affected areas, “If a reactive OCV campaign succeeds in Guinea, it can be deployed anywhere in Africa.” The ongoing epidemic in Guinea provided a “natural” window of opportunity for the vaccine as a control tool.

Two campaigns with two rounds of vaccination were planned, the first in Boffa on the North Shore in April and May 2012 and in May and July in Forecariah, including Kaback Island. During the first campaign in Boffa, Dr. Sakoba was the first to take the vaccine in front of an audience of journalists. Despite short time frames and logistical challenges, both campaigns were well-accepted and successful in terms of coverage and efficacy (Luquero et al., 2014).

By the end of the summer of 2012, the cholera epidemic had subsided, with impacts extending beyond Guinea's public health outcomes. Cholera vaccine proponents could capitalize on the results of this first African reactive OCV campaign. They believed that the vaccine's success story in a difficult terrain like Guinea would allow it to travel to other regions facing similar challenges.

Guinea, it worked very well, because we vaccinated in rural areas, not very accessible, in islets, we had to bring the vaccines by boat. What we've seen is that it's a super easy vaccine to administer, it's super *safe*, compared to injections where you have to have a whole waste management system for needles, it's an oral vaccine, which people could [in the future] do in *self-administration*, but you can do it with *Community Health Workers*. It is very easy to do. In fact, the last time, we managed to eliminate the constraints of *cold chain* because it is a vaccine that is very thermostable, we kept the vaccines in a central stock, we did the distribution outside the cold chain, it becomes a vaccine that is very easy to distribute. (Calico, interview, Geneva, July 2018)

There was another benefit of the vaccine: "It doesn't require a change in habits, you know, so it's an action you do at some point, and people, they become protected" (Calico, interview, Geneva July 2018).

In 2013, based on the successful OCV introductions, the Geneva-based Gavi made the decision to fund an OCV stockpile for USD \$115 million as part of its Vaccine Investment Strategy for 2013–2018.

Addressing the Concerns of Beneficiaries' Vaccine Overconfidence and Refusal

As the OCV was deployed in different global south settings, stakeholders opposing the vaccine continued to be concerned regarding beneficiaries' reactions to the vaccine. Given its relatively limited protection at the individual level, OCVs require high coverage rates for two doses to achieve herd (population level) immunity. As a result, during the introduction campaigns, the public's anticipated vaccine confidence became particularly important. Studies usually found acceptance rates around 90%, for instance, in Kenya,

Zanzibar, the Democratic Republic of Congo (Sundaram et al. 2016) and Haiti (Ivers et al. 2013). Actual vaccine uptake for the Guinean campaign, however, ranged from 69 to 84% depending on prefectures (Luquero et al. 2014). Despite encouraging vaccine acceptance studies, it is important to note that such studies do not inform on these populations' preference for vaccines compared to WASH strategies.

Another lasting concern continuing after the successful Haitian and Guinean campaigns has been the effect of vaccination on an individual's protective behaviour,

Opponents always said, “[vaccinated] people will not protect themselves and then they will do anything, they will not follow hygiene measures.” To my knowledge, there are two studies on this, one on Haiti and one on Thailand, I believe, for the CDC. They say the same thing: what happens is quite the opposite. (Morgane, telephone interview, January 2017)

Morgane referenced research conducted after the WHO's decision to prequalify the Shanchol vaccine. Prior to these studies, discussions relied on data from clinical trials conducted in the 1980s and early vaccination efforts, such as those in 1997, which were not designed to assess the effects in epidemic contexts.

During our interview, I shared a contrasting piece of evidence from the Malawi OCV campaign. During participant observation, a colleague had observed an elderly woman drinking water from an unprotected well and offering it to others, confidently asserting that “everyone was protected by the vaccine.” When I mentioned this, Dr. Morgane dismissed it with a shrug and insisted:

What is clear in these campaigns is that people were afraid of this disease. In case we didn't already know, it is very clear. From there, I can hardly imagine someone saying, “*Oh no I'm going to drink anything.*” — I cannot imagine that. Unless you're completely crazy, but otherwise, it doesn't make sense! Nobody is going to do that, you know. (Morgane, interview, Geneva, July 2018)

Dr. Calico was more receptive and acknowledged the possibility that cholera vaccination campaigns might lead to a relaxation of individual preventive practices. To mitigate this risk, he suggested that these campaigns could also serve as platforms for raising awareness:

There was this question, by giving the vaccine people may relax a bit the hygiene measures. [KAP studies] have shown that, in fact, if you use this opportunity to do *health promotion*, it's the opposite, you can turn the vaccination campaign into a tool to improve the rest of the knowledge. So vaccination is an opportunity to train people; you take it as an opportunity and not as a constraint, you explain to people that the vaccine does not protect 100%, that we must continue to wash our hands, we must continue to chlorinate the water, you explain well. (Calico, interview, Geneva, Switzerland, July 2018)

However, the reality of organizing a reactive vaccination campaign in the midst of a cholera epidemic leaves little room for detailed communication. Nuances about the vaccine's protective levels are often lost. In Malawi, for example, during the introduction of the OCV in Lake Chilwa, the same rumour that had plagued the Bilivacin vaccine nearly a century earlier resurfaced—claiming that the vaccine caused cholera rather than preventing it (Heyerdahl et al. 2018). Some participants reported that individuals had developed cholera shortly after vaccination, reflecting a failure of information campaigns to effectively communicate that the vaccine does not offer immediate or complete protection. On this point, Morgane conceded that communicating actual protection levels to populations was complicated:

During information campaigns, those are messages that need to be communicated, but at the same time, it is a bit tricky because the message ends up being “Come and get vaccinated to be protected against cholera, but you might still get it.” (Morgane, telephone interview, January 2017)

Fearful of provoking negative public reactions, communicators hesitated to fully disclose the vaccine's limitations. Consequently, cases of cholera occurring among vaccinated individuals were often interpreted as malevolent acts, fueling rumours and distrust of vaccinators. This issue could potentially arise with other “leaky vaccines” as well.¹⁰

Eventually, concerns regarding public overconfidence in vaccines were dissipated by these warrants and a few data points, cited by Morgane, which appeared reassuring. Yet the systematic integration of WASH initiatives in vaccination campaigns paradoxically also meant that they became increasingly regarded as companion interventions to vaccines rather than the staple of cholera control, progressively erasing the distinct importance of WASH.

The Measurement High Ground

While Singh agreed with an integration approach that combined vaccines with WASH, he focused on the difficulty of measuring the impact of WASH interventions to advance the added value of vaccines.

We've always been talking about vaccine as it integrated with WASH. And we keep talking about that, but unfortunately, we don't have good examples of exactly what that means. What do we mean when we're talking about WASH? Are we talking about high chlorinated water in every house? Somehow that doesn't seem feasible. So, you're either talking about that very heavy investment in infrastructure or, alternatively, the point-of-use chlorination. And again, yes that works sort of as long as you do it. But it doesn't seem to be very sustainable. So, in the WASH side, we keep saying, "Yes, we want to include WASH." But we really don't know what we're talking about. And when we say integration, we really want to integrate the entire package of control, meaning the clinic, the laboratory, WASH, the vaccine. These all have to fit together in an integrated way. (Singh, interview, telephone, July 2018)

Professor Singh supplanted water and sanitation interventions, grouping them together as a messy and ill-defined whole that disrupts the coherence of the epidemic response. Unlike the vaccine, contained in a vial and delivered in a single action, WASH interventions require ongoing adaptation and maintenance. The measurable benefits of the vaccine, such as quantifiable effectiveness and outcomes, align with the trend in evidence-based medicine that emphasizes the quantification of intervention evaluations. By setting the bar for the intrinsic quantification of the effects and outcomes of each intervention, those who supported the vaccine know that others would not be able to meet this. As part of evidence-based medicine, the major trend in global health, pride of place, is given to the quantification of intervention evaluations. All interventions that are difficult to measure or that cannot undergo randomized controlled trials become difficult to defend (Adams 2013). This is the case when using DALY (Disability Adjusted Life Years) measurements, a leading indicator for measuring the effectiveness of population health interventions. DALYs are particularly difficult to measure when interventions rely on the behaviour of the beneficiaries, such as many WASH interventions. Vaccines, on the other hand, respond particularly well to DALY measurements. Yet DALY vaccine assessments do not calculate potential co-infections and reflect shortcomings in approaches focusing on a single disease (Biehl and Petryna 2013). They are

also blind to the cultural weight of different forms of disability resulting from diseases (Nichter 2008).

Lastly, WASH advocates have frequently argued that research on cholera vaccine efficacy, effectiveness, cost-effectiveness, or acceptance is biased by funders with vested interests in promoting vaccines. George, a known proponent of WASH interventions and a skeptic of cholera vaccines, has been vocal about this concern:

In doing this work on vaccination, I sometimes go against what is usually said, because *it's not the same thing*. The endpoint is not the same. I work on *the effect* of an activity, and I do not work to *promote* or *prevent* that activity. As a result, a lot of research is paid for by companies that promote this or that activity, including obviously the Bill and Melinda Gates Foundation, which promotes cholera vaccination. (George, interview, Paris, July 2018)

At the same time, a review of George's own funding sources reveals that his pro-WASH studies are partially funded by large water and energy corporations, highlighting a broader issue of private funding influencing public health research.

The Philanthrocapitalist Art of Market Shaping

The stockpile served three key functions: in the short to medium term, it provided cholera vaccines to countries as donations to help control outbreaks. Additionally, it secured purchase orders, which encouraged investment in production and attracted new vaccine manufacturers, steadily increasing vaccine availability. In the long term, the goal was to reduce vaccine prices through economies of scale, making them more affordable for low-income countries.

Singh emphasized that while Shanchol™ was relatively affordable, it alone could not meet global demand. If more low-cost vaccines were available, a stockpile might not have been necessary. However, the limited supply created a need for efficient distribution through market-shaping mechanisms. Singh explained that initially, in 2011, despite WHO prequalification, demand for the vaccine was low, resulting in a vicious cycle of low supply and low demand. Gavi's support for the stockpile broke this cycle, boosting demand and encouraging a second manufacturer, EuBiologics, to enter the market, which in turn increased supply and created a virtuous cycle.

The introduction of the Euvichol vaccine in 2016 further lowered costs, reducing the price per dose from USD \$1.85 to \$1.30, making it even more accessible. However, this system heavily relies on Gavi's funding, which is not guaranteed. Morgane explained that Gavi's initial investment in the cholera stockpile was for five years (2013–2018), and there is significant competition for funding with other vaccines. The critical question remains the “added value” of the cholera vaccine compared to other interventions, both in water and sanitation (WASH) and other vaccines, with cost-effectiveness being a crucial measure.

Relying on the stockpile required ongoing data collection and experimenting with novel, cheaper ways to administer the vaccine. The vaccine's future hinged on demonstrating its efficiency not only in terms of the cost of the vaccine itself but also in minimizing the operational costs associated with its deployment. It had to be cheaper at saving lives than other interventions. This has led to innovations such as single-dose regimens (Qadri et al. 2016) and self-administration strategies (Grandesso et al. 2018), despite initial concerns about their practicality and effectiveness.

Ironically, the substantial resources dedicated to gathering additional data and the associated costs are often not accounted for in cost-effectiveness studies and the decision-making process for selecting control strategies. These resources could otherwise be directed toward directly addressing the immediate needs of affected populations. This concern was poignantly expressed by a participant in the assessment of Lake Chilwa's innovative OCV campaigns, who questioned why an investigating team would come to his remote village and ask about vaccines and the reasons behind drinking muddied water, instead of simply providing access to clean, drinkable water.¹¹

It Came from Geneva: The Double-Edged Commodification of Oral Cholera Vaccines

In 2018, Gavi renewed its support for the oral cholera vaccine (OCV) stockpile, a commitment that continues to this day. OCVs have become central to the Global Task Force for Cholera Control's (GTFCC) roadmap for eliminating cholera by 2030 (Global Task Force on Cholera Control 2018). Between 2016 and 2023, Gavi's stockpile funded 70 million doses, with annual production soaring from 2.5 million in 2016 to an estimated 50 million by 2024 (UNICEF 2024). Despite these substantial increases, the World Health Organization (WHO) reported a global shortage of OCVs in 2023, noting that the 40 million doses produced that year were insufficient to meet country demands amid significant outbreaks (Rigby et al. 2024). These developments underscore the success of vaccine proponents in

transforming a once-marginalized tool into a cornerstone of twenty-first-century cholera control strategies.

Cholera outbreaks continue to pose a serious threat, particularly in Africa, where yearly case numbers fluctuate significantly (see Figure 1). In Haiti, where the 2010 cholera outbreak was brought under control by 2019, a new outbreak emerged in 2022 and is ongoing, having already claimed over a thousand lives (PAHO 2024).

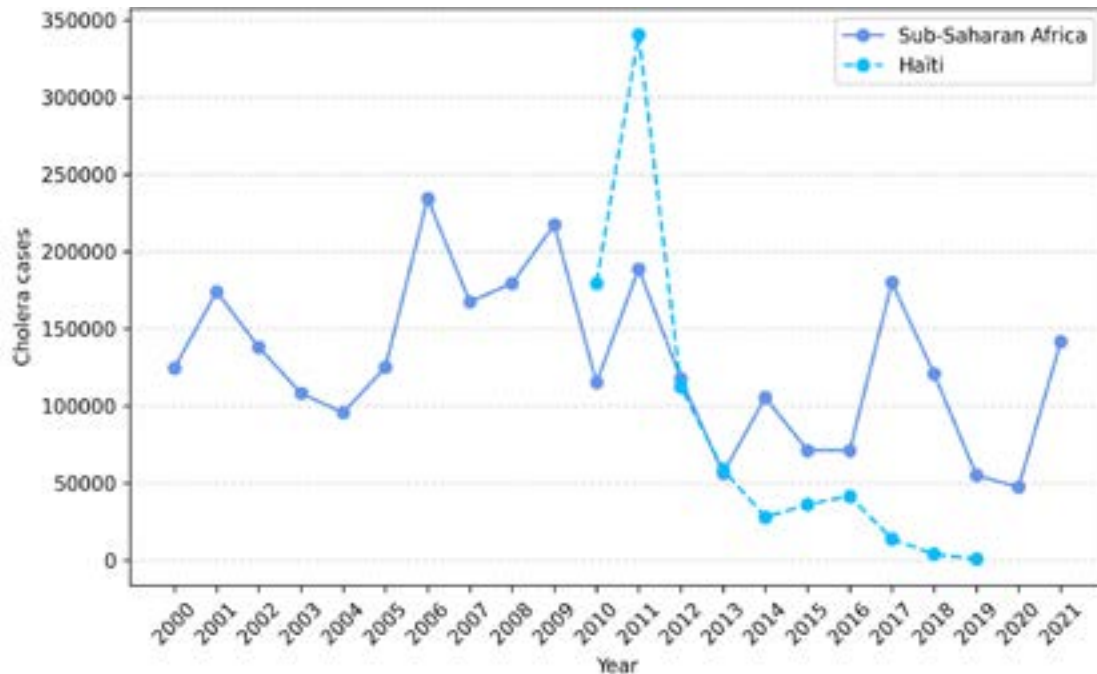


Figure 1. Reported cholera cases in Sub-Saharan Africa and Haiti (2000-2021).

Globally, access to safe water and sanitation improved between 2000 and 2020. However, in sub-Saharan Africa—where most cholera cases are reported (Mengel et al. 2014)—the situation has worsened. The number of people lacking access to safe water increased from 350 million in 2000 to 387 million in 2020, while those without access to sanitation rose from 490 million to 737 million (World Bank 2023). Today, only 39% of Africa’s population has access to safe water, and just 27% have access to safely managed sanitation services. To meet the Sustainable Development Goals (SDGs) by 2030, investments in safe water would need to increase *twelvefold*, and sanitation investments *twentyfold* (UNICEF 2022). This, however, appears unlikely. Although aid flows for water and sanitation in Africa increased steadily from 2000 to 2012, they plateaued between 2013 and 2020 and have sharply declined since the COVID-19 pandemic (see Figure 2).

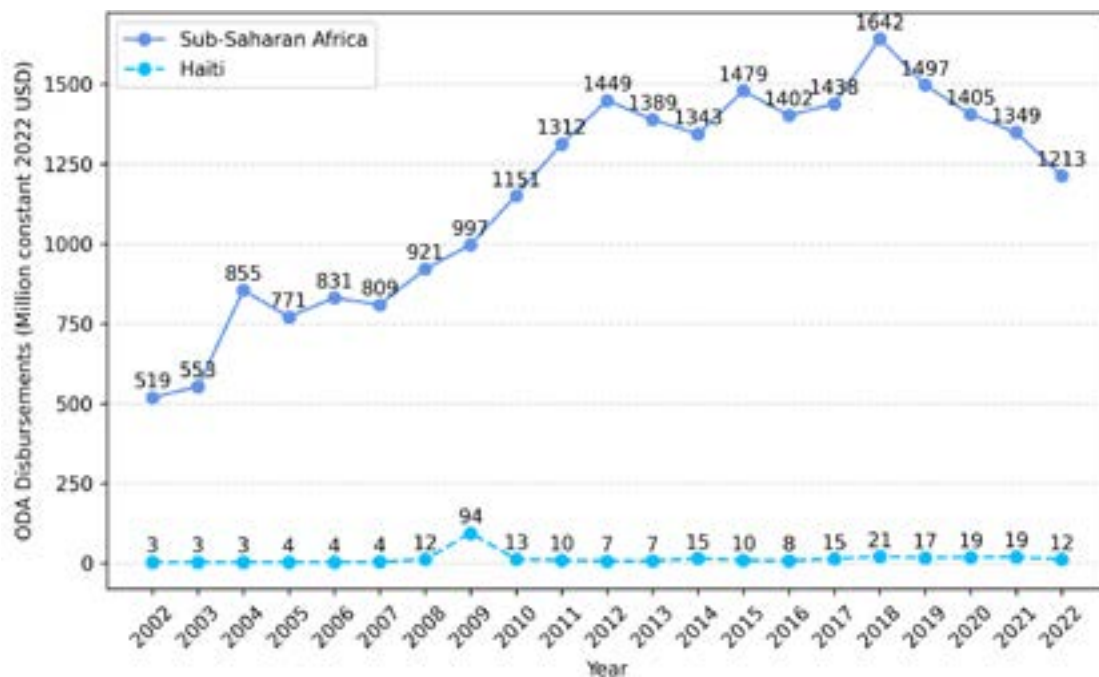


Figure 2. Official Development Assistance Disbursements for Water Supply & Sanitation in Sub-Saharan Africa and Haiti (2002-2022).

While the rise of cholera vaccines alone cannot fully explain the decline in water and sanitation aid in sub-Saharan Africa, it is important to consider that other waterborne diseases, such as typhoid and rotavirus, have also seen significant vaccine introductions over the past two decades. Twelve years after the introduction of novel oral cholera vaccines, the anticipated “maximalist” approach—integrating vaccines with substantial investments in water and sanitation—has not materialized as expected. Instead, the concern now is the emergence of a new form of “minimalism,” in which the existence of vaccines reduces the emphasis on critical water and sanitation improvements, with vaccines perceived as a fallback during outbreaks.

This shift in cholera control strategies represents an extreme form of the pharmaceuticalization of global health. For over 150 years, water and sanitation have been recognized as the fundamental solution to cholera (Snow 1855). However, cholera vaccines have experienced an *irresistible rise*, becoming the cornerstone of cholera control in the twenty-first century. Humanitarian actors played a key role in this shift, representing OCVs as the pragmatic and morally imperative choice—akin to the campaign for access to antiretroviral treatments (ARTs) for HIV/AIDS in the global south—to control massive cholera outbreaks, such as Haiti’s 2010–2019 epidemic.

Interestingly, Paul Farmer, a central advocate for the initial OCV rollout in Haiti, had previously warned of the dangers of pragmatism. He criticized human rights activists who, out of “pragmatism,” focused on narrow political and civil rights struggles while neglecting the fight for economic and social equality—an approach he argued could quickly become a resignation to the political status quo (Farmer 2004:9–10).

The imperative to save lives during outbreaks is indisputable. Yet, over a decade into OCV introduction, it is crucial to focus on fulfilling the commitment to prevent an institutional side effect of vaccine deployment: the midterm displacement of broader, less quantifiable, but ultimately essential investments in universal safe water and sanitation infrastructure.

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Notes

1 I served as a project operations manager and medical anthropologist for the Agence de Médecine Préventive (AMP), a French NGO, from 2010 to 2018. During this period, I was extensively involved in cholera-related projects across Africa. From 2010 to 2016, I contributed to the African Cholera Surveillance Network (Africhol), a project funded by the Bill and Melinda Gates Foundation (BMGF), which aimed to establish and enhance cholera surveillance systems in eleven African countries.

Between 2015 and 2017, I focused on operational research related to oral cholera vaccine (OCV) acceptance in Zambia, Malawi, and Mozambique as part of the Vaxichol initiative, another BMGF-funded project.

In 2018, I served as a consultant anthropologist for a Wellcome Trust-funded case study on data sharing practices during cholera outbreaks.

2 Between 10 and 60 dollars for complete immunization of an adult, depending on years, countries and intended use of the vaccine.

3 Later made public and available online: <https://iris.who.int/handle/10665/59012>.

4 Water Sanitation and Hygiene (WASH) also known as *Watsan*, refers to activities that enhance access to drinking water (such as boreholes and well disinfection) and sanitation (including organization of waste pre-collection and construction of latrines),

as well as community education and hygiene promotion. In NGO environments, the term “Watsan” is also used to refer to the professional who manages these activities.

- 5 Position papers are documents authored by the WHO staff that present state-of-the-art disease epidemiology and the tools available for its control. Their purpose is to convey the WHO’s stance on these tools, clearly identifying those the organization endorses and those it advises against using.
- 6 All interviewee names have been pseudonymized.
- 7 Cost-efficiency refers to a ratio established between the cost of an intervention and its effectiveness on health. In more detail, it involves a medico-economic analysis to determine the efficiency (in terms of the number of lives saved, years of life saved, duration of symptoms, etcetera) of a health intervention compared to a reference intervention for a given cost. See <https://www.frontiersin.org/articles/10.3389/fpubh.2021.722927/full>
- 8 Vaccination Against Cholera Finally Begins In Haiti, Richard Knox, NPR 2012, <https://www.npr.org/sections/health-shots/2012/04/12/150493770/vaccination-against-cholera-finally-begins-in-haiti> . Accessed 23 February 2019.
- 9 Including Doctors Without Borders (MSF in French), Action Against Hunger (ACF in French), the Guinean Red Cross, UNICEF and WHO, and the Agence de Médecine Préventive (AMP).
- 10 In this supplement see J. Graham and K. Peeters Grieten’s piece for a deeper dive into the multifaceted stakes of leaky vaccines.
- 11 Author fieldnotes from the Lake Chilwa OCV acceptance assessment.

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