Simulation-based Assessment of Cholera Epidemic Response:
Al-Hudaydah, Yemen

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For all of you who have come into my learning journey in the past two years, I am truly grateful.

As students, we were often asked, “Why do you learn system dynamics? Do you like SD?”. Saying “I like system dynamics” is not really on the top of my answer list; at least not in the beginning of the program, and probably not among the OG study group members that have been through many late-night discussions in the first semester. Thanks to the study group, the first few months seemed less scary. Of course, I was also showered with tips and "how-to" by the teaching assistants, whom one of them became my thesis supervisor, Anaely. The mentorship goes beyond classes and thesis, I am deeply grateful for having such a supportive supervisor. With more modeling, more practice, and more modeling, overtime, I become the one that saying, “I really like SD”. (As a SD student, I am obliged to talk about feedback loop in the acknowledgement!)

Now, I must thank some of the seniors from the SD program, Nathalia, Wang, Henry, and many more for their kindness to share their experiences, and also feedback to some of my models. The future after graduation seems less intimidating knowing that I am not alone.

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Thesis completion is a milestone, it is also a reminder that the kindness, support, and opportunities that I received, in time, shall be passed on to other students.

Abstract

Cholera can kill up to 50% of patients who do not receive adequate rehydration; however, the case fatality rate can be as low as 1% with prompt treatment. As of November 2020, the World Health Organization reported 2.5 million suspected cholera cases and nearly 4,000 deaths in Yemen. Humanitarian response in Yemen is particularly needed when epidemics occur during or as a consequence of conflict and political upheaval. In 2017, the main problem was a lack of adequate cholera preparedness and response: vaccination implementation was delayed (after 16 months into the epidemic); water and sanitation (WASH) intervention was the primary preventive measure.

Lessons learned from Yemen's cholera response are well-documented, with the majority taking a qualitative approach. This study aims to quantify and evaluate the lessons learned from the 2017 and 2018 cholera responses using system dynamics modeling. The model is useful to understand impactful policies before, during, and after cholera epidemics. A user-friendly interface was created to facilitate policy testing and engage multi-sector stakeholders in more effective communication. The model built upon a classic infection structure with empirically grounded operational structures: oral rehydration corner, diarrhea treatment center, WASH, vaccination, and data surveillance system. The data collected during the model's development and validation are epidemiological data: and cholera response (interventions) data.

The findings show a profound difference of interventions for asymptomatic and symptomatic infected individuals, especially the ratio between the two disease states is 75% to 25%, respectively. For prevention, if vaccination began in June 2017 (close to the peak of epidemic) with the same number of vaccines (that were delivered 16 months into the epidemic) would still be effective in longer term if there is a following second vaccination campaign. Second, a single dose vaccine results in a more favorable short-term response, which has significant implications for epidemic management under severe logistical and security constraints. The findings highlight the unintended consequences resources are disproportionately directed toward WASH intervention. Such policies are likely to result in the "Shifting the Burden" system archetype, an overdependence on reactive quick fixes that results in fewer resources for other interventions. Deconstructing the interventions from historical implemented interventions (BASE) to no intervention (Business as Usual [BAU]) has demonstrated significant impacts from the humanitarian cholera response in 2017. The model simulation shows 55% more deaths if nothing has been done. The simulation result also projects a potential 30% of death can be prevented if interventions, can be initiated earlier.

The insights gained from the intervention are not only applicable to the cholera epidemic but also to other infectious disease response modeling in general. The next step is to adapt this Al-Hudaydah model to other cholera-affected countries through collaboration with humanitarian actors.

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1. Introduction

1.1 Cholera and response

Cholera is an acute diarrheal infection caused by consuming food or water contaminated with the bacterium Vibrio cholerae (Médecins Sans Frontières, 2018; WHO, 1993). Vibrio cholerae causes profuse watery diarrhea and vomiting that can quickly progress to dehydration and hypovolaemic shock, killing up to 50% of patients who do not receive adequate rehydration (Médecins Sans Frontières, 2018). Even healthy people can die within hours if developing severe cholera symptoms. The good news is that if symptomatic individuals receive healthcare treatment in time, the case fatality rate can be less than 1%. How does cholera kill between 21,000 and 143,000 people globally each year? The World Health Organization (WHO) stated cholera as an inequitable disease that disproportionately affects the poorest and most vulnerable people (Global Task Force on Cholera Control [GTFCC], 2022).

Cholera treatment, control, and prevention are the responsibility of national government health ministries and non-governmental organizations (NGOs) (Federspiel and Ali, 2018; Harpring et al., 2020; Spiegel et al., 2018). Once cases are identified, interventions to control and prevent cholera include surveillance and case management (treatment), WASH interventions, provision of oral cholera vaccinations, and strengthening education programs (Davis, Narra and Mintz, 2018; Médecins Sans Frontières, 2018; WHO, 2021). While universal access to clean water and sanitation is the long-term solution to cholera, this is typically linked with the country's economic and political development; and is therefore vulnerable to environmental and humanitarian crises (Spiegel et al., 2018).

WHO (2020) reported 2.5 million suspected cholera cases and nearly 4,000 deaths in Yemen as of November 2020. The literature identifies two groups of problems that allowed an epidemic of this magnitude: Yemen's precarious conditions and the humanitarian response.

1.1.1 Yemen's precarious conditions

Yemen has been devastated by a complex civil war between government forces in the south backed by the US and UK-backed Saudi-led Coalition Forces (SLC) and Houthi forces in the north allied with former President Saleh's forces since 2014 (Burki, 2016; Spiegel et al., 2018). Yemen was classified as a level 3 emergency by the United Nations (UN) in 2015, triggering the highest level of resource mobilization across the humanitarian system (Spiegel et al., 2018). By 2016, only 46% of all healthcare facilities remained operational. In addition to severely damaged water and sewage infrastructure, the dire situation has been exacerbated by a lack of energy (electricity and fuel), spare parts, operating and maintenance funds, and three years of unpaid civil servants (Burki, 2016; Federspiel and Ali, 2018; Spiegel et al., 2018; Qadri, Islam and Clemens, 2017).

Furthermore, most civilians' movement is confined by the ongoing conflicts; and food insecurity has put more than half of the population at risk of famine. Yemen has the highest number of people in need of humanitarian assistance of any country. On September 28, 2016, a large-scale cholera epidemic began. The number of people in need reached as high as 20 million in 2017 (ECHO, 2021).

1.1.2 Cholera response

Humanitarian organizations prepare for, respond to, and assist in disasters, whether man-made or natural, or a combination of the two. Humanitarian interventions are particularly needed when disasters occur during or as a consequence of conflict and political upheaval (Harpring et al., 2020; Rocca, 2021). The man-made and environmental factors of the cholera epidemic complicate how, when, and where the international aid resources are distributed (Baboo et al., 2022; Harpring et al., 2020).

Lessons learned from Yemen's cholera response are well documented (Al-Mekhlafi, 2018; Bellizzi, 2021; Federspiel and Ali, 2018; Spiegel et al., 2018; Qadri, Islam, and Clemens, 2017). The primary issue was that Yemen lacked an adequate cholera preparedness and response plan, despite previous outbreaks, regional endemicity, and active conflict. The timeline of the cholera response in Yemen is presented in Figure 1, including the cholera prevalence. The highlighted vaccination campaign in Figure 1 is a question asked by most of the lessons learned studies: Could the largest cholera outbreak ever recorded have been avoided or at least managed, had enough Oral Cholera Vaccine (OCVs) been deployed earlier on in the conflict? (Spiegel et al., 2018).

The reviewed studies concluded that the delayed response was due to two factors: first, a lack of a functioning surveillance system; second, multi-sector coordination structures were confused with the mandates and roles of the clusters, cholera task force, and incident management system; either overlapping or incompletely developed. Lack of coordination across these areas hampered management, technical output, and agency trust (Bellizzi, 2021; Burki, 2016; Federspiel and Ali, 2018; Harpring et al., 2020; Spiegel et al., 2018).

The overall recommendations focus on improving the laboratory and surveillance capacities and collaboration across sectors. These recommendations are repeatedly outlined in lessons learned studies conducted not only in Yemen but also in other countries experiencing cholera outbreaks. The key questions revolve around: How can the recommendation be implemented? How does one actualize what ought to be done into how it can be done?

1.2 Ending cholera by 2030: A Global Roadmap

The Global Task Force on Cholera Control (GTFCC) brings together more than 50 institutions (including governments, non-governmental organizations (NGOs), academic institutions, and United Nations agencies) to adopt a strategy to end cholera by 2030 and to reduce cholera deaths by 90% within the next decade (GTFCC, 2020). The GTFCC is built on three pillars that parallel the Yemen lessons learned: early detection and response to outbreaks, integrated prevention strategies, and country-to-country coordination. To facilitate early response, the task force and several Yemen lessons learned studies argued for the use of modeling to guide and assess cholera control measures, particularly vaccination (Federspiel and Ali, 2018; Parker et al., 2017; Qadri et al., 2017).

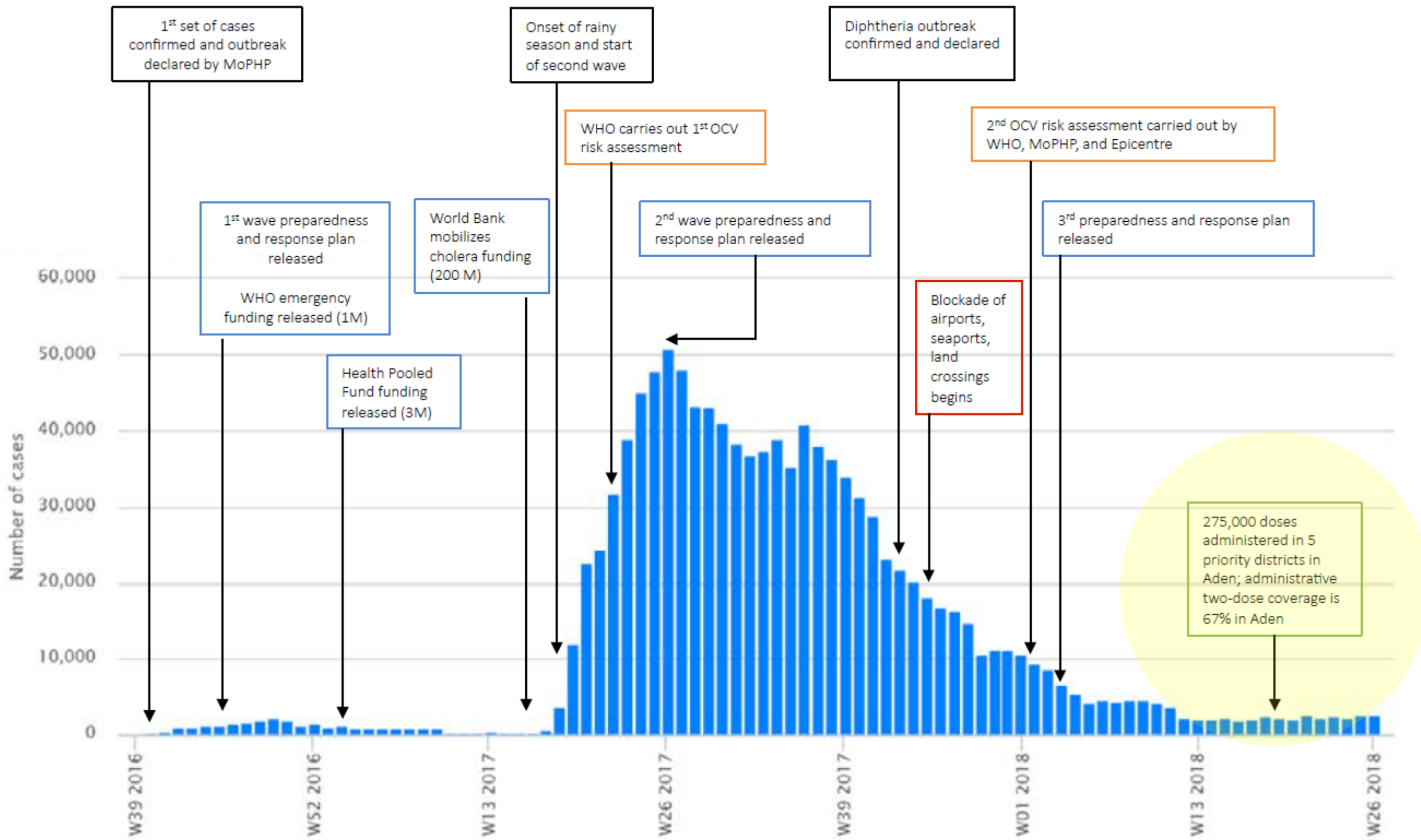


Figure 1. Timeline of key events in Yemen cholera epidemic from 2016 to 2018, weekly number of cases (Spiegel et al., 2018).

1.3 Why faster can be slower: Shifting the burden archetype

Barciela et al. (2021) has developed a Cholera Risk Model (CRM) for cholera control in Yemen. It is a predictive tool that integrates data on rainfall, temperature, and social determinants such as human mobility and water security to determine the risk of cholera trigger and transmission. Instead of a firefighting alarm, the CRM acts as a waterfighting alarm, dispatching water fighters whenever the system detects excessive rainfall. For example, with the rainfall forecast, the model assigns districts to one of three categories: 1 (low risk), 2 (moderate risk), or 3 (extreme risk) (high).

Humanitarian actors such as UNICEF then respond by increasing water system chlorination, sewer clearing, water truck preparation, and risk communication. Without a doubt, WASH intervention is critical for preventing and controlling cholera transmission; thus, implementing WASH rapidly has a significant impact. However, Barciela et al. (2021) noted that UNICEF is starting to notice fatigue, both the beneficiaries (Yemenis) and the humanitarian actors.

The following question is: Can implementing WASH rapidly be the answer to preventing cholera transmission? Are the actions being taken in response to acute problems (in this case, a cholera outbreak), reinforce the use of quick fixes? Is this a sign of the "Shifting the Burden" systems archetype?

An epidemiologist, who was interviewed in Spiegel et al. (2018) study, asked a critical question, "*Why the second wave was so big, even with rainy season (it is a factor), but why was it so massive'*. The interviewee response indicates that studies or predictive tools that focus solely on the exogenous factors on cholera transmission such as rain and precipitation is insufficient to understand the complexity of the problem. Recognizing endogenous Susceptible-Infected-Recovered (SIR) feedback loops can shed light on such question.

Harpring et al. (2022) study used system dynamics (SD) causal loop diagram to visualize the compounding factors influencing the cholera outbreak in Yemen. Along with the SIR dynamics, they discovered a strong connection between humanitarian response and the existing infrastructure development to the cholera epidemic.

Pryut (2013) developed a cholera epidemic SD model for Zimbabwe that aimed for introductory System Dynamics courses. The model tested two policies: sanitary infrastructure and health services state. The policy impacts on the SIR structures are tested through the percentage change on these two policy parameters instead of detail operational policy structures.

On the other hand, ordinary differential equation cholera models were reviewed and half of them contain only SIR model structure (Fung, 2014). To study the implications of different interventions and testing strategies, the SIR model must be extended with intervention structures. The other half of cholera transmission models included a maximum of three interventions focusing mainly on vaccination, antibiotics, and water provision. A model with more interventions does not necessarily mean better; it largely depends on the model objective and boundary. This cholera response model aims to identify the dynamic structures of humanitarian responses in Al-Hudaydah; hence, most treatment and preventive interventions are included.

Cholera control and death reduction need a multifaceted approach. None of the reviewed models include structures of both asymptomatic and symptomatic individuals as well as WASH and health interventions. In extending the existing system dynamics models, this cholera response model bridge the endogenous feedbacks driving cholera epidemic dynamics with empirically-grounded operational structures.

1.4 Research objectives

1. Identify the dynamic structures of humanitarian responses that build upon the classic infection (epidemiological) SD models.

2. Identify leverage points and test recommendations from Yemen cholera response lessons learned literature.

3. Use the developed cholera response model for humanitarian preparedness and humanitarian multi-sectors cholera response communication.

1.5 Research Questions

1.1 What are the driving factors which exacerbate the cholera epidemic?

1.2 What are the operational dynamics of the identified factors relating to the cholera epidemic? What are the feedback mechanisms that responsible for the cholera epidemic?

2.1 What are the high-impact interventions that can potentially alleviate the cholera epidemic in Yemen?

2.2 What were the lessons learned from the past interventions?

3.1 How can the model be used as a tool to have quick response to contain outbreaks at an early stage?

3.2 How can the model be used for humanitarian multi-sectors cholera response communication?

2. Methodology

2.1 System Dynamics and values of modeling

System Dynamics (SD) is the research methodology used in this study. Given the fact that SD incorporates both qualitative and quantitative components, it can be considered a mixed-methods research approach (Sterman, 2000). Infectious disease research has demonstrated that using SD models enables the exploration of alternative scenarios, the identification of previously unknown feedback loops, unintended consequences, and the identification of potential policy leverage points (Harpring et al., 2020; Pruyt, 2013; Rahmandad et al., 2021; Struben, 2020).

SD is best suited to providing dynamic projections of the course of a humanitarian crisis and exploring the implications of various interventions. SD can therefore shed light on how to improve humanitarian response to meet the diverse needs of populations (Gonçalves, 2011; Rocca, 2021). In comparison to network and agent-based modeling, Rocca's (2021) research determined that System Dynamics is the most appropriate technique for piloting complex systems modeling in the humanitarian sector because it enables humanitarian response simulation even in contexts with limited data. Rocca’s (2021) findings highlighted a need to model Yemen's cholera response, thus inspired the building of this cholera response model.

2.2 Specific considerations for this project

This cholera response model is exactly what its name implies: cholera as SIR endogenous feedback loops, and response as exogenous operational dynamics balancing effect on the SIR. Wheat (2015) and Sterman (2000) emphasized that policy design is much more than changing the value of parameters. The operational policy structure should specifically include tangible resources, perceptual adjustments, institutional capacity, and time required to implement changes (delay) that result in the desired parameter value (Wheat, 2015).

This cholera response model aims to build an operational component of cholera intervention implementation. The following question is how such a structure can be helpful to humanitarian actors. Usually, a programme manager considers two main aspects during proposal development. What is the current need (also referred to as people in need - demand), and how many potential beneficiaries can be reached by the project (activities outputs - supply)[1]. Hence, to make this cholera response model useful to humanitarian actors, the intervention inputs (in the model interface) should be constructed in a way that a programme manager can navigate the model interface quickly and effectively; with the objective to increase the users' trust, acceptance, and adoption of the tool. This is especially crucial in an emergency response when the pressure is high, time to make decisions is scarce.

Wheat (2015) provided an example of a vaccination policy structure that included inputs such as vaccine demand, vaccine supply, vaccination rate, staff size, and productivity. A programme manager and staff, on the other hand, may struggle to make sense of vaccination rates. In the author's experience as an aid worker, rate was rarely used in activity inputs. Additionally, the reviewed humanitarian literature makes relatively limited use of vaccination rates (note that this is about intervention inputs, humanitarian actors make use of rates such as death or infection rates in other aspects). For instance, during a multi-sector meeting to plan a cholera emergency response, a programme manager from WHO or UNICEF may state, "If 500,000 vaccines (input 1) can be procured in 30 days (delay - input 2), our team will be able to conduct a seven-day vaccination campaign (input 3) beginning May 1." (Input 4).

Therefore, it is more helpful for this cholera response model to have numerical inputs rather than rate inputs (this applies to interventions other than vaccination in this model). Also, the programme manager is usually well aware of the team's capacity and will adjust it in accordance with available resources; staff productivity is unnecessary in this case.

Furthermore, similar to the SIR core structure, the policy structure determines the type of data required. For example, it is difficult to collect data on the total number of staff and their productivity across all humanitarian organizations. OCHA (2017) WASH database records only the types of interventions implemented, the number of people reached, and the timeframe. Fung concluded that while illustrating ranges of possibilities (impacts of interventions in cholera models) is beneficial, future studies should be designed to provide data to parameterize these models.

This model collected data of each intervention for three main reasons. First, the historical data obtained results from all implemented interventions in 2017. Quantifying impacts from interventions should be done from the beginning of the modeled horizontal time together with the core SIR structure in replicating the historical data. Second, while this model has not yet been validated with expert inputs due to the study's resource constraints, incorporating historical data increases confidence in the model, particularly for uncertain parameters. Finally, the data indicate past implementation challenges. For instance, the starting date of the interventions; the maximum number of people that could be supported; the preparation (delay) that is needed for the intervention implementation. With the data, the policy testing in the model will be structured within a feasible range.

[1] This is based on the author personal opinion from working experience in the humanitarian field: as a monitoring and evaluation specialist, and a project officer, in managing and implementing projects.

2.3 Data collection

The data collected during the model's development and validation can be classified into two categories:

Epidemiological data: information on the characteristics of Vibrio cholerae infections (e.g. duration of infection, severity proportions), as well as their prevalence in Al-Hudaydah governorate (e.g. number of suspected and confirmed cases, deaths).

Cholera response (interventions) data: WASH sector (OCHA, 2017) and health sector (EOC, 2018; UNICEF, 2018).

Data quality issues have been regarded as a significant obstacle to an effective humanitarian response to the cholera epidemic. Inadequate access to health facilities may have resulted in underestimating the cholera burden, most notably mortality (Spiegel, 2018). For example, infected individuals who choose traditional medicine or private clinics over these specialized treatment centers are not captured by the surveillance system. Even mortality statistics are subject to reporting errors when deaths occur beyond the treatment facilities. On the other hand, Camacho et al. (2018) stated that overreporting of other AWD cases was likely to contribute to underestimates of the epidemic's case fatality rate.

Regardless of the lack of data, policy decisions must be made, frequently under high uncertainty and pressure conditions. Where a lack of data makes precise predictions impossible, simulation models may still provide valuable insights to aid decision-making under unknown circumstances. Such scientifically informed exploration can add clarity to decisions, allowing for more effective policy choices. The model analysis chapter discusses how this cholera response model incorporates structures to account for over-and under-reporting.

2.4 Research ethics

The ethical concerns about the research participants are not applicable since this study does not involve collecting primary data. While modeling can help explore solutions to complex problems, it also increases the stakes: Alongside the possibility of real benefit comes the risk of real harm (Lim, 2021). To be aware of such risk, one requires reflection, not only on the modeler positionality but throughout the whole modeling process. Along with reflection for action, it is a modeler's responsibility to adhere to best practices in developing, testing, and documentation models following guidelines in the SD field (Barlas, 1996; Rahmandad and Sterman, 2012).

Since the cholera model aimed to understand the lessons learned in 2017 to 2018, the main purpose is not to recommend specific policies. Limitations and uncertainties in both parameter values and structural components of the cholera model, as well as a lack of Yemen field work, limit the model's ability to be used as a policy recommendation tool at its current iteration (Gkini, 2021).

Cholera SIR Stock and Flow Diagram

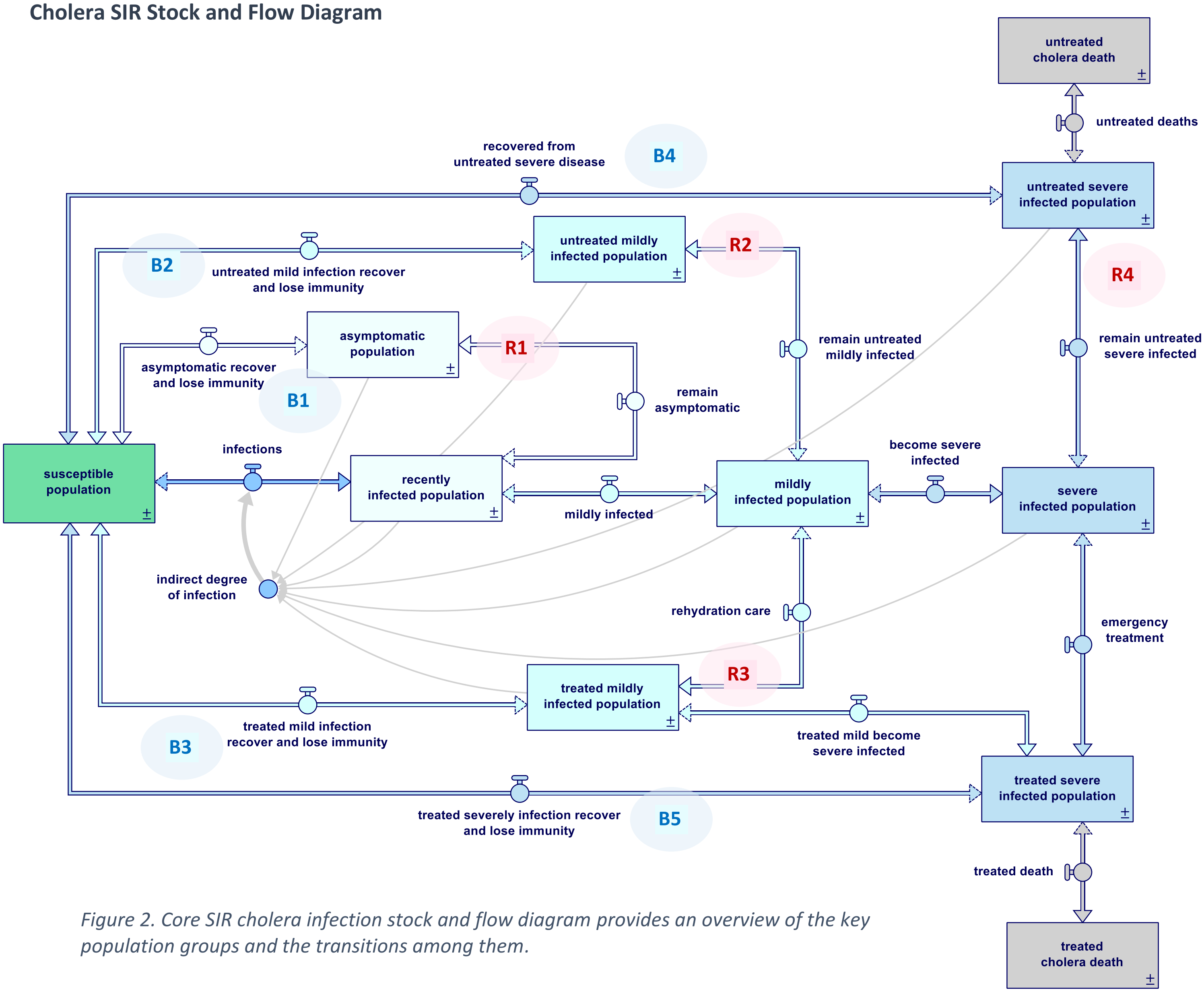


Figure 2. Core SIR cholera infection stock and flow diagram provides an overview of the key population groups and the transitions among them.

Table 1. Summary of feedback loops in SIR components.

Infectious states	Treatment	Loops	Shown
Asymptomatic (75%)	No	Asymptomatic infected loop	R1
		Asymptomatic recovered loop	B1
Mild symptom (15%)	No	Untreated mildly infected loop	R2
	No	Untreated mildly recovered loop	B2
	Yes	Treated mildly infected loop	R3
	Yes	Treated mildly recovered loop	B3
Severe symptom (10%)	No	Untreated severe infected loop	R4
	No	Untreated severe recovered loop	B4
	Yes	Treated severe recovered loop	B5

3. Model and Policy Analysis

3.1. Cholera Susceptible-Infected-Recovered, SIR

In brief, the cholera response model is an extended SIR model that integrates the epidemic response's operational dynamics. Building on Harpring et al. (2020) Yemen cholera response - causal loop diagram, and Pruyt's model (2009) that simulates the 2008 cholera outbreak in Zimbabwe, this section will address the research question: What are the driving factors which exacerbate the cholera epidemic?

Al-Hudaydah governorate had a population of 3,238,199 in 2017. (OCHA, 2017). In an SIR model, population are divided into several compartments called stocks, depending on their status of being susceptible to the infection (S), being infected and infectious (I), and having recovered from the infection (R) (Sterman, 2000). Individuals in each stock are assumed to be homogeneously mixing. Figure 2 is a stock and flow diagram illustrating the SIR major feedback loops.

3.1.1 Indirect infection

This model only incorporates indirect infection through contaminated water by infected individuals. When susceptible individuals become infected with cholera, they shift to the *recently infected population* after one day. The rate of cholera infection is a product of the *indirect degree of infection* and the size of the *susceptible population* (S). In turn, the indirect degree of infection depends on the *connectedness of aquifers* and *smoothed fraction of contaminated water*.

Although sporadic cholera cases may occur as a result from ingestion of insufficiently cooked seafood contaminated with Vibrio cholerae, humans are the primary reservoir for the pathogen during periods of active transmission (epidemic) via fecal contamination of drinking water or food (Davis, Narra, and Mintz, 2018; Médecins Sans Frontières, 2018; Mwasa and Tchuenche, 2010, Pryut, 2009). A meta-analysis of the role of water, sanitation, and hygiene exposures in 51 case-control cholera studies found that cases were significantly more likely than controls to report the use of an untreated drinking water, open defecation, unimproved sanitation, and poor hand hygiene (Wolfe et al., 2018). Hence, the *smoothed fraction of contaminated water* is water contaminated by bacteria shedding from the infected individuals (Pryut, 2009).

The *smoothed fraction of contaminated water* uses the (third-order) water contamination from *total bacteria shedding from the fraction of infected* with a delay of two and a half days. According to Nevondo and Cloete (2001), Vibrio cholerae survival in the aquatic environment is highly dependent on the chemical, biological, and physical conditions of the aquatic environment: Vibrio cholerae surviving in surface waters for periods ranging from one hour to thirteen days (cited from Okoh, 2015).

Three days are used for *time to affect water in aquifers* in this model. A third-order delay is used to account for the fact that there are different stages in the process (Sterman, 2000) between bacteria shedding by the infected individuals to contaminating the water.

Connectedness of aquifers is the "contact rate" between the susceptible population with contaminated water. More than 19 million Yemenis are believed to be without access to safe drinking water and sanitation (Burki, 2016; Camacho et al., 2018; Ng et al., 2020). According to WHO-UNICEF statistics, only 55% of the population had access to drinking water from improved water sources in 2014 (Qadri, Islam, and Clemens, 2017). Grad et al. (2012) explained that "contact rate" is largely unknown in most contexts, and there are no simple methods for converting experimental study results into "contact rate" between susceptible individuals and bacteria in water. Since various factors determine the rate at which susceptible individuals become infected, the c*onnectedness of aquifers* is calibrated to the historical data, 0.44 is used in this model.

3.1.2 Asymptomatic reinforcing feedback loop (R)

Individuals in the *recently infected population* leave the stock after an average incubation time of one day and flow in two directions: as asymptomatic infected to the asymptomatic population if they show no symptom as mildly infected to the mildly infected population if they show mild symptoms. Pryut's model (2009) makes no distinction between asymptomatic and symptomatic infections. Other works highlight that these are essential elements and incorporated into their model an asymptomatic feedback loop (Chao et al., 2014; Kaper, Morris, & Levine, 1995; Leung & Matrajt, 2021; Médecins Sans Frontières, 2018; Okoh et al., 2015)

First, most infected individuals (75% of infections) remain clinically unapparent, while the remaining 25% develop mild to severe symptoms (depending on the strain involved) (Médecins Sans Frontières, 2018). Only symptomatic infections from treatment centers are captured in surveillance data (Fung, 2014; Médecins Sans Frontières, 2018). When calibrating modeling outputs to historical data, Fung (2014) concluded that underreporting of cases, including asymptomatic cases, should be considered. Chao et al. (2014) found their model sensitive to the fraction of infected people who became symptomatic: The higher the symptomatic proportion, the higher the incidence of reported cases.

Second, the bacterial shedding rate is lower in asymptomatic individuals than in symptomatic individuals (60 percent - 90 percent of infected individuals are asymptomatic). Studies (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Okoh et al., 2015) have reported that some individuals can be infected with Vibrio cholerae and yet show no symptoms but then tend to shed the organism into the environment, even for only a few days. In a non-cholera epidemic area, Vibrio cholerae can be isolated from wastewater effluents (Okoh et al., 2015).

Third, research emphasizes the distinction between immunity from asymptomatic infection and protection from disease (symptomatic) following recovery (Kaper, Morris, & Levine, 1995; Leung & Matrajt, 2021).

3.1.3 Bacteria shedding

The model includes bacteria shedding as part of the indirect infection pathway. According to Kaper, Morris, and Levine (1995), doses of 10^11 Colony Forming Units (CFU) of Vibrio cholerae were needed to trigger diarrhea in healthy North American volunteers. For example, ingestion of 10^6 Vibrio cholerae with fish and rice resulted in a high attack rate (100%). On the other hand, a symptomatic mild infected individual can shed Vibrio cholerae in the stool in low but potentially infectious concentrations, up to 10^8 Vibrio cholerae organisms per g of stool (Nelson et al., 2013). For an individual with acute cholera, severely disease, excretes 10^7 to 10^8 Vibrio cholerae organisms per gram of stool; for patients who have 5 to 10 liters of diarrheal stool, the total output of Vibrio cholerae can be in the range of 10^11 to 10^13 CFU (Kaper, Morris, and Levine, 1995).

This model uses 10^6 Vibrio cholerae as the amount to infect an individual. The value of:

i. bacteria shedding from symptomatic is 10^4,
hence, normalized to 10^4/10^6 = 0.67
ii. bacteria shedding from a mildly infected individual is 10^8,
hence, normalized to 10^8/10^6 = 1.23
iii. bacteria shedding from a severely infected individual is 10^12, hence, normalized to 10^12/10^6 = 2

3.1.4 Symptomatic reinforcing feedback loops (R)

Mildly infected population are mild cases of Vibrio cholerae infection that may be clinically indistinguishable from other causes of diarrheal illness (LaRocque & Harris, 2020). Hence, not all seek healthcare services (Médecins Sans Frontières, 2018). Depending on healthcare services access, this model disaggregates mildly infected individuals into two different feedback loops: treated and untreated mildly infected individuals. Mildly infected individuals leave the stock after the time progress to the next stage (one day) and flow to three directions: *treated mildly infected population*, *untreated mildly infected population,* and progresses into *severe disease population stocks*.

Severe infected population is severe cases of Vibrio cholerae infection that is characterized by a sudden onset of acute voluminous watery diarrhea described as 'rice water stools' and vomiting leading to rapid dehydration (fluid losses of up to one liter per hour), and death if left untreated (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018). Among individuals developing symptoms, 60 to 80% of episodes are of mild or moderate severity (Médecins Sans Frontières, 2018; Pryut, 2004). In other words, only 5 to 10% of the *recently infected population* in the base model becomes very ill. Mildly infected individuals move to *severely infected population* after an average *time to progress next stage*. Severely infected individuals then move into two different feedback loops based on access to healthcare services: treated and untreated. *Treated severe infected population* stock does not attribute to the infectious reinforcing feedback loop as the excreted wastewater is disinfected at the healthcare sewage treatment facilities (Médecins Sans Frontières, 2018).

3.1.5 Recovered balancing feedback loops (B)

All individuals belonging to the *asymptomatic population, treated and untreated mildly infected population* recover after average illness duration (asymptomatic for five days and symptomatic for nine days) (Chao et al., 2011; Nelson et al., 2009). On the other hand, individuals in *treated and untreated severe infected population* either die (cholera deaths) or recover and become immune (recovered from heavy infection) after the same average duration of the illness of nine days.

The proportion of the treated severely infected population dying or recovering is determined by the capacity of healthcare services, overloading in health services resulting in lower care quality. Hence, an increase in fatality fraction. In 2017, the case fatality rate in Al-Hudaydah governorate was 0.19 percent (OCHA, 2017). For severely infected individuals who are not accessing healthcare services, the *untreated fatality fraction* uses 0.004, assuming that the fatality fraction is double the case fatality rate with *treated death fraction* of 0.0021.

3.1.6 Immunity waning

Studies have shown a difference between protection from asymptomatic infection and protection from disease (symptomatic) after recovery (Kaper, Morris, & Levine, 1995; Leung & Matrajt, 2021). Pryut model (2004) aggregates both mildly and severely infected population into one stock of *recovered temporarily immune population* where they flow back to the *susceptible population* after an average immunity period of six years. Studies reported that clinical cholera (symptomatic) conferred protection against subsequent cholera for at least three years (Kaper, Morris, & Levine, 1995), while a study by Leung and Matrajt (2021) identified asymptomatic protection period lasts between 3 to 12 months. The model uses six months for the *average asymptomatic infection acquired immunity period* and three years for the *average symptomatic infection acquired immunity period* (Kaper, Morris, & Levine, 1995; Leung & Matrajt, 2021).

Limitations:

For models that simulate an outbreak within a short period (two years in this model), one limitation is that they can ignore the dynamics of population growth (birth rate and death rate, gray arrows) and assume a constant population (Fung, 2014). There is no further subdivision of subpopulations according to health, living conditions, environmental conditions, geographic concentration as these are not part of the model boundary.

Multiple Vibrio cholerae infections within the same household can occur due to secondary transmission from one household member to another via the fecal-oral route (Weil et al., 2014). To explicitly account for the concentration of hyperinfectious bacteria in drinking water, modelers include a separate compartment for these hyperinfectious bacteria with very high infectiousness for "human-to-human" transmission (Chao et al., 2014; Hartley et al., 2006; Miller et al., 2010). However, Pascual et al. (2006) argued that the additional compartment is redundant unless one has specific questions to study the hyperinfectious state. The hyperinfectious state of bacteria is not included in this cholera response model.

3.2. Cholera response - intervention structure

In the event of a cholera epidemic, the focus must be on limiting mortality and stopping the disease from spreading. It should be comprehensive and multi-sectoral, encompassing epidemiology (surveillance), case management, water, sanitation, hygiene, logistics, community engagement, and risk communication (GTFCC, 2020). This section addresses the following research questions: *What are the operational dynamics of the identified factors relating to the cholera epidemic?* What are the feedback mechanisms that responsible for the cholera epidemic? *What are the* *high-impact interventions? How can this model help shed light upon the lessons learned from the past interventions in Yemen?*

3.2.1 Water, sanitation and hygiene Interventions (WASH)

Water, sanitation, and hygiene (WASH) interventions are commonly used to prevent and control cholera by deterring exposure to risk factors for disease transmission (Wolfe et al., 2018). Water interventions improve the quantity of water (water trucking), the quality of water (chlorinating water), or the management of water (safe storage). In Yemen, water trucking, latrine construction, chlorine tablet distribution, filter distribution, and hygiene kit distribution are the primary focuses of WASH (Spiegel et al., 2018).

Fung (2014) discussed transmission dynamic models used to simulate the effects of water, sanitation, and hygiene interventions. WASH interventions, their effectiveness, and coverage substantially impact the outcomes. A poorly defined WASH intervention could inadvertently misinform policymakers about which programs should be expanded in cholera response. While it is useful to illustrate ranges of possibilities, Fung noted that future studies should be designed to provide data to parameterize these models. The present cholera response model includes data on WASH interventions implemented in Al-Hudaydah governorate from OCHA's (2018) online database - the Cholera Response Dashboard.

3.2.1.1 Clean water provision

In Al-Hudaydah, clean water provision activities comprise of chlorination of wells, communal water tanks, distribution of chlorine tablets, and the daily chlorination of water trucks at water filling stations. The outputs of the activities are measured in terms of the number of people reached over time. While data are only available from May to December 2017, they enable parameterization of the intervention structure. More importantly, the intervention data demonstrate the capacity of humanitarian actors and the implementation challenges associated with cholera response, even in the absence of Yemeni stakeholders and experts' inputs.

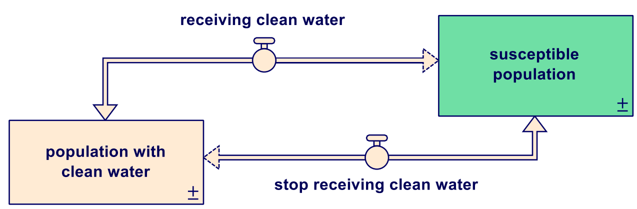


Figure 3. Stock and flow diagram of water provision intervention.

Arguably, the weakest link in modeling WASH interventions is a lack of data connecting intervention variables to infection coefficient reduction (intervention impacts) (Fung, 2014). Bertuzzo et al. (2014) reported on a "set of sanitation measures" that would contribute to a 40% reduction in "contact rate" over a month in Haiti. It will help readers if details demonstrating how the 40% reduction was achieved in the Haiti context are available. On the other hand, Tuite et al. (2011) estimated the number of people who would require clean water to achieve the same effect as 500,000 people receiving two doses of vaccine in Haiti (they showed that one million people need water provision). The implied assumption was that providing safe drinking water would result in a 100% reduction in cholera transmission (but not human-to-human transmission). However, it is unclear to readers by such a comparison without further description on how to achieve three years of water provision in a cholera epidemic response.

For example, it is feasible to vaccinate 500,000 people in a two-week vaccination campaign and provide up to three years of immunity protection to those vaccinated. To achieve the same three-year immunity through clean water intervention, the water trucks would likely need to deliver water to a million people (the study provided this Figure 3) each day. Perhaps the capacity (resources) estimation should be 365*3 years*number of trucks needed for one-million-person water provision per day.

In this cholera response model, susceptible individuals who receive clean water shift to *population with clean water* stock after one day. Compared to Tuite et al. (2011) model on 100% reduction of "contact" rate if covered by clean water provision, this model assumes only 70% of individuals who receive clean water shift into the *population with clean water* stock. Having clean water does not ensure a 100% reduction in susceptibility (Wolfe et al., 2018). Figure 4 below illustrates the different pathways of cholera transmission. In addition, not all the water provision goes directly to the *susceptibility population*. The water provision is shared among all SIR sub-populations since there is disaggregation among the recipients in this model. Hence, only a fraction of individuals from the *susceptible population* stock receives clean water.

Individuals with clean water leave the stock after one day and flow back to *susceptible population* stock after water provision ceases. In other words, this water intervention structure shows one-day protection from infection. One might argue that the water provision should eventually transit from emergency water trucking or chlorine tablets to building water treatment plants. Nevertheless, such long-term WASH development strategy is not part of the emergency cholera response model boundary.

Furthermore, this water intervention structure comprises a capacity-building structure (water supply capacity). Considering implementation challenges such as delay in building capacity from the supply side limitations, the capacity to distribute water is expressed as the number of people that can be provided with clean water. Building capacity to distribute water is a goal-seeking function. The current capacity to distribute water is closing the gap

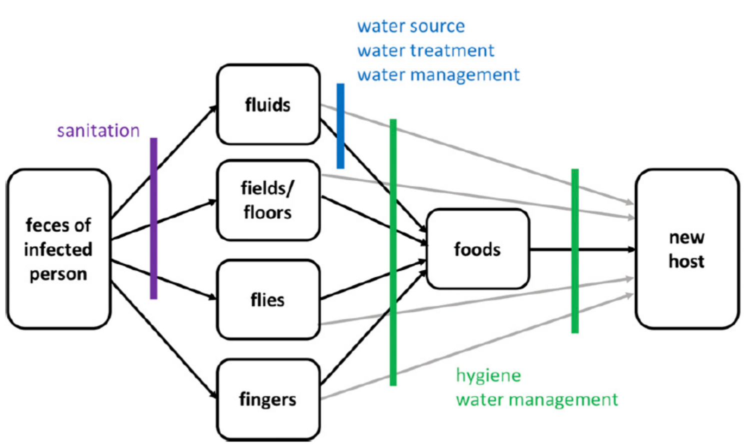


Figure 4. Pathways of fecal–oral cholera transmission and opportunities to interrupt transmission from Water 1st International (cited from Wolfe, 2018).

with desired water distribution capacity (target by the humanitarian actors) over time to increase their distribution capacity (first-order delay). *Time to increase distribution capacity* is an assumptive duration (days) needed to increase the current capacity. The WASH experts can change the value for different scenario simulations through the developed model interface.

Result

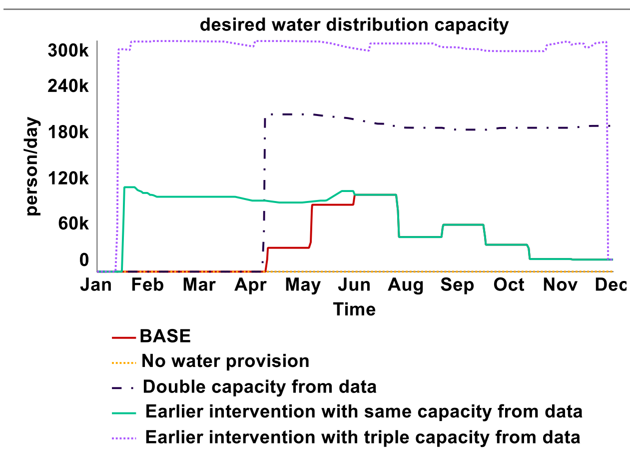
Table 2 presents the water provision input (*desired water distribution capacity*) and the result (impact from the intervention on *recently infected population*). The behavior over time graphs in Table 2 only portrays the timeline from January to December 2017 for a clearer behavior (result) analysis. The *desired water distribution capacity* is the number of person reached for clean water intervention activities (Y-axis). BASE is the scenario simulation that replicates the historical data of cholera epidemic in Al-Hudaydah (including all the intervention data). The capacity from BASE (intervention data in red line) in the input graph shows a maximum of 100,000 recipients reached by the humanitarian actors in a governorate of three million population.

No substantial difference between double the capacity (black line) to BASE (red line) is observed. Without any clean water provision intervention, the yellow line peaks at 12,000 persons while BASE line peaks at 11,000 persons. When the intervention begins earlier with the same capacity as in data, the blue line peaks at the same magnitude as BASE but peaks after one month delay in September. This indicates an important role of water provision as an immediate response (with a relatively short delay) compared to other interventions with longer delay such as building DTC or procuring vaccines from global stockpile.

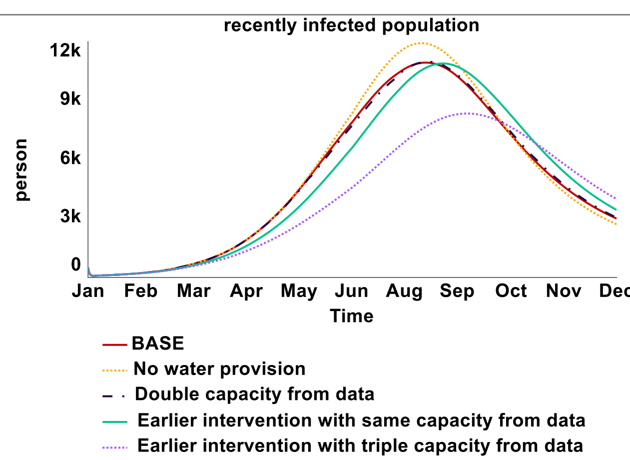
One might anticipate a greater impact of water provision on cholera control, given that WASH intervention is considered a critical component of such an emergency response (Médecins Sans Frontières, 2018). The result does not negate the importance of water provision as a preventive measure. Water provision can have a significant impact

Table 2. Clean water provision intervention simulation.

Intervention input



Result



on flattening the cholera epidemic curve if capacity is tripled (purple line) or increased to 1,000,000 daily recipients; however, based on 2017 intervention data, the plan was deemed unattainable in Al-Hudaydah due to its precarious condition.

3.2.1.2 Sewage treatment plant

The highest number of cholera cases has been reported in areas with non-functional sewage treatment plants (Abu-Lohom, Muzenda, & Mumsse, 2018). Without functional sewage treatment plants, sewage effluents are frequently diverted to impoverished neighborhoods and agricultural lands, contaminating shallow aquifers and wells used by local civilians and private tankers (Médecins Sans Frontières, 2018; Okoh et al., 2015). The reuse of sewage effluents for irrigation is an essential alternative water source for Yemen.

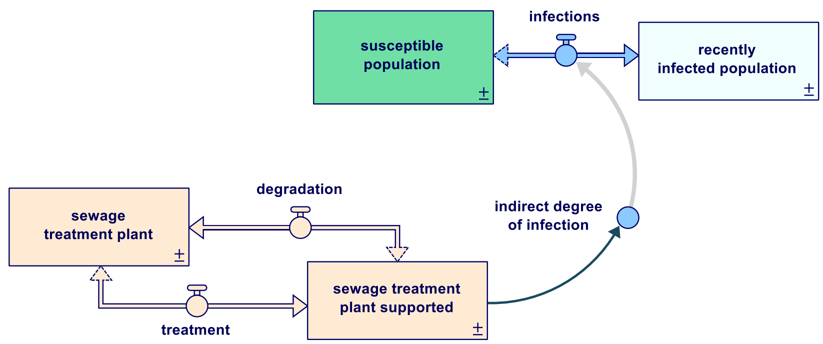


Figure 5. Stock and flow diagram of sewage treatment plant intervention.

Sewage treatment helps remove contaminants from sewage to produce effluent suitable for discharge to the surrounding environment or reuse (Al-gheeti et al., 2014; Médecins Sans Frontières, 2018; Okoh et al., 2015). For instance, farmers in Yemen collect sewage effluent directly from stabilization ponds to irrigate various crops (Al-gheeti et al., 2018). A study by Al-Sharabee in 2009 (cited in Al-gheeti et al., 2014) reports that the zone area near the Sana'a wastewater treatment plant depends upon the sewage effluents by 95% to irrigate crops. However, Yemen's current sewage effluent quality is generally poor since none of the existing sewage treatment plants produces effluents comply with the effluent quality regulations (Al-gheeti et al., 2018).

Sewage management and food safety are two critical areas for preparedness and response to the cholera outbreak. However, because these fields are not mandated by health or the WASH cluster, they are frequently overlooked or dealt with ad hoc during the response (Bellizzi, 2021; Wolfe, 2018). This problem is also indicated by the lack of cholera modeling literature on sewage treatment. In this cholera response model, a simplified need-based sewage treatment structure is constructed because it is unnecessary to model the effluent disinfection process.

Most humanitarian responses are based on estimates of the number of people in need in each sector (Roberta, 2021). In Yemen, the humanitarian actors have provided operational support for sewage treatment plants in Al-Hudaydah governorate, particularly Al Hali, Al Hawak, and Al Mina districts. Apart from the number of people reached through implemented activities, humanitarian actors detailed their WASH activities in their annual reports (UNICEF, 2019). UNICEF, for example, has provided 3.2 million liters of fuel per month to ensure the continued operation of urban water supply and sanitation systems (including sewage treatment plants) in 15 major cities.

Although reports specifying project impact evaluation are uncommon in the published literature (Fung, 2014), a well-maintained sewage treatment plant is assumed to produce effluents that meet quality regulations, thereby improving sanitary conditions and reducing Vibrio cholerae contamination in drinking water sources (Médecins Sans Frontières, 2018; Okoh et al., 2015). The sewage treatment plant intervention structure in this model addresses the ongoing maintenance and treatment needs of the existing plants (sewered population) in Al-Hudaydah.

In Figure 5, sewage treatment plant is a stock that represents the sewered population in Al-Hudaydah - 69.3% a*verage sewered population* (Ministry of Electricity and Water, 2003). The sanitation intervention of additional treatment and maintenance to the sewage plants during the epidemic shifts the sewered individuals to *sewage treatment plant supported* stock. The sewered individuals covered by treatment and maintenance of the sewage plants then leave *sewage treatment plant supported* stock after an average degradation time, flows back to the *sewage treatment plant.* The degradation time assumes that a sewage treatment plant needs maintenance and treatment after 30 days. More data and expert input is required for this parameter.

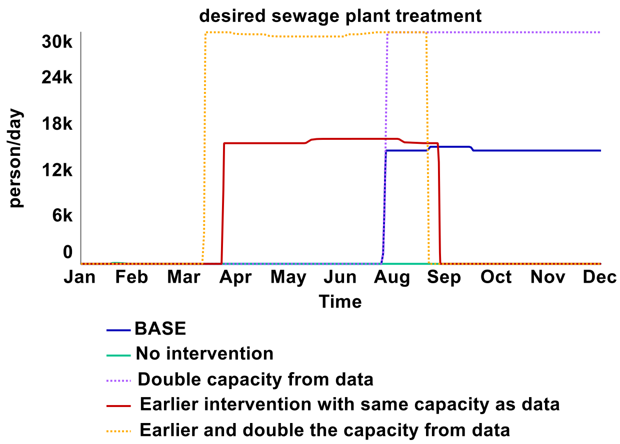
The effect of the intervention depends on the need for maintenance and treatment. *Sewage treatment plant need* is the stock *sewage plant treatment* relative to the initial value of *sewage plant treatment (average sewered population)*. If the value is 1, it indicates 100% need. Once the intervention is implemented, the number of sewered persons reduces, causing the value to be less than one; hence, a reduced need and a positive effect of the intervention on sanitary conditions. The *effect of sewage plant treatment on sanitary condition* has a graphical function of S-shape decay. When the sewage treatment plant need is value 1 (no intervention), the effect is 1 (no effect to the normal sanitary condition). The maximum effect is limited at 2 to constrain the sanitary condition at its maximum at 100%. Like the clean water provision model structure, this intervention also adds a capacity component to show the delay: time needed to procure resources and implement the intervention.

Result

The following table 3 summarizes the sewage treatment plant support input (desired sewage treatment) and the results (impact from the intervention on recently infected population). The behavior over time graphs in Table 3 depict only the period from January to December 2017 to enhance analysis of behavior (results). The desired sewage plant treatment capacity is determined by the number of people who will be targeted by intervention activities (Y-axis). BASE is a scenario simulation that replicates the historical data of the Al-Hudaydah cholera epidemic (including all the intervention data). The capacity from BASE (intervention data in blue line) indicates that humanitarian actors reached a maximum of 15,000 sewered population in an average sewered population of 2.2 million.

There is no noticeable difference between doubling capacity (purple dashed line) and no intervention (green line) to BASE (blue line). This indicates that the intervention began too late (shortly before the epidemic's peak in August 2017) where doubling the resources has a minimal impact. An earlier intervention in March or April has a significant impact on epidemic control.

Table 3. Sewage treatment plant support intervention simulation.

<table>
<tr><th>Intervention input</th><th>Result</th></tr>
<tr><td>
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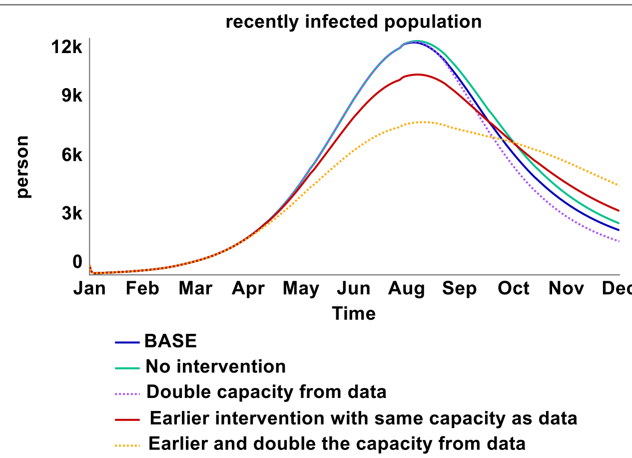
<td>
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3.2.1.3 Latrine construction

According to the World Bank (2021), 1% of people in Yemen's urban areas practiced open defecation in 2017. Open defecation refers to feces are discarded in fields, bodies of water, and other public areas (Wolfe, 2018). Like non-functional sewage plants, open defecation near water sources, or poorly constructed latrines, can become sources of infection, particularly during the rainy season (Médecins Sans Frontières, 2018; Okoh et al., 2015; Spiegel, 2018). None of the cholera transmission models examined so far incorporate latrine structures. However, Médecins Sans Frontières (2018) highlights the importance of safe excreta disposal in a manual on Management of a Cholera Epidemic. For instance, whenever there is a high concentration of people, and there are no or few latrines, emergency measures should be implemented, taking the context and habits of the population into account.

This model latrine construction intervention is based on the need for latrine capacity: the 1% population openly defecating. While the manual recommends prioritizing public latrine placement in areas with a high risk of transmission (markets, train stations, and bus stations), this model intervention structure does not disaggregate to infection hotspots level. The latrine intervention consists of a capacity-building structure (*added latrine capacity*). The stock *added latrine capacity* is expressed as number of people who can be provided with latrine facility. *Latrine construction* has a goal-seeking function at which the *added latrine capacity* (stock) is closing the gap with desired latrine construction over the time to build latrine (first order delay). In other words, the capacity building takes into account the time needed to build new latrines (delay). The intervention effect is represented by the *effect of additional latrine on sanitary condition* on the sanitary condition. The effect variable uses a graphical function of S-shape decay. When the latrine need is value 1 (no intervention), the effect is 1 (no effect on the normal sanitary condition). The maximum effect is limited at 2 to limit the sanitary condition to its maximum at 100%.

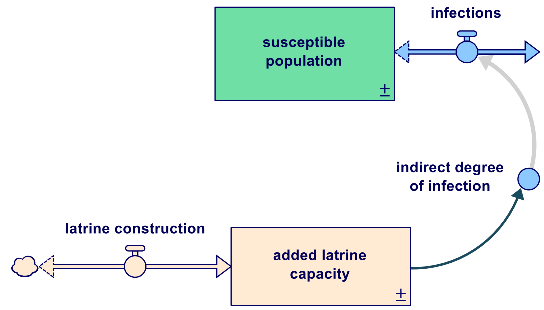

Figure 6. Stock and flow diagram of latrine construction intervention.

Result

Figure 7 is a behavior of time graph that portrays the simulation result from various intervention inputs (in 2017). The intervention is composed of three inputs: the desired number of latrines, the duration required to build this desired number of latrines, and the start date for latrine construction. There is no information on latrine construction in the WASH data from OCHA's cholera response dashboard (2018). Other WASH activities were prioritized; for example, latrines were constructed as part of the ORC and DTC facilities, rather than as public latrines (Médecins Sans Frontières, 2018).

BASE (dashed black line) shows no latrine intervention. Other simulated scenarios test the intervention starting time and the delay (duration to build new latrines). The most favorable behavior is starting the intervention early and having the latrines ready for public use the fastest. The intervention impact might not significantly impact the epidemic curve; however, this intervention plays a vital role in preventing water sources from Vibrio cholerae contamination, especially in the rainy season.

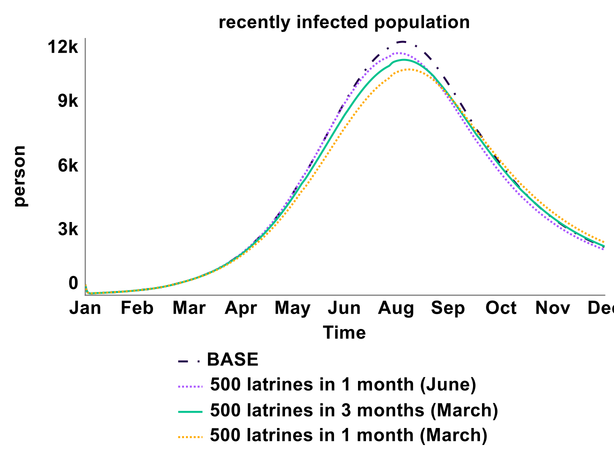

Figure 7. Latrine construction intervention simulation result.

Effect of WASH on sanitary condition

In Gkini's COVID-19 transmission model (2020), each of those intervention is multiplied by their associated weight to give its total contribution to the overall costs of hygienic behaviour. In this model, the *normal sanitary condition* adopts the same weighted average approach to "combine" the effects of WASH intervention. Each intervention activity is multiplied by their associated weight to give their total contribution (effect) to the overall sanitary condition.

According to WHO–UNICEF statistics, in 2014, only 53% of the population in Yemen used improved sanitation facilities (cited from Qadri, Islam, and Clemens, 2017). Hence, the value of *normal sanitary condition* is assumed to be 0.5 functioning.

Weight of sewage plant support assigns the weight of sewage plant state in influencing the *indicated sanitary condition*. It is assumed to be 0.4 of the sanitary condition. The value is conceptualized with a higher weight than latrine use and other infrastructure states.

Weight of latrine use assigns the weight of latrine state in influencing the indicated sanitary condition. It is assumed to be 0.2 of the sanitary condition. More data/expert input is required for this parameter.

Weight of other sanitary interventions assigns the weight of another sanitation state in influencing the indicated sanitary condition. It is assumed to be 0.4 because this parameter considers household and personal level sanitation is different from community-level interventions on sewage treatment plant and latrines. Although personal and household sanitation conditions play an essential role on fecal-oral cholera transmission, it is beyond the boundary of this model. Hence, the parameter value remains constant.

Limitations:

The intervention data (OCHA, 2017) includes activities of Basic Hygiene Kit (household) distribution, and hygiene promotion in 2017. These activities are designed to minimize 'human-to-human' infection, particularly among members of the same household. Additionally, Chao et al. (2014) developed a model educational campaign to promote improved hygiene and sanitation in conjunction with a vaccination campaign. They simulate the effect of a 10% or 30% (additional) reduction in areas targeted by vaccination campaigns. Nonetheless, no empirical data source for hygiene education effectiveness was provided in Chao et al. study.

Modeling behavior change is possible, but more explanation is necessary because a change in knowledge does not guarantee behavior adoption or maintenance. Wolfe et al. (2018) mentioned that knowledge and attitudes toward WASH interventions and standard practices may also impact intervention effectiveness, but these factors were rarely reported. Modeling behavior change in relation to hygiene practices is outside the scope of this cholera response model.

3.2.2 Healthcare Interventions

3.2.2.1 Diarrhea Treatment Centre (DTC)

Infected individuals who are severely dehydrated, need intravenous fluids and hospitalization. In Yemen, they are admitted to a DTC. The mortality rate without treatment can reach 50%; with adequate healthcare, it is less than 1% (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009).

A DTC is a specialized inpatient healthcare facility dedicated to managing severe cholera cases. DTC is located outside the main hospital to prevent disease spread and is completely self-sufficient in general services (toilets, showers, kitchen, laundry, morgue, and waste area), stocks, and resources (medical and logistics, waters, and electricity).

None of the reviewed cholera transmission models includes DTC as the treatment component. Miller et al. (2010) and Mwasa and Tchuenche (2011) simulated the cholera treatment structure with symptomatic infected individuals receiving combined rehydration and antibiotic treatment. Those receiving this treatment are assumed to have an increased recovery rate and a decreased death rate due to cholera. Oral rehydration therapy (ORT) is the primary treatment for cholera patients, as it prevents dehydration and reduces mortality (Médecins Sans Frontières, 2018). While antibiotics are not advised for mild or moderately ill patients, they can help reduce stool volume, diarrhea duration, and Vibrio cholerae shedding in severely ill patients when used with rehydration therapy (Davis, Narra, Mintz, 2018).

DTC is added as the main treatment component for *severe infected population* who seek emergency treatment in this cholera response model. Emergency treatment at DTC has three impacts: The effect of antibiotic treatment is not explicitly constructed in the DTC structure since mass antibiotic administration is not recommended because it has no proven effect on cholera transmission and may contribute to antimicrobial resistance (WHO, 2021). However, an increased recovery rate (five days rather than nine days in untreated individuals) is included, as Médecins Sans Frontières (2018) reported that a patient with severe dehydration or complications might require hospitalization for four to five days.

Second, in addition to the antibiotic function of reducing the water contamination rate by treated patients in terms of Vibrio cholerae concentration in the water reservoir (Davis, Narra, Mintz, 2018), this model excludes treated severe infected population stock from the cholera infection feedback loop. In other words, they function as a balancing feedback loop when their bacteria shedding does not attribute to the water contamination. DTC adheres to strict guidelines for safe external waste disposal at the facility's waste treatment system.

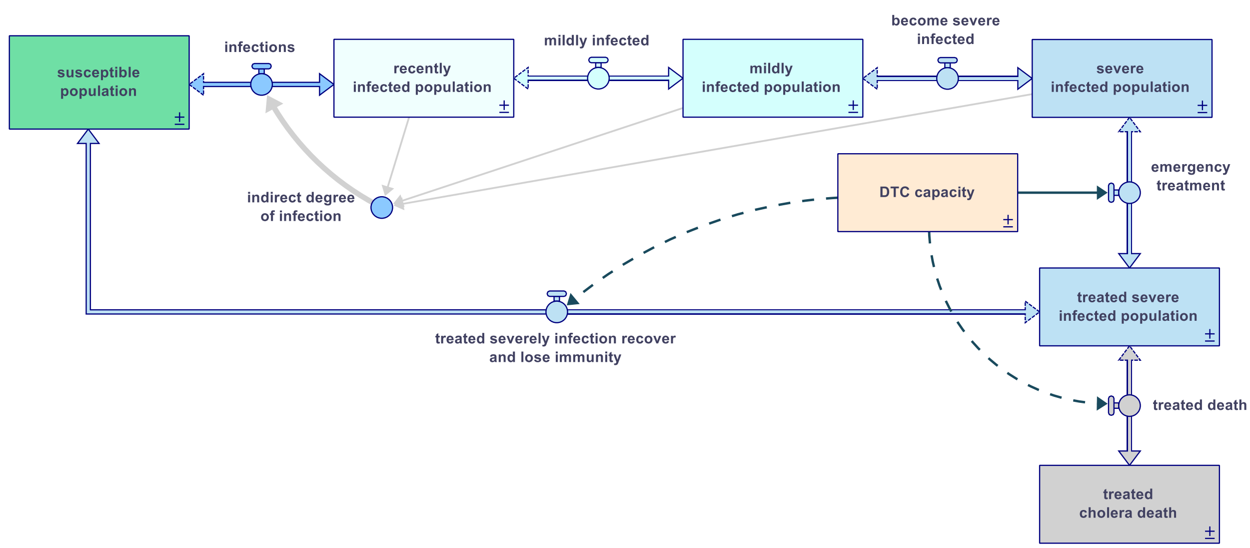

Figure 8. Stock and flow diagram of emergency treatment intervention.

Third, the DTC structure takes into account the impact of current healthcare facility capacity. This is a critical step as it models both supply and demand issues, which is not possible simply by adding an antibiotic treatment structure. For example, a COVID-19 system dynamic model by Deaton (2021) incorporates hospital capacity in treating severely disease COVID-19 patients. This structure tracks the number of hospital beds. Once those beds are full, COVID-19 patients in need of hospital care are placed on a waiting list and are admitted as space becomes available. Patients who cannot receive healthcare in time die at a significantly higher rate than those who receive it. Additionally, Fiddaman's COVID-19 system dynamic model (2020) includes a hospital capacity structure that considers the effect of care quality sensitivity to capacity strain on the patient death rate. Similarly, Médecins Sans Frontières (2018) stated that the case fatality rate (CFR) is used to evaluate the quality of healthcare services (case management) provided by cholera treatment centers.

This model adopts Fiddaman's structure, where the fatality fraction on treated death is affected by the strain on DTC services capacity. The formula includes the sensitivity of care quality to health services strain. The negative exponent indicates an inverse relationship, whereby an increase in health services strain leads to decreased care quality. Hence, an increase in fatality fraction.

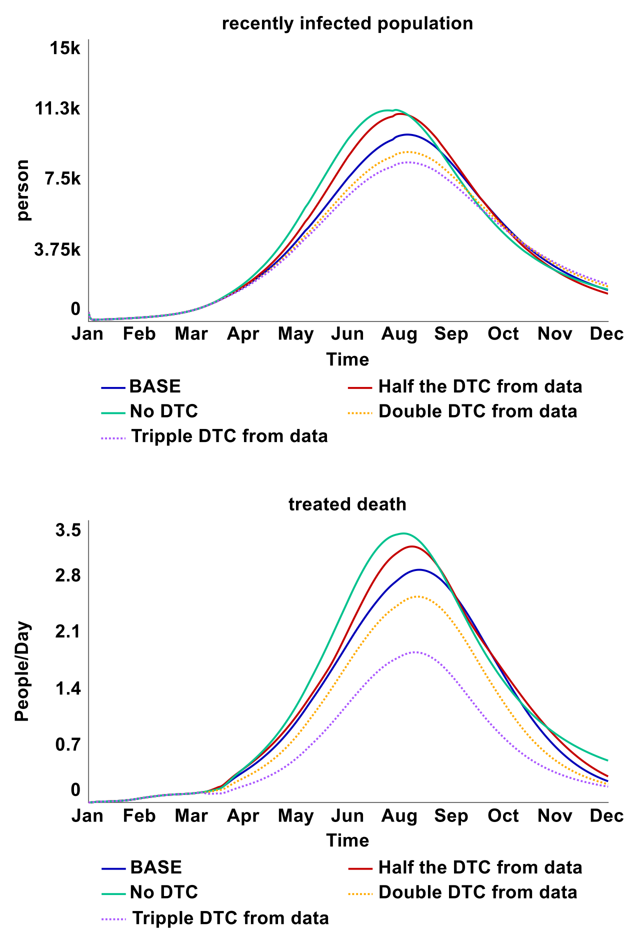

Figure 9. DTC intervention simulation result of recently infected population (top) and treated death (bottom).

Result

Figure 7 shows two behavior of time graphs that presents the result of *recently infected population* (top) and *treated death* (bottom). BASE is the scenario simulation that replicates the historical data of cholera epidemic in Al-Hudaydah (including all the intervention data). The DTC number in BASE (intervention data in blue line) is 18 DTC.

Different DTC capacity simulations substantially change both cholera transmission and death rate. The changes for both graphs are relatively similar for the first three scenarios of BASE (blue line), No DTC (green line), and Half the DTC (red line). The DTC need is more the DTC supply in these three scenarios: DTC is overload. The DTC strain has deteriorated healthcare service quality, and negatively impacted the death rate and health-seeking among severely infected individuals. In other words, a lack of DTC strengthens the untreated severe infected reinforcing loop, R5.

However, once the number of DTC increases to double and triple the capacity from data), both infected population and death drop (dashed yellow and purple lines). Interestingly, the drop in the infected population has a smaller magnitude than the drop in death. One of the reasons is that, DTC has a more substantial impact on preventing deaths: the mortality rate reduces from 50% to less than 1% (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009).

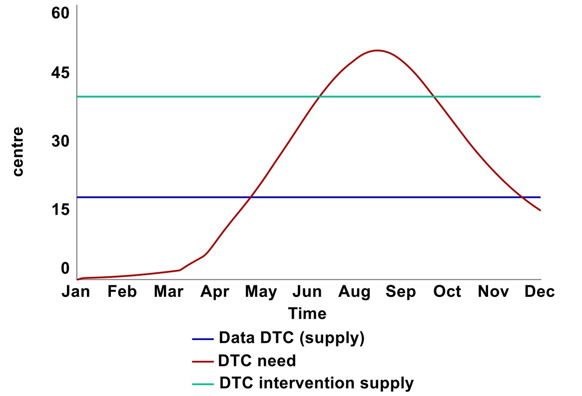

Figure 10. A behavior over time graph protraying whether the need for DTC are met by intervention input.

When the supply in these two scenarios is now meeting (and over) the demand, the *health seeking ratio* is slightly affected, positively. However, the impact is minimal since various factors affect health-seeking behavior; accessibility, availability, affordability, and acceptability. This model boundary focuses on the availability of the DTC. This model does not include interventions that increase health-seeking among severely infected individuals. Improving demand among the infected individuals can potentially be included in future studies.

3.2.2.2 Oral Rehydration Corner (ORC)

ORCs are small, decentralized outpatient care facilities that operate only during daylight hours (8 to 12 hours per day). They are primarily used to administer oral rehydration therapy. Early oral therapy can help prevent the onset or aggravation of severe dehydration, which requires hospitalization (Médecins Sans Frontières, 2018; Miller et al., 2010; Mwasa and Tchuenche, 2011). If a patient's condition worsens, ORC transfer severe or complicated cases to a DTC.

As with DTC, none of the cholera transmission models reviewed specifically extend the structure of ORC, with the exception of Miller et al. (2010) and Mwasa and Tchuenche (2011), who simulated oral rehydration therapy but not the health facilities. ORC is included as an intervention component for mildly infected individuals seeking rehydration care. There are two primary outcomes of ORC's rehydration care. First, assuming all patients at the ORC receive oral rehydration therapy: adequate volumes of a solution of oral rehydration salts. It prevents dehydration, thereby reducing mildly infected individuals' progression into severely diseased individuals.

The ORC structure includes the impact from the existing healthcare facility capacity. If the ORC capacity is strained by high demand from the infected individuals, the care quality reduces. Médecins Sans Frontières (2018) explained that a mild clinical state can rapidly deteriorate (or remain unchanged) if the volume of fluid prescribed is insufficient (the degree of dehydration is underestimated); the volume is not administered within the appropriate time frame (rehydration too slow or too fast, interruptions in treatment). When the quality of healthcare declines, more mildly infected individuals become severely infected. Additionally, ORC overload has a negative effect on the health-seeking behavior of infected individuals.

Result

Figure 11 shows three behavior over time graphs that presents the result of *recently infected population* (top), *recorded suspected and confirmed cases* (middle), and *treated and untreated death rate (bottom)*. BASE is the scenario simulation that replicates the historical data of cholera epidemic in Al-Hudaydah (including all the intervention data). The ORC number in BASE (intervention data in blue line) is 144 ORC. Different ORC capacity simulations give three distinct behavior observations.

First, one might assume *recorded suspected and confirmed cases* graph (middle) portrays the same behaviors as *recently infected population* graph (top) when increased number of ORC strengthens the treated recovered balancing feedback loop, B3. Why does double the ORC capacity (yellow line) show the highest peak among all the *recorded suspected and confirmed cases (rate)* simulations?

ORC and DTC are the primary sources of data for the country's surveillance system (McCrickard et al., 2017; Spiegel et al., 2018). Hence, the data depends on the availability of ORC and DTC. However, cases are still recorded in the graph when there is no ORC (red line). Even though the destruction has limited health care delivery, infected individuals are assumed to seek healthcare services at hospitals if ORC and DTC are not available. In this scenario, the surveillance system relies on the existing hospital to provide treatment to the infected individuals. Hence, no ORC does not mean a flat red line in the recorded cases (middle) graph.

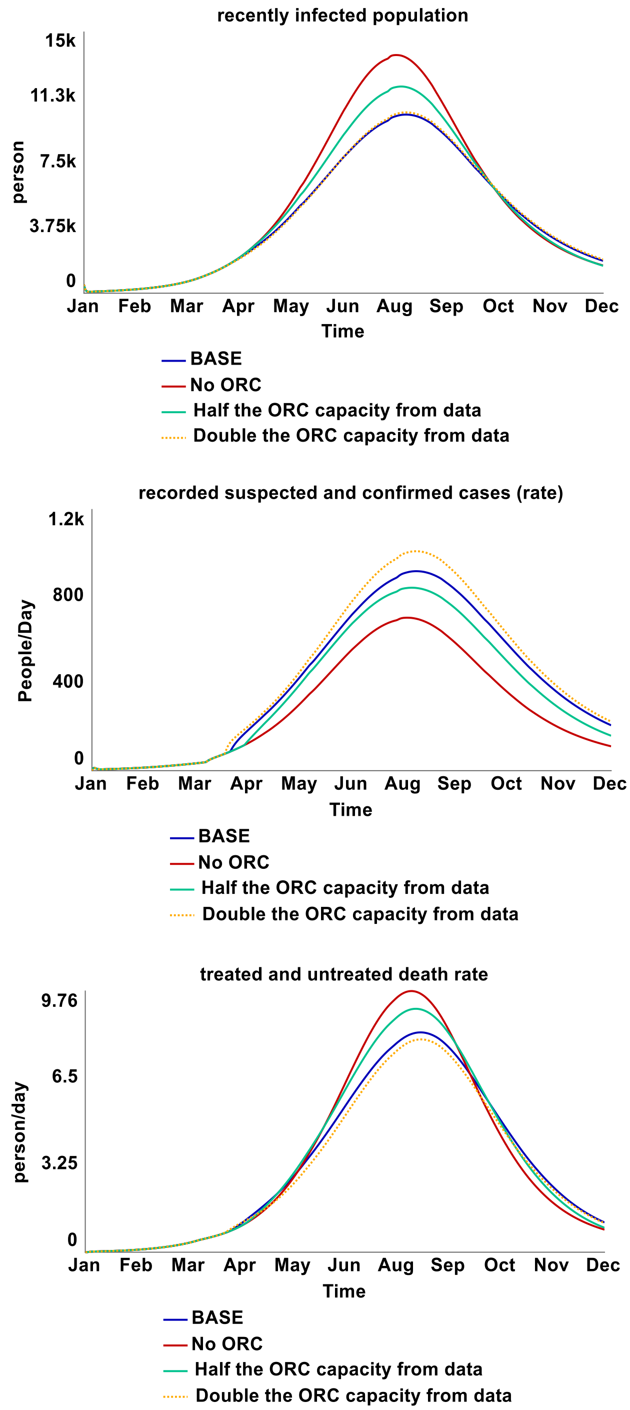

Figure 11. Behavior of time graphs that presents the result of recently infected population (top), recorded suspected and confirmed cases (middle), and treated and untreated death rate (bottom) under ORC intervention.

Second, one might puzzle over the result of double the ORC capacity (yellow line) slightly more than the BASE (blue line) in *recently infected population graph* (top). This observation is related to the result in *treated and untreated death* graph (bottom). Figure 12 is an overtime graph that shows the supply and demand on ORC. It indicates the ORC services strain situation if the demand is more than the supply of ORC. For example, in BASE scenario (blue line), the ORC (supply) is lower than the ORC needs (demand in red line). Overloading in ORC results in less impact of the intervention in preventing cholera death.

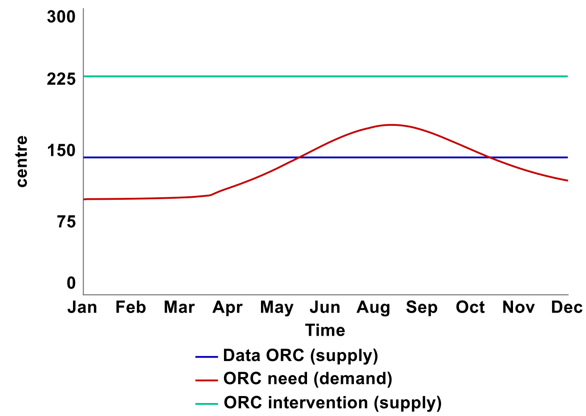

Figure 12. A behavior over time graph protraying whether the need for ORC is met by intervention input.

Nonetheless, an increase in ORC does not lead to a 100% reduction in death (as shown in treated and untreated death graph). In other words, once the supply is over the demand, good quality care help prevent the symptoms deteriorates to severely infected stage: The treated mildly recovered balancing loop (B3) is strengthened. When there is a less severely infected population, there is less death; the total population in Al-Hudaydah is higher in scenario double the ORC capacity compared to BASE. There are more susceptible individuals in scenario double the ORC capacity. Hence, the *recently infected population* graph (top) shows a slightly higher infected number in scenario double the ORC capacity compared to BASE.

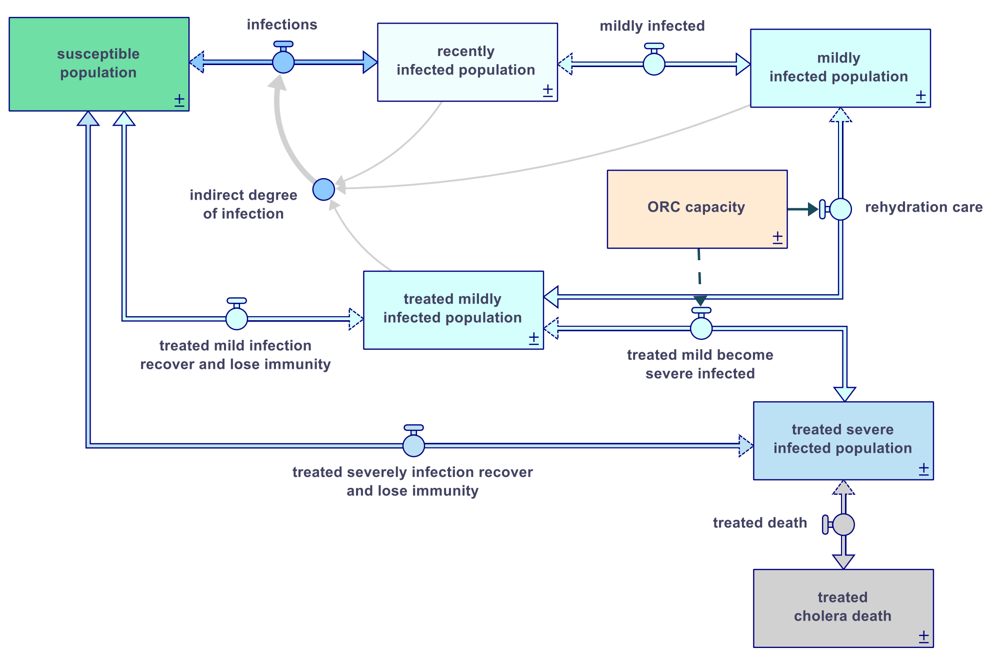

Figure 13. Stock and flow diagram of oral rehydration care at ORC intervention.

Nonetheless, an increase in ORC does not lead to a 100% reduction in death (as shown in treated and untreated death graph). In other words, once the supply is over the demand, good quality care help prevent the symptoms deteriorates to severely infected stage: The treated mildly recovered balancing loop (B3) is strengthened. When there is a less severely infected population, there is less death; the total population in Al-Hudaydah is higher in scenario double the ORC capacity compared to BASE. There are more susceptible individuals in scenario double the ORC capacity. Hence, the *recently infected population* graph (top) shows a slightly higher infected number in scenario double the ORC capacity compared to BASE.

3.2.2.3 Vaccination

Vaccination decreases the number of fully susceptible individuals, decreases infectiousness (the rate of water contamination), and decreases the likelihood of becoming symptomatic when infected (Camacho et al., 2018; Grad et al., 2012). OCV has been shown to be safe, logistically feasible, and acceptable by recipients (Federspiel and Ali, 2018; Parker et al., 2017; WHO, 2017). OCV is also inexpensive in a variety of settings, with total costs including procurement and delivery per fully vaccinated individual being less than USD 10 (Federspiel and Ali, 2018; Parker et al., 2017; WHO, 2017).

Vaccination is the most common simulated intervention among cholera transmission models that extend beyond the SIR explanatory component. For example, Fung (2014) has reviewed 14 ordinary differential equation (ODE) models that focus on the Haitian cholera epidemic. Eight models incorporated intervention components where all eight of them simulated impact from vaccination.

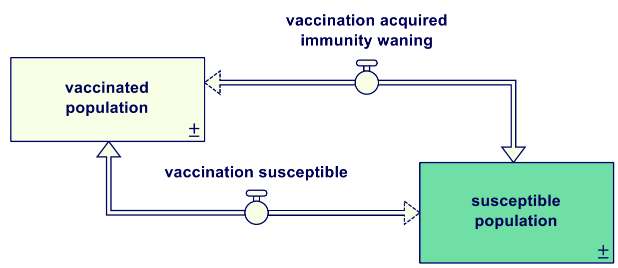

Figure 14. Stock and flow diagram of vaccination

In this cholera response model, the stock and flow diagram in Figure 14 illustrates that the vaccination transfers individuals from *susceptible population* to *vaccinated population*. Once immunity wanes, people are transferred back to the *susceptible population* from the *vaccinated population*. However, not vaccine recipients come directly from the *susceptible population*, especially when there is no mass testing (such as COVID-19 screening) during the cholera epidemic. Even mass testing is possible for COVID-19, healthcare providers do not screen the recipients. Hence, the vaccines procured for Al-Hudaydah are shared among the: *susceptible population, recently infected population, asymptomatic population, and recovered asymptomatic population* (refer to Appendix B documentation for detailed equations, Figure 14 is a simplified SFD). In addition, not everyone vaccinated will be immune to infection. A recent meta-analysis of seven randomized trials and six observational studies reported the mean effectiveness of a standard two-dose killed oral cholera vaccination at 76% with protection lasting at least three years (Shim and Galvani, 2012). Vaccine effectiveness is included in this model but not vaccine efficacy.

Result

Most of the Yemen cholera response lessons learned literature centers on the question: Could the largest cholera outbreak ever recorded have been avoided or at least managed, had enough OCVs been deployed earlier on in the conflict? In the total infected population graph (bottom), BASE has the same total number of infected population (red line overlapping with blue line), indicating that vaccination in August 2018 has a minimal impact.

The result indicates that the earlier the vaccination starts, the better the impact in flattening the curve in the first wave. Although starting the vaccination during the height of the epidemic (in June 2017) has a lesser impact than early response in April, starting in June still reduces infection profoundly compared to starting vaccination in August

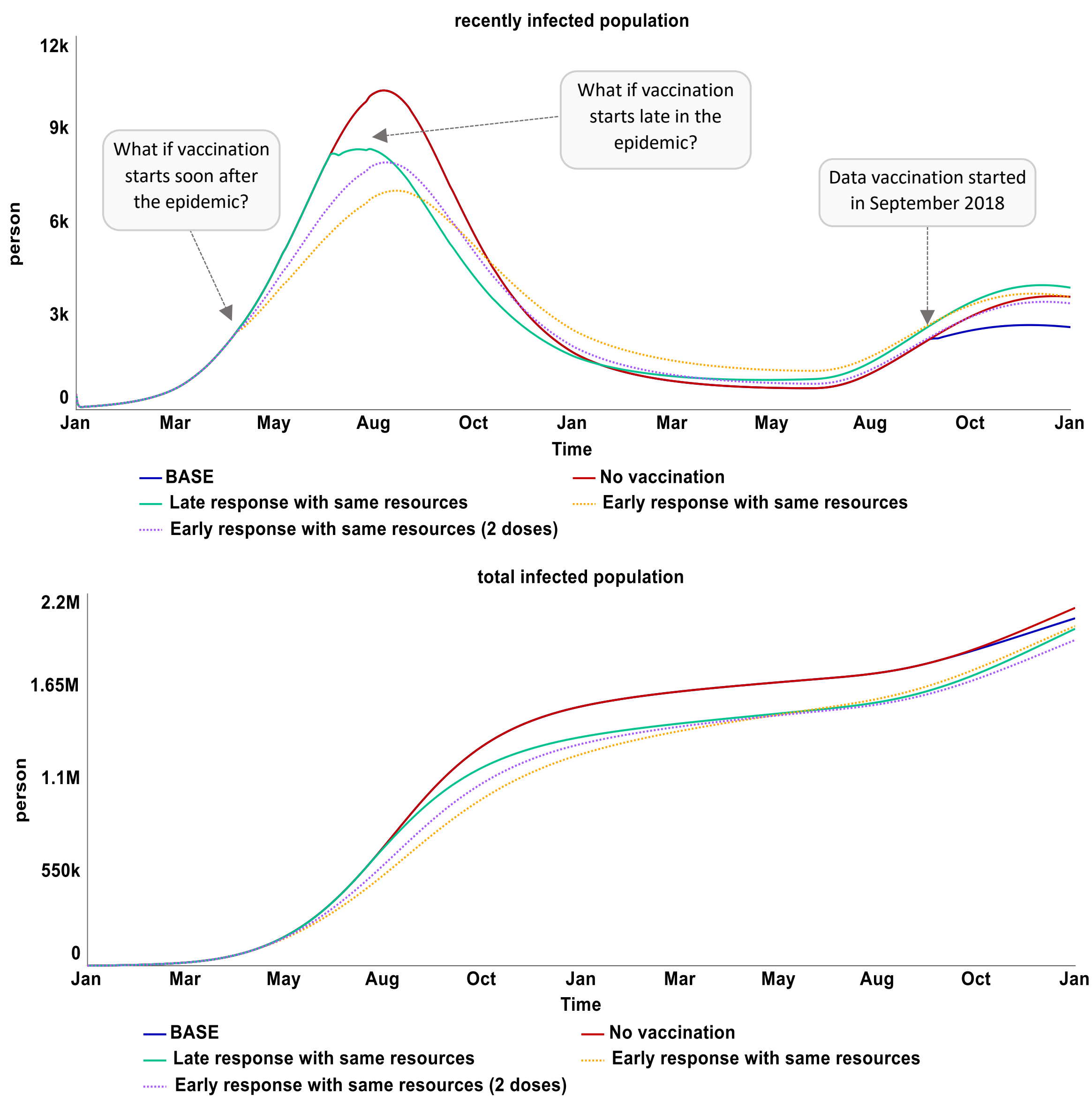

Figure 15. Simulation of different vaccination starting time with the same resources as in 2018 vaccination data.

2018 (historical data). Surprisingly, late response in June (green line) would result in a lower total number of infected population over the entire course of the epidemic than earlier vaccination compared to early response (dashed yellow line) shown in total infected population graph (bottom). This is because more vaccinated individuals would remain in the vaccinated stock at the end of 2018, thereby protecting them during the second wave of 2018. Those vaccinated earlier have a more favorable impact on the first wave in 2017; however, they return to susceptible population stock sooner after the protection period ends.

Two-dose policy: Médecins Sans Frontières (2018) reports that immunity develops one week after administration and lasts up to six months after a single dose and at least three years after two doses. The comparison between single and two doses (dashed yellow and purple respectively) in Figure 15 shows that single dose has a more favorable impact in short term response, although both interventions end up with similar total infected population late in 2018. This result is in line with a study by Pezzoli (2020) where the author claimed that, although OCV currently used in mass campaigns are administered according to two-dose regimen 14 days apart, a single dose provides short-term protection, within the first year, which is crucial for epidemic management. For a population of 3 million people in Al-Hudaydah that received 260,000 vaccines in 2018, giving a single dose vaccine to double the population results in a more favorable impacts under severe logistical and security constraints; buying more time to procure more vaccines.

Revaccination

Figure 16 portrays simulation result of implementing a second vaccination campaign in 2018. As expected, the early vaccination can significantly flatten the epidemic. Surprisingly, a substantial reduction of infection is observed even when the vaccination starts late in the epidemic (July 2017) (dashed black and purple lines). Interestingly, with the same resources and two campaigns, the late vaccination that has a lesser impact than early vaccination in the first wave, has however, more impact than early vaccination in the second wave, 2018.

This indicates that revaccination is necessary to maintain immunity in previously vaccinated individuals after the protection has waned. Second,

In 2018, these two populations shift back to the *susceptible population*. When the balancing feedback loops weaken, the infection reinforcing feedback loops strengthen again. The result suggests revaccinating the population in Al-Hudaydah to strengthen the balancing feedback loops and prevent future epidemics. Durham et al. (1998) and UNICEF (2018) also recommended revaccinating at-risk populations every two years (given that the duration of vaccine protection is about two years) in areas that are potentially facing annual outbreaks. If one dose policy is used in conflict affect areas while waiting for more vaccines, revaccination should be done earlier since the protection period from one dose is about 180 days.

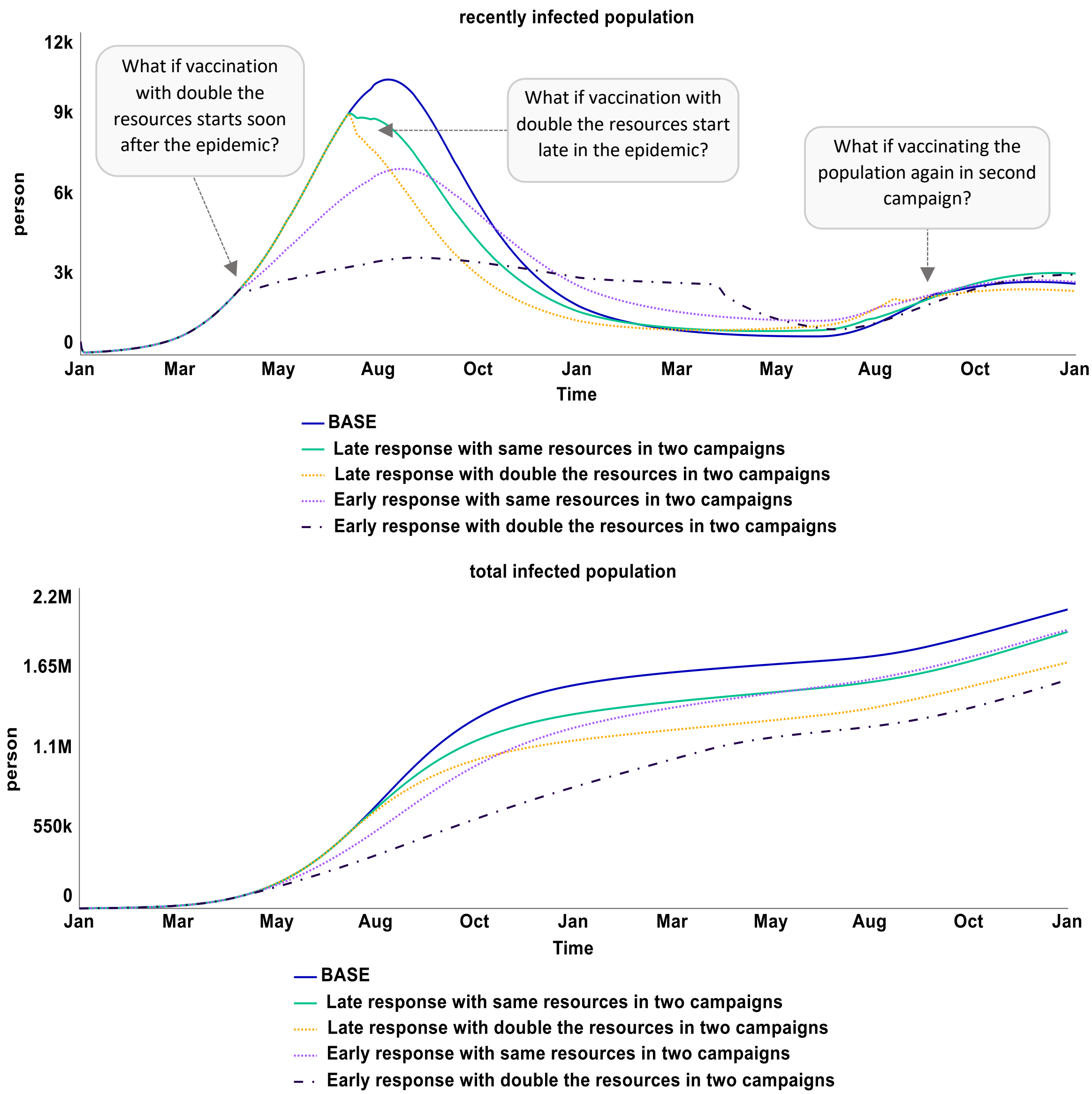

Figure 16. Re-vaccinate the public in 2018 simulation results.

3.2.3 Surveillance system

According to Camacho et al. (2018), Yemen's health authorities established a national cholera surveillance system to collect data on suspected cholera cases presenting to health facilities (no mass screening, the data depends on the availability of ORC, DTC, and health seeking ratio). Only symptomatic infections are likely to seek treatment and be reported. Camacho et al. further reported that only 32.4% of suspect cholera cases in Yemen visited a DTC on the same day of symptom onset, while for 10.2% of patients it took two or more days to access care. Moreover, there may be a degree of under ascertainment from cases who visited private health facilities and were not reported to this system. The DTC and ORC system cannot capture cases that sought traditional healers or self-medication instead of formal health care or deaths outside the healthcare facilities (Houatthongkham et al., 2016).

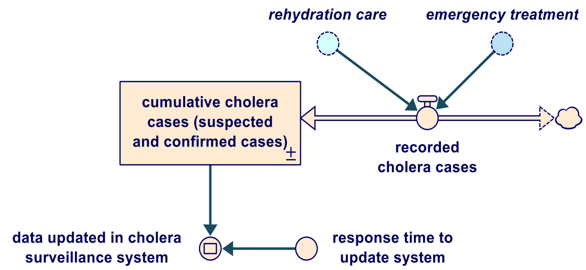

Figure 17. Stock and flow diagram of data surveillance system.

In this cholera response model, simulated suspected and confirmed cases that replicate the historical data are a product of individuals seeking rehydration care and emergency treatment with suspected cholera infection.

Result

Total infected population in Figure 18 (top) illustrates the comparison between reported cases (yellow line) and all infected individuals (including asymptomatic) as 212,000 and 2,060,000 people respectively at the end of 2018. In other words, this simulation result shows that only 10% of infected individuals are recorded in the surveillance system. This finding is consistent with the WHO statement that cholera is underreported, resulting in underestimating the disease's global burden. Officially reported cholera cases account for only 5–10% of the total number that occurs annually worldwide, owing to

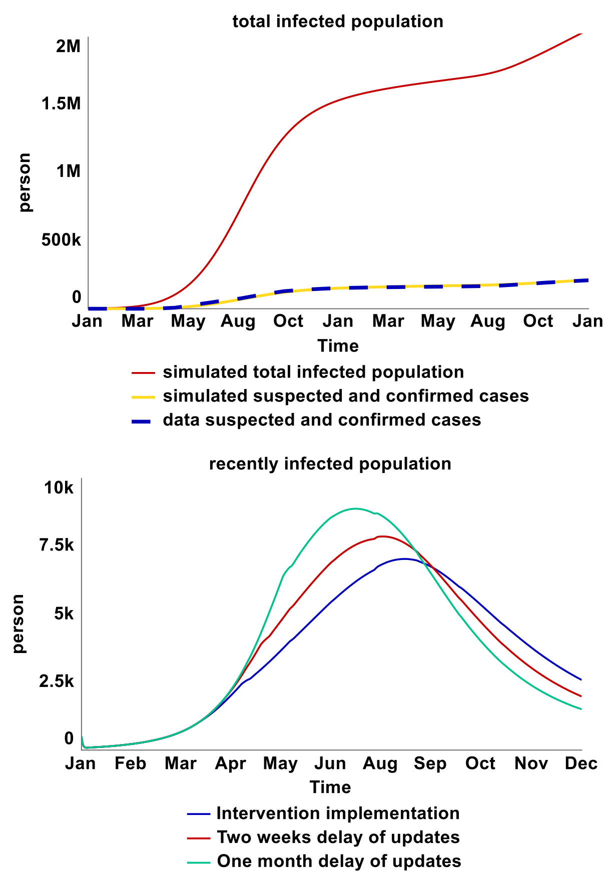

Figure 18. Behavior of time graphs that presents the result of total infected population (top) and recently infected population (bottom).

insufficient laboratory and epidemiological surveillance systems and economic, social, and political disincentives to report cases. (Ali, Nelson, and Sack, 2015).

Besides, other infectious disease modeling also highlights the under-reporting issue. For instance, a COVID-19 model by Rahmandad, Lim, and Sterman (2021) found that official data substantially underreport prevalence and mortality: Estimated cumulative COVID cases are approximately 7 times greater than official reports while deaths are 1.44 times larger than official reports.

The bottom behavior over time graph presents scenarios of different response time to update the system. Smooth function is used to incorporate the delay from the surveillance system in all intervention start time. The result is significantly impact as expected since the intervention start time is highly sensitive in controlling the epidemic. This structure is not endogenized into the model as the objective is to show the interface users regarding the importance of response time.

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Cholera Response Model Stock and Flow Diagram

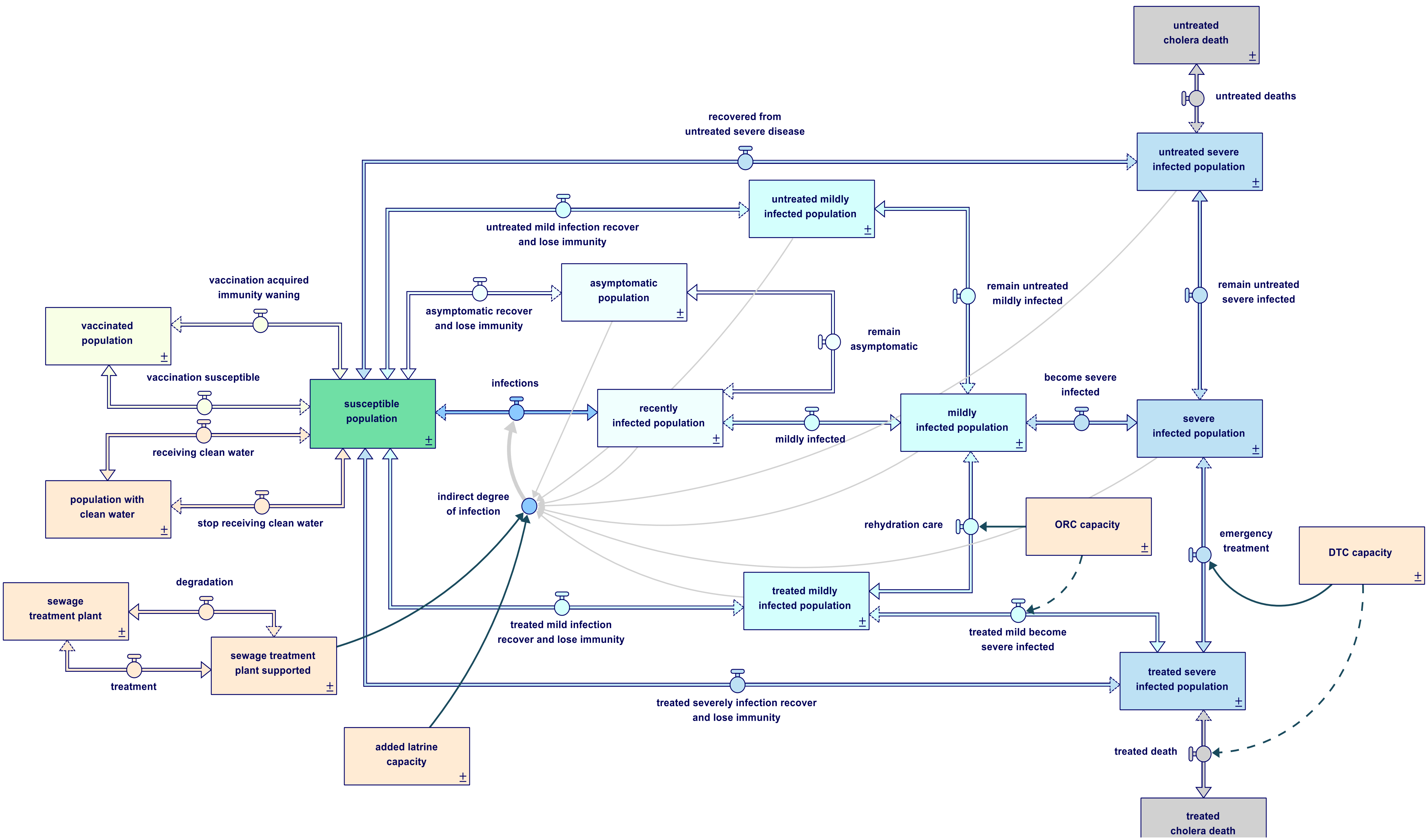

Figure 19. Stock and flow diagram of the cholera response model.

3.3 Other Model Setting

The model conceptual framework and structure has now been discussed elaborately (refer to Appendix B for detailed model documentation). This section explains additional modeling decisions made during the development of this model.

3.3.1 Time Horizon Choice

This model has a relatively short time horizon, as its purpose is to explore the implications of cholera response interventions during the 2017 and 2018 epidemics. As such, the model commences on January 1, 2017 and continues for 730 days, ending on December 31, 2018. One of the research objectives is to quantify the lessons learned from the reviewed literature; thus, a retrospective analysis and policy testing were conducted rather than the more conventional future timeline projection for epidemic preparedness.

3.3.2 DT and Integration Method

A DT of 1/4 with Euler's integration method is used to run this model.

3.3.3 Calibration

Three uncertain parameter values: *connectedness to aquifer, initial value of recently infected population*, and *time* (of bacteria shed by infected individuals) *to affect water in aquifer,* were estimated using a calibration routine.

3.3.4 Parameterization

Table 4 below outlines key parameters used in SIR structure. For more information and complete parameters record, refer to Appendix B (model documentation) and C (sensitivity test analysis)

Table 4. Literature sources for key parameters in SIR structure.

Indicators: Sensitive Highly sensitive

No	Parameters	Sensitivity Test		Values	Unit	Sources
		Numerical	Behavioral			
1	connectedness of aquifers			0.5	1/day	Calibrated; Pryut, 2013; Tuite et al., 2011
2	time to affect water in aquifers			8	day	Calibrated; Pryut, 2013
3	ratio of asymptomatic			0.75	dmnl	Kaper, Morris and Levine, 1995; Médecins Sans Frontières, 2018
4	average incubation time			1	day	Kaper, Morris and Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009
5	average duration of illness asymptomatic			5	day	Chao et al., 2014; Kaper, Morris and Levine, 1995; Médecins Sans Frontières, 2018
6	susceptible population			3,238,199	person	OCHA, 2017
7	recently infected population			500	person	Estimation from OCHA, 2017
8	normal ratio of severe disease			0.3	dmnl	Kaper, Morris and Levine, 1995; Médecins Sans Frontières, 2018

9	average duration of illness symptomatic			9	day	Chao et al., 2011; Nelson et al., 2009
10	average asymptomatic infection acquired immunity period			180	day	Leung & Matrajt, 2021
11	average symptomatic infection acquired immunity period			1095	day	Kaper, Morris, & Levine, 1995; Leung & Matrajt, 2021
12	fraction mildly infected seeking care			0.3	dmnl	Estimation from Camacho et al., 2018
13	fraction severe infected seeking care			0.4	dmnl	Camacho et al., 2018; Médecins Sans Frontières, 2018
14	treated fatality fraction			0.0021	dmnl	OCHA, 2017
15	bacteria shedding from asymptomatic			0.67	dmnl	Kaper, Morris, & Levine, 1995 (normalized value)
16	bacteria shedding from mildly infected			1.33	dmnl	Nelson et al., 2013 (normalized value)
17	bacteria shedding from severely infected			2	dmnl	Kaper, Morris, & Levine, 1995 (normalized value)

3.4 Model Validation

Barlas (1996) explains that validating a model fundamentally assesses "its usefulness with respect to its purpose". Adhering to Barlas (1996) and Sterman (2000) guidelines, formal model analysis, and validation procedures were conducted to support model developing and testing throughout the research process. The procedures involve iterative cycles of data collection, model building, simulation, analysis, validation, and documentation. The procedures were repeated until the result produced the right behavior for the right reasons.

Table 5. Summary of conducted validity tests.

Type of Test	Test	Results
Direct structure tests	Parameter confirmation	**Are the parameter values used known or reasonable estimates of the real-world values?** Parameter values were chosen after reviewing both empirical and modeling studies (refer to Table 5 above and model documentation Appendix B). It is important to mention that certain parameter values identified in the literature result from modeling research. For example, the connectedness to aquifer value in Pryut (2014). To a certain degree, modeling studies make parameter estimations based on calibration to replicate the historical. As such, certain parameter values are intrinsically linked to the model structural components. Hence, parameter values that "best-fits" the underlying SIR models from literature must be changed to match this cholera response model. Three uncertain parameters are calibrated to the historical data: *connectedness to aquifer, initial value of recently infected population*, and *time* (of bacteria shed by infected individuals) *to affect water in aquifer.*

	Dimensional consistency	**Are the units of measurement consistent without scaling or dummy variables?** This test is automatically run by the simulation software (Stella Architect). In this model, all units are dimensionally consistent.
	Structure confirmation	**Is the model structure consistent with the knowledge of the real-world system?** The literature that served as the theoretical framework for developing this model provides structural confirmation for the model (refer to model analysis section). While the structure simplifies the real-world cholera epidemic (as all models do), the processes included in the model have sufficient theoretical support to increase the model confidence; The model structure reasonably and adequately represents the real-world cholera epidemic.
	Extreme conditions	**Do the equations in the model return logical outputs even if the input to each equation takes on extreme values?** The test verifies that all equations in the model are rigorous under extreme conditions. Each equation has been examined to ensure that it is sufficiently robust in the presence of extreme inputs. Wherever possible, the MIN or MAX functions have been used to prevent the equations from taking absurd values. The upper and lower bounds of table functions have also been estimated in this test.
Structure-oriented behavior tests	Behavior sensitivity	**Is the model's behavior appropriately sensitive to changes in its various parameters as if in the real-world epidemic dynamics?** Sensitivity analysis was performed on the model for each of the key parameters. The test also reveals which parameters require additional data collection for quantification. Appendix C provides additional analysis of the test results.
	Boundary adequacy	**Is model aggregation appropriate? Does the model include all relevant structures for the model?** The most important question in determining the boundary is the model objectives. The model differentiates asymptomatic and symptomatic infection for two main reasons. First, to explore the under-reporting problem as silent spreaders strengthening the infection reinforcing feedback loop. Second, treatment intervention is disease-specific: ORC for mildly infected individuals and DTC for severely infected individuals. Disaggregating the population to asymptomatic and symptomatic population enables the model to capture the stated dynamics, particularly when the asymptomatic individuals are 75% of the total infected population. It would be unrealistic to provide treatment to asymptomatic individuals who would not seek healthcare in the first place. The model result shows that only 10% of total infected individuals are recorded, similar to the global statistic of cholera prevalence data by WHO. To conclude, the model's boundary is determined to be adequate.

<table>
<tr>
<td>Behavior pattern test</td>
<td>Behavior reproduction test</td>
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Is the model capable of reproducing the behavior patterns observed in the real-world system?

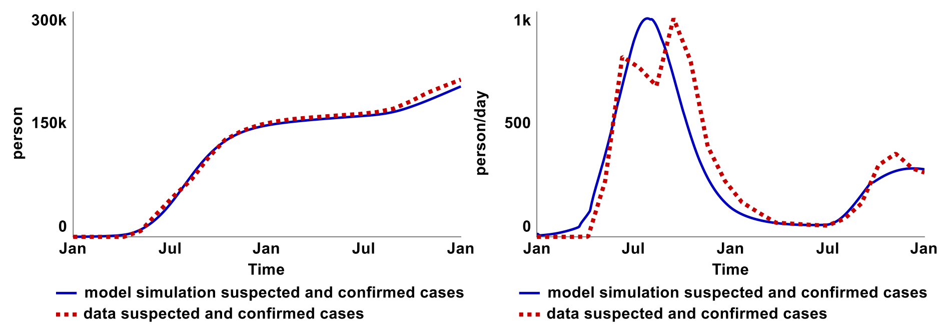

Figure 20. Comparison between model behaviors and historical data in total suspected and confirmed cases graph (left) and in the infection rate of suspected and confirmed cases graph (right).

The Figure 20 demonstrates a good fit between the model simulation results and the historical data as expected. First, the model incorporates the dynamic of asymptomatic feedback loop as the collected data are the suspected and confirmed cases in Al-hudaydah. In other words, infected individuals who are sick enough to seek healthcare services (symptomatic). Second, the model takes account of the data source; suspected and confirmed cases were collected from the DTC. Hence, the capacity structure of the DTC is built as part of the intervention structures.
On the other hand, the infection rate of suspected and confirmed cases graph (right) illustrates the marginal difference in infection rates between suspected and confirmed cases (right). The plausible explanation is that DTC and ORC lacked capacity at the epidemic inception due to a delay in capacity development (constructing new DTC and ORC).

Camacho et al. (2018) explained that scarcity of adequate treatment is more common during the initial phase of unexpected outbreaks and in crisis settings. The absence of DTC and ORC indicates a data collection gap (according to Yemen's surveillance system). When infected individuals have access to the DTC and ORC, there is an over-reporting problem because other patients with acute watery diarrhea (AWD) seek care at the ORC and DTC (Federspiel and Ali, 2018, Spiegel et al., 2018). It is reasonable for the simulated infection rate to be slightly higher than the data at the start and slightly lower than the data following the establishment of DTC and ORC.

No explanation regarding the two peaks of the data behavior is available from the literature. One plausible reason is that the healthcare system was over-stretched by the drastic increase in infected patients; healthcare and the data surveillance system could not perform as usual under such an overloaded condition. Once the system has an increased capacity (after a delay), the data collection function also increases, resulting in a second peak. Another reason could be the rain precipitation that intensifies the infection rate during heavy rain (Barciela et al., 2021).

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Loops That Matter (LTM)	Loops dominance	**Are the feedback loops shown in LTM test producing the right results for the right reasons?** The visualization and aggregation of feedback loops in a behavior over time graph enable the analysis of the dynamics of various loops. If a loop's behavior deviates from expectations, for example, a sudden drastic reduction in the treated recovery balancing loop without any intervention, it indicates a questionable structure. By working backward and examining the variables in the causal pathway, the problematic equations can be identified. Schoenberg, Davidsen, and Eberlein (2019) noted that LTM is less appropriate for models where external forcing functions dominate the model's feedback effects, as LTM focuses exclusively on endogenously generated behavior. The effects of interventions are a type of external balancing effect. Since vaccination has the potential to bring an epidemic to a halt, one would assume there will be an obvious feedback loop. However, it is not shown in the LTM result, unless the horizontal time frame of the graph is narrowed to the six days of the vaccination campaign. Still, the vaccination causal loop appears as a very minimal impact within the LTM result. The reason is that vaccination has created a favorable condition for other feedback loops: the reduction of the susceptible population then weakens the infection reinforcing feedback loops. Schoenberg, Davidsen, and Eberlein (2019) suggested that such structure can be analyzed using the Loop Impact method. This method will be explored in future studies.

4. Scenario Analysis

4.1 (BAU-BASE-Early response)

The previous section analyzes each intervention independently while this section analyses impact from a joint-interventions and answers the research question: *How can the model be used as a tool for quick response in containing outbreaks at an early stage?*

BASE

BASE is the simulation that replicates the historical data. This scenario included implemented interventions in 2017.

Business as Usual (BAU)

BAU is the scenario where all interventions are deconstructed from BASE to explore the worst-case scenario of the cholera epidemic.

Early response

An early response would explore the impact of all interventions if the starting day were in April 2017, using the same capacity from the BASE. This is to avoid unrealistic policy recommendations, particularly in a conflict-affected context where intervention implementation faces immense challenges.

Deconstructing the interventions from BASE to BAU has shown significant impacts from the humanitarian cholera response in 2017. 55% more deaths if nothing has been done in Al-Hudaydah. The simulation result also reveals a potential 30% of death can be prevented if interventions, especially vaccination, can be initiated earlier.

Studies have reported that concern was raised by Yemeni government and some humanitarian actors regarding mass immunization would be logistically difficult with ongoing security problems (Al-Mekhlafi, 2018; Federspiel and Ali, 2018; Qadri, Islam and Clemens, 2017). Another reason is that vaccination would have a minimal effect given the magnitude of the outbreak: it may be too late for vaccination, and the benefits would not outweigh the risks of initiating a campaign.

Yemen's government, the United Nations, and the WHO stated that the decision was made on a technical basis to ensure that efforts would be concentrated on WASH intervention targeting approximately 16 million people (Al-Mekhlafi, 2018). Vaccines were finally distributed to 540,000 people by the WHO and UNICEF in August 2018, nearly 16 months after the outbreak began. Al-Hudaydah vaccinated 260,000 people with two dose OCV.

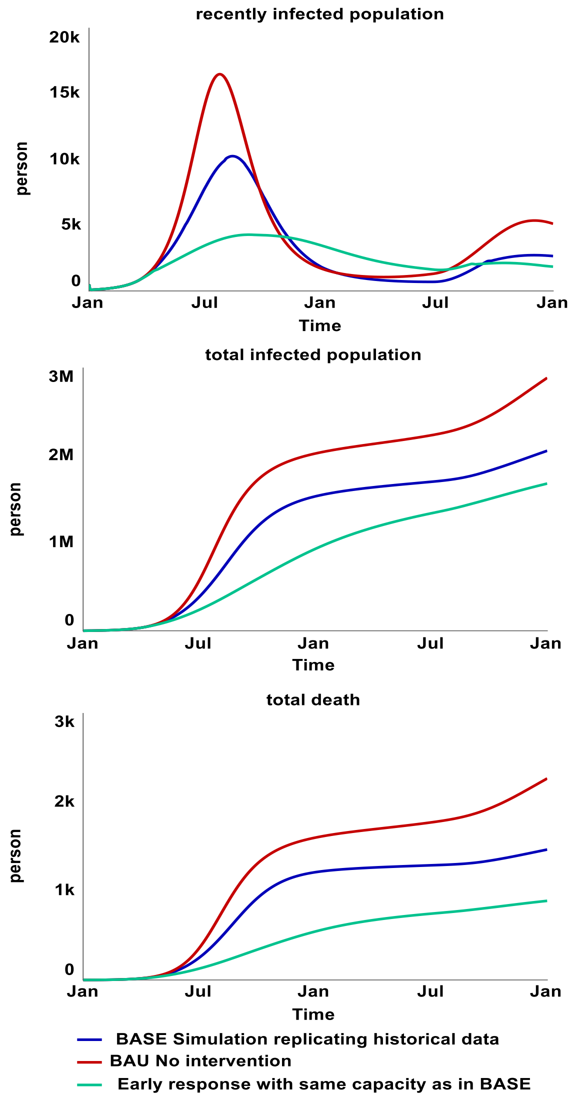

Figure 21. Behavior of time graphs that presents the result of recently infected population (top), recorded suspected and confirmed cases (middle), and treated and untreated death rate (bottom) of BAU-BASE-Early response simuation.

Indeed, the conflict situation posed significant logistical challenges for mass vaccination. Burki (2016), on the other hand, reported that coverage of the pentavalent vaccine is expected to be around 88% in 2015 — the same as in 2014. Past pentavalent vaccine campaign indicates that mass vaccination campaign is feasible if well-planned and supported. Moreover, Médecins Sans Frontières' (2018) cholera response manual stated that OCVs are administered orally (not via injection) and rarely cause serious adverse effects; mass cholera vaccination campaigns do not require a large number of medical personnel. Hence, an earlier vaccination campaign is not impossible in Yemen.

Table 6. Numerical result of BAU-BASE-Early response simuation.

Number of people	BASE	BAU		Early response	
total infected population	2055712	2888484	+41%	1681105	-18%
total death	1468	2268	+55%	891	-39%

On the other hand, the intervention analysis on WASH and vaccination (page 16) has outlined that three-year protection provided by vaccination compared to a one-day protection by clean water provision. Additionally, it is unrealistic to assume that those who receive clean water are 100% protected from cholera infection, as cholera is transmitted via multiple pathways (as illustrated in Figure 4); thus, removing a single source of infection may not effectively prevent disease, whereas contamination introduced via a single pathway can effectively cause disease.

Additionally, water can be viewed as a source of cholera outbreaks. Even when routine water treatments are carried out, cholera can still be transmitted when: dosing errors are made, treatment is forgotten, or the piped water supply is contaminated (Wolfe et al., 2018). In fact, Jon Snow made history in public health by tracing and discovering that the source of the London cholera epidemic in 1854 was contaminated water from a water pump.

This discussion does not intend to discredit the crucial role of clean water provision. Having access to safe drinking water is central to living a life in dignity and upholding human rights (WHO, 2017). However, it is problematic when resources are overly focused on WASH intervention. First, during the major wave of the epidemic, when stakeholders chose not to vaccinate the public but instead prioritized WASH (Al-Mekhlafi, 2018); second, after the epidemic, when humanitarian actors utilize the waterfighting system, Cholera Risk Model predictive tool (Barciela et al., 2021) without considering the endogenous feedback loops of cholera transmission. Such policy is very likely to result in the "Shifting the Burden" system archetype. This system archetype demonstrates a reliance on reactive quick fixes that leads to

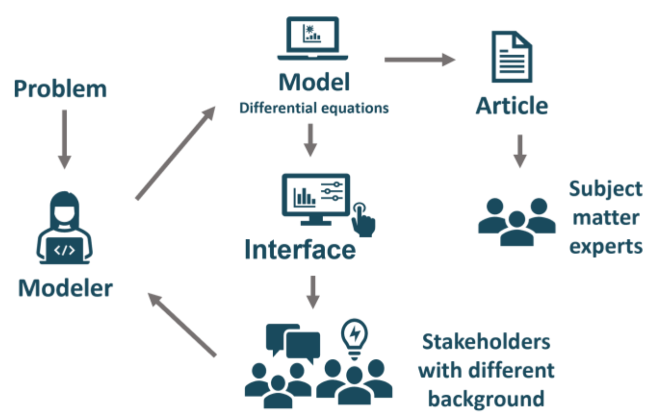

Figure 22. Communicating model insights through a user-friendly model interface.

unintended consequences of low priorities and fewer resources for other interventions. This cholera response model simulation can shed light on previously unknown unintended consequences and pave the way for a more robust cholera response in the future.

In general, the model demonstrates that individual and joint-interventions can have varying degrees of effectiveness depending on the supply, demand, and progression of the epidemic (timing). As a result, the decision must be made on a case-by-case basis by the humanitarian response stakeholders. Possessing a model does not guarantee its utility if stakeholders do not adopt it. This brings us to the critical role of science communication that influences decision-making. The next section answers the last research question: How can the model be used for humanitarian multi-sectors cholera response communication?

4.2 Model interface

The model interface has been designed to communicate insights from the model simulation in a safe environment using a self-learning approach. For example, the climate–energy simulation En-ROADS enables decision makers to gain firsthand knowledge about how a low carbon economy can be achieved and how climate policies affect physical and transition risks, through the use of a science-based tool (Kapmeier et al., 2021).

Additionally, the model interface can facilitate in cross-sector communication, fostering collaboration between agencies working in different humanitarian clusters. Such an integrated model is especially essential in times of crisis, particularly in countries undergoing internal conflict. Bellizi et al. (2021) identified dysfunctional collaboration in Yemen as a result of conflicting mandates and the relationship between non-governmental organizations and their donors. WASH and health services are the responsibility of a number of agencies and stakeholders, which frequently results in complicated and occasionally confusing approaches to addressing gaps and barriers, particularly during an emergency response.

In addition to "Shifting the Burden", a common challenge identified by Sterman (2015) is that, rather than implementing risk-mitigating strategies, managers are frequently caught in "firefighting" and capability traps, depleting the resources required to manage problems. The model interface enables stakeholders to gain such insights and to learn from previous policy decisions.

Similar to En-roads, this model interface can be conducted in a workshop setting, with the facilitator(s) running the model and delving into the results with the participants. Typically, the workshop can gather information, with participants sharing their insights and reactions. This type of discussion frequently provides critical feedback to the modeler. For example, humanitarian actors' capacity to implement interventions may change over time, either increasing or decreasing. The model can then be updated based on the feedback received from participants: a virtual reinforcing feedback loop. A facilitation guide is developed for this purpose (attached to interface).

The developed interface is primarily intended for public health professionals and program managers who involve in cholera response. These include, for example, staff working at ministries of health, public health institutions, United Nations agencies, and non-governmental organizations.

On the other hand, Struben (2020) noted that much of the success of interventions is largely dependent on broad support and involvement from a variety of actors such as local policymakers who lack direct access to experts, volunteers working within communities, compliant citizens, and communicative media. As a result, making the model available via a web interface can increase the model's accessibility and sustainability.

A brief overview of the interface is listed in the next two pages in Figure 23 to 26. The interface is divided into five major sections: model briefing, guidance on how to use the dashboard, main dashboard, control panel, and debriefing.

5. Conclusion

Cholera kills up to 50% of patients who do not receive adequate rehydration; with treatment in time, the case fatality rate can be less than 1%. World Health Organization reported 2.5 million suspected cholera cases and nearly 4,000 deaths in Yemen as of November 2020. How could an epidemic of this magnitude occur? In Yemen, humanitarian response is particularly needed when epidemics occur during or as a consequence of conflict and political upheaval. Lessons learned from cholera response in Yemen are well-studied where most of the reviewed literature employed a qualitative approach. The primary problem was that Yemen lacked an adequate cholera preparedness and response in 2017; with two main findings pointing at the late implementation of vaccination (after 16 months into the epidemic). The initial attempt to vaccinate the public failed as the stakeholders decided that the vaccine would have a minimal impact. Instead, resources were channeled into WASH interventions as the main preventive measure in controlling the epidemic.

When a community is threatened by a rapidly spreading cholera epidemic, it can be difficult to know how to save lives. This study uses system dynamics modeling to quantify and evaluate the lessons learned from the 2017 and 2018 cholera response. The model is used to answer some of the debated questions in the lessons learned literature. More importantly, the model enables decision-makers to test policies that would be impractical or unethical in the real world and learn from their errors in this virtual Al-Hudaydah. A user-friendly interface was built for policy testing and to engage multi-sector stakeholders to communicate more effectively in cholera response. The model can be used prior to an epidemic to aid in prevention and preparedness; during an outbreak to organize and monitor the response; and following an outbreak to assess the response.

The model extended the classic infection structure with empirically grounded operational structures: oral rehydration corner, diarrhea treatment center, water and sanitation intervention, vaccination, and data surveillance system. The data collected during the model's development and validation are epidemiological data: and cholera response (interventions) data. The model demonstrates that individual and joint-interventions can have varying degrees of effectiveness depending on the supply, demand, and progression of the epidemic (timing).

The model shows the importance of implementing different interventions for asymptomatic and symptomatic infected individuals, especially the ratio between the two-disease state is 75% to 25%, respectively. Both treatment and preventive interventions are tested. One of the most debated questions from lessons learned studies is, could the largest cholera outbreak ever recorded have been avoided or at least managed, had enough OCVs been deployed earlier on in the conflict? The model findings show that the 260,000 vaccines that arrived 16 months into the epidemic would still be impactful even if the vaccination started in June 2017 (height of the epidemic).

First, although starting the vaccination during the height of the epidemic (late response in June) has a lesser impact than early response in April, starting in June still reduces infection. Surprisingly, late vaccination in June has resulted in lower total number of infected population compared to early vaccination. During the end of 2018, more vaccinated individuals remained in the vaccinated stock due to the late vaccination, hence protecting them during the third wave in 2018. However, those vaccinated earlier have a more favorable impact in the second wave in 2017; however, they return to susceptible population stock earlier after the protection duration. This indicates that revaccination is needed for the early vaccinated individuals to be protected again after immunity wanes. Second, a single dose vaccine has a more favorable short-term response, which has important implications for epidemic management when logistical and security constraints are high.

It is problematic when resources are overly focused on WASH intervention. Such policy is likely to result in the "Shifting the Burden" system archetype; relying on reactive quick fixes that leads to unintended consequences of low priorities and fewer resources for other interventions. For instance, vaccination provides three-year protection compared water provision of a one-day protection.

Deconstructing the interventions from BASE to BAU has shown significant impacts from the humanitarian cholera response in 2017. 55% more deaths if nothing has been done in Al-Hudaydah. The simulation result also reveals a potential 30% of death can be prevented if interventions, especially vaccination, can be initiated earlier.

While this cholera response model is useful for clarifying policy problems in the past and reshaping mental models; just as important, is to be transparent regarding the model’s limitations, assumptions, and boundary conditions.

The cholera response model has several limitations where many of them stem from data quality or availability problems to approximate or estimate more detailed quantified representations of important dynamics. For instance, a lack of information regarding the weight of various WASH intervention impacts on the overall sanitory conditions in Al-Hudaydah. SD does not shy away from building such structures in the model as it is a basic tenet of SD modelling that crucial structures or variables should not be excluded from a model simply because they are difficult to quantify (Lim, 2021). However, estimating parameters necessary to quantify such structures still depends on having relevant data. In this case, subject experts' inputs are essential. Besides, sensitivity test analysis has been used to provide some insurance against such uncertainties.

The model's limitations nonetheless restrict the quantitative precision of the model's projections which should be borne in mind when interpreting its results. In other words, this cholera response model is not intended for high-precision quantitative forecasting or prediction.

Regardless of the outlined limitations, this cholera response model has shown both the compounding factors that exacerbate the epidemic and the operational dynamics in controlling the epidemics. The developed interface can be used to explore high impacts interventions as well as to communicate among different humanitarian sectors. More importantly, the insights gained from the model are not only applicable to the cholera epidemic but also to other infectious disease response modeling. The next step is to adapt this Al-Hudaydah model to other cholera-affected countries through collaboration with humanitarian actors.

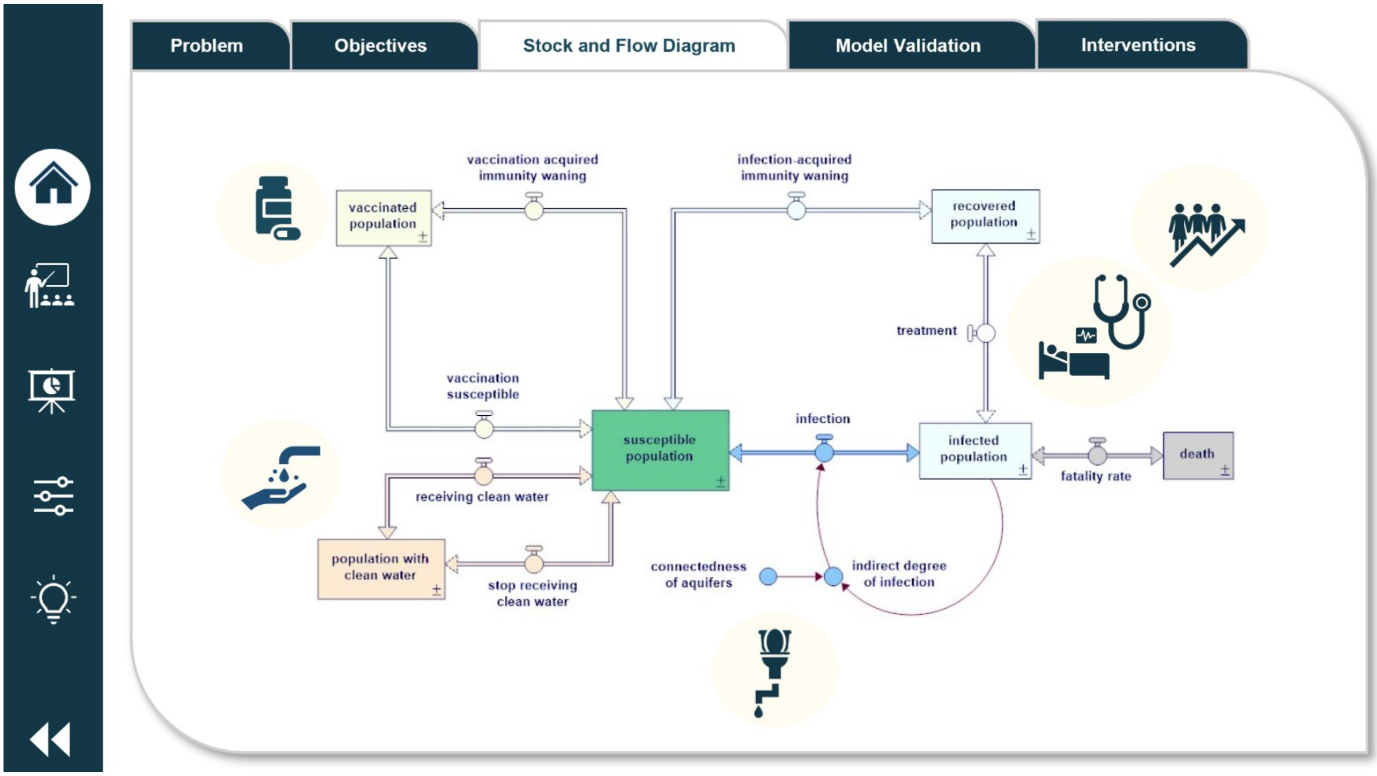

Figure 23. Figure shows a top-level stock and flow diagram of the cholera response model as part of the model briefing aside from description on the problem, interface objectives, model validation, and interventions.

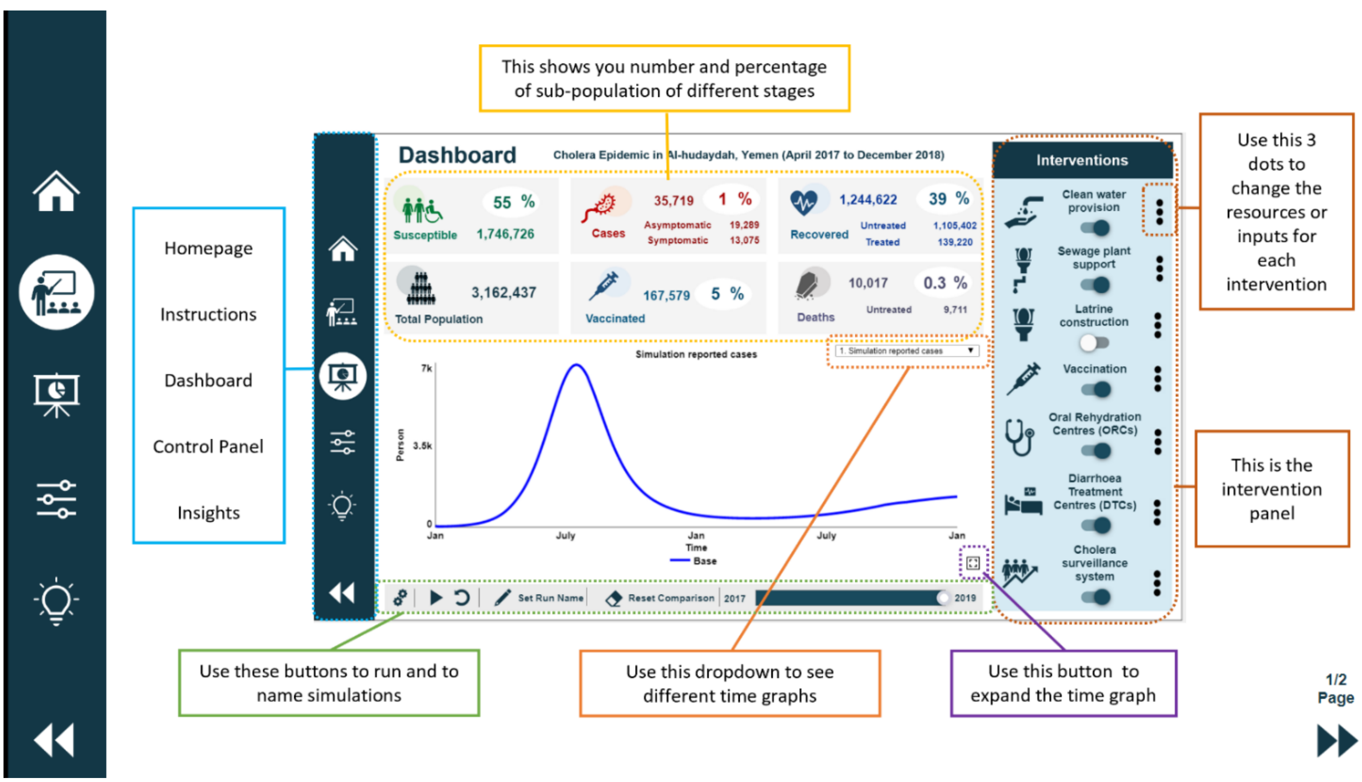

Figure 24. Guidance on how to use the dashboard for policy testing.

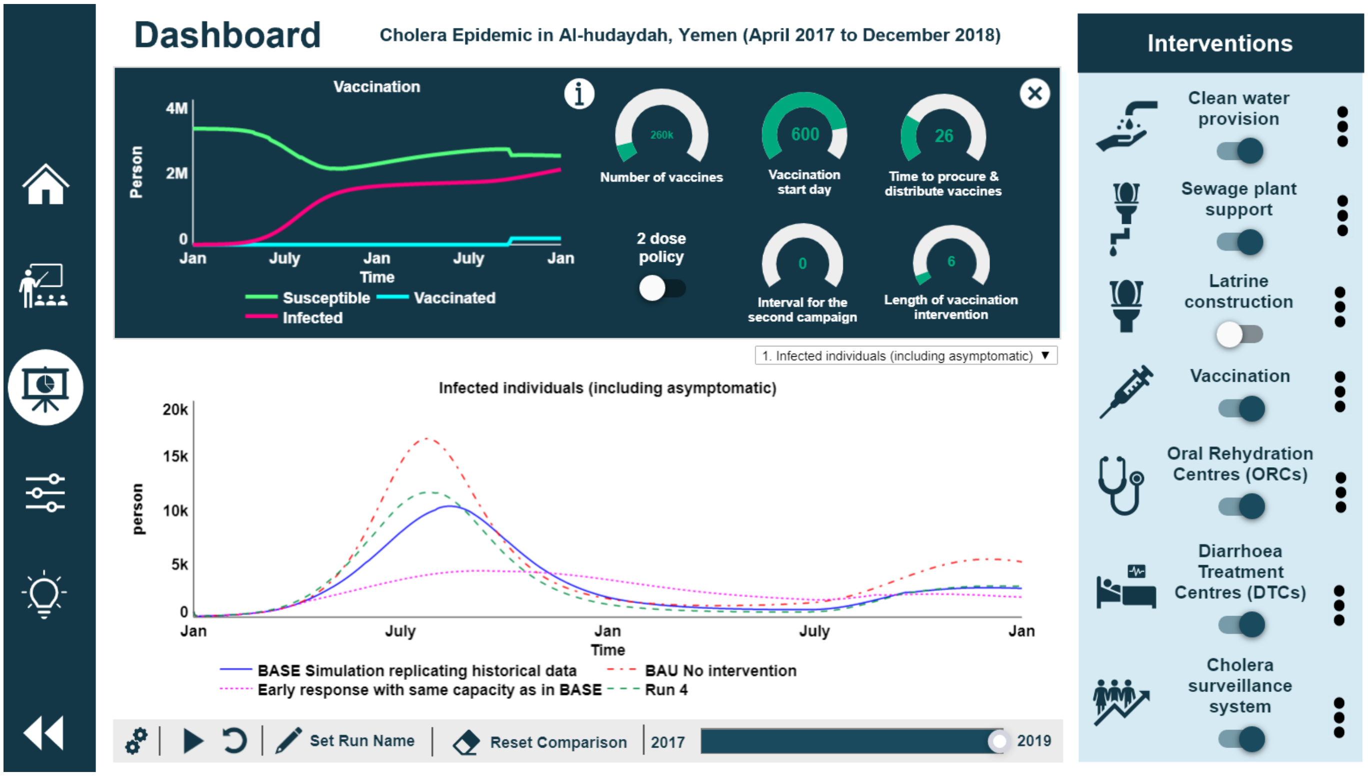

Figure 25. The intervention panel that allows further adjustment on various policy testing. The vaccination graph on the top left show the need of vaccination by indicating the susceptible population. Other intervention panels also contain such indicators to help users make decision based on the need for such interventions.

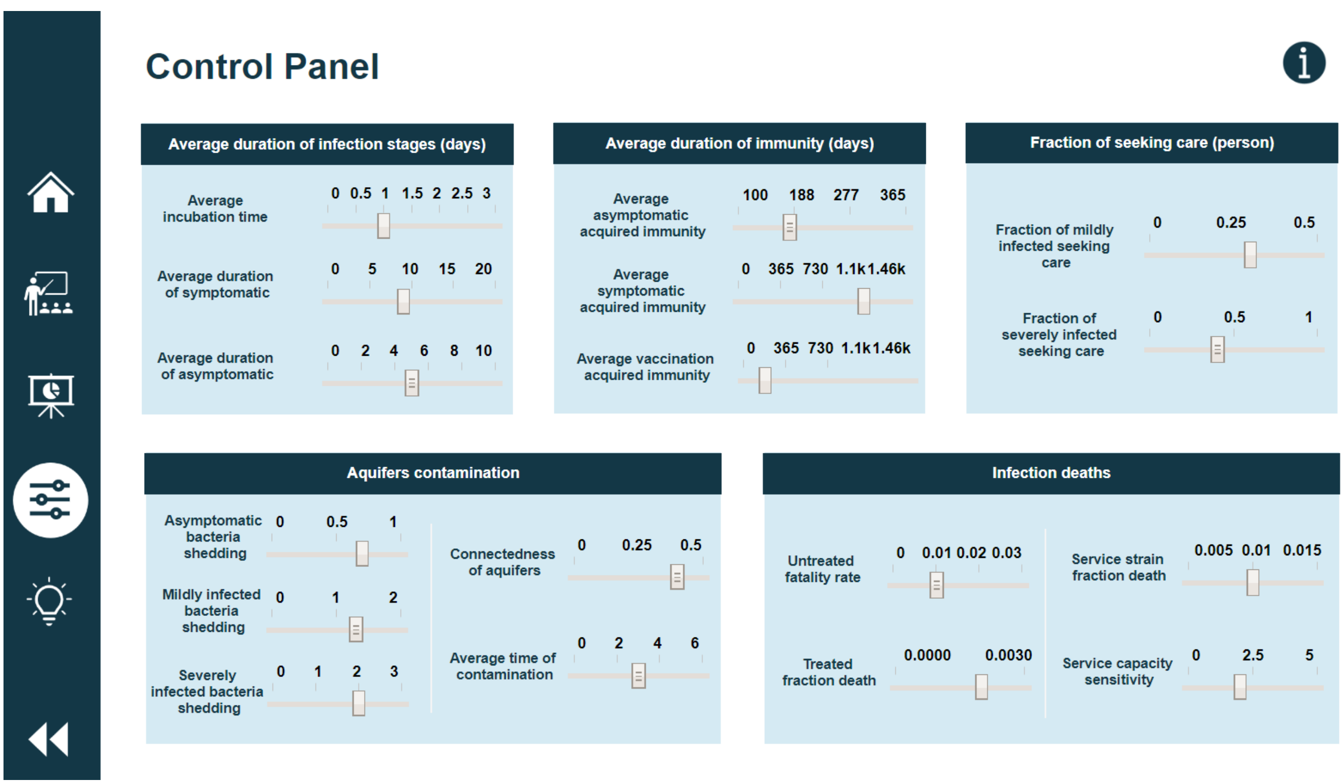

Figure 26. The control panel enables the users to change the parameter values. For instance, what will happen if the average duration of infection is longer.

6. Supplementary materials

6.1 Appendix A: References

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6.2 Appendix B: Documentation

	Equation	Units	Documentation
SIR component			
asymptomatic	MAX(recently_infected_population*ratio_of_asymptomatic/average_incubation_time, 0)	person/day	"asymptomatic" flow is the rate at which recently infected individuals leave the stock through multiplication with (ratio of asymptomatic) after an average incubation time of 1 day (material delay). The MAX function is to ensure the flow is more than 0.
asymptomatic_infection_acquired_immunity_waning	MAX(0, recovered_asymptomatic_population/average_asymptomatic_infection_acquired_immunity_period-vaccination_recovered_asymptomatic)	person/day	"asymptomatic infection acquired immunity waning" flow is the rate at which recovered asymptomatic individuals leave the stock after an average asymptomatic infection acquired immunity period of 6 months (material delay). The MAX function is to ensure the flow is more than 0. The flow also minus the vaccination flow once the intervention is activated.
asymptomatic_population(t)	asymptomatic_population(t - dt) + (asymptomatic - recovered_from_asymptomatic - vaccination_asymptomatic) * dt	person	"asymptomatic population" are cholera infected individuals who show no symptom. Asymptomatic individuals who shifted to the "asymptomatic population" stock then leave after an average duration of asymptomatic illness of 5 days and flow towards "recovered from asymptomatic population" stock. The "asymptomatic population" is assumed to be 0 initially.
average_asymptomatic_infection_acquired_immunity_period	180	day	Subclinical infections, or infections confirmed by positive stool culture but unaccompanied by diarrhea, have been documented. Leung and Matrajt (2021) study highlights the difference between protection from infection and protection from disease. They identified 3 challenge studies in which most participants were reported among the participants without diarrhea on initial challenge developed symptoms upon rechallenge (3 to 12 months) (Leung & Matrajt, 2021)
average_duration_of_illness_asymptomatic	5	day	The shedding of bacteria typically ends within 7 to 10 days.
average_duration_of_illness_symptomatic	9	day	The symptomatic infectious period ranges from 7 to 14 days (Chao et al., 2011; Nelson et al., 2009). Médecins Sans Frontières (2018) similarly reports bacteria shedding of bacteria among symptomatic patients typically ends within 7 to 10 days. The "average duration of illness symptomatic" uses 9 days.

average_duration_of_recovery_under_treatment	5	day	Findings indicate that antibiotics reduced volume of stool output by 8–92%, duration of diarrhea by 50–56%, and duration of positive bacterial culture by 26–83% (CDC, 2020). However, mass administration of antibiotics is not recommended, as it has no proven effect on the spread of cholera may contribute to antimicrobial resistance (WHO, 2021). A patient with severe dehydration or complications may remain hospitalised 4 to 5 days (MSF, 2018).Hence, the "average duration of recovery under treatment" uses 5 days.
average_incubation_time	1	day	The incubation period of cholera can range from several hours to 5 days (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009). The "average incubation time" uses 1 day as the symptomatic individuals will then progress to either mild or severe disease stage with "time to progress to next stage".
average_symptomatic_infection_acquired_immunity_period	3*365	day	Studies found that clinical cholera conferred protection against subsequent cholera for at least 3 years (Kaper, Morris, & Levine, 1995; Leung & Matrajt, 2021)
bacteria_shedding_from_asymptomatic	0.67	1	Some patients can even be infected with V. cholerae and yet show no symptoms but then tend to shed the organism into the environment, even for only a few days, explaining why vibrios can be isolated in wastewater effluents in a non-Vibrio and/or non-cholera epidemic area (Okoh et al., 2015). According to Kaper, Morris, and Levine (1995), doses of 10^11 CFU of V. cholerae were required to consistently cause diarrhea in healthy North American volunteers when the inoculum was given in buffered saline (pH 7.2). When stomach acidity was neutralized with 2 g of sodium bicarbonate immediately prior to administration of the inoculum, attack rates of 90% were seen with an inoculum of 10^6. Food has a buffering capacity comparable to that seen with sodium bicarbonate. Ingestion of 10^6 vibrios with food such as fish and rice resulted in the same high attack rate (100%) as when this inoculum is administered with buffer. For Yemen context, the model uses 10^6 vibrios as the amount to cause an infection. 10^6 vibrios is normalized to 1. An asymptomatic infected individual can shed vibrios in the stool in low but potentially infectious concentrations (10^3 to 10^5 V. cholerae organisms per g of stool) for several days (Kaper, Morris, & Levine, 1995). The variable "bacteria shedding from asymptomatic" uses 10^4, hence, normalized to 10^4/10^6 = 0.67

bacteria_shedding_from_mildly_infected	1.33	1	According to Nelson et al. (2013), a symptomatic, mildly infected individual can shed vibrios in the stool in low but potentially infectious concentrations, up to 10^8 V. cholerae organisms per g of stool. For Yemen context, the model uses 10^6 vibrios as the amount to cause an infection. 10^6 vibrios is normalized to 1. The variable "bacteria shedding from a mildly infected individual" uses 10^8, hence, normalized to 10^8/10^6 = 1.23
bacteria_shedding_from_severely_infected	2	1	According to Kaper, Morris, and Levine (1995), individual with acute cholera excretes 10^7 to 10^8 V. cholerae organisms per g of stool; for patients who have 5 to 10 liters of diarrheal stool, total output of V. cholerae can be in the range of 10^11 to 10^13 CFU. Even after cessation of symptoms, patients who have not been treated with antibiotics may continue to excrete vibrios for 1 to 2 weeks. For Yemen context, the model uses 10^6 vibrios as the amount to cause an infection. 10^6 vibrios is normalized to 1.The variable "bacteria shedding from severely infected" uses 10^12, hence, normalized to 10^12/10^6 = 2 (Kaper, Morris, & Levine, 1995).
become_severe_infected	(mildly_infected_population/time_progress_to_next_stage-rehydration_care)*normal_ratio_of_severe_disease	person /day	"become severe infected" flow is the rate at which part of the mildly infected individuals leave the stock through multiplication with the normal ratio of severe disease after the time progress to next stage - 1 day (material delay).
connectedness_of_aquifers	0.5	1/day	The "connectedness of aquifers" is the rate of contact with contaminated water. This is an abstract concept that in the context of this model must be related to the amount of reservoir water consumed, but is not expressed in units that include volume and has no upper or lower bounds (Pruyt, 2013). The "connectedness of aquifers" is a simplified and uncertain factor. The variable is calibrated to the historical data, amount to 43% in the base model.
data_IDP	362292	person	Data is obtained from online database from International Organization for Migration (2018) who has an IDP tracking system (DTM). Due to the intensified conflict in Al-Hudaydah from June 2018, an increase of IDP from June to November 2018 was recorded: 133830 to 362292 IDP within 6 months.
duration_IDPs_movement	180	day	Data is obtained from online database from International Organization for Migration (2018) who has an IDP tracking system (DTM). Due to the intensified conflict in Al-Hudaydah from June 2018, an increase of IDP from June to

			November 2018 was recorded: 133830 to 362292 IDP within 6 months. Hence, 180 days is used.
emergency_treatment	IF switch_data_collection =0 THEN emergency_treatment_at_hospital ELSE MAX(emergency_treatment_at_hospital, seeking_care_at_DTC) {IF switch_DTC=0 THEN severe_infected_population*fraction_severe_infected_seeking_care*effect_of_DTC_strain_on_seeking_emergency_treatment*seeking_care_at_hospital ELSE severe_infected_population*fraction_severe_infected_seeking_care*effect_of_DTC_strain_on_seeking_emergency_treatment	person/day	"treatment at DTC" flow is the rate at which severe infected individuals leave the stock by seeking treatment at DTC. The flow depends on the fraction severe infected seeking care and it is affected by the ORC strain.
emergency_treatment_at_hospital	fraction_seeking_care_at_hospital*severe_infected_population/time_progress_to_next_stage	person/day	"emergency treatment at hospital" flow is the rate at which mildly infected population seek emergency treatment at hospital.
fraction_mildly_infected_seeking_care	0.3	1	Only symptomatic infections are likely to be reported. Camacho et al. (2018) demonstrated that only 32.4% of suspect cholera cases in Yemen visited a DTC on the same day of symptom onset, while for 10.2% of patients it took two or more days to access care (Yemen report). For mildly infected individuals who may experience short period of cholera symptoms and may be clinically indistinguishable from other causes of diarrheal illness, are likely to not seek treatment. Hence, the value is assumed to be 0.1 (less than 0.32 who seek treatment in DTC).
fraction_of_Infected_IDP	0.1	1	Assuming 10% of the IDP are infected. Many IDPs live in forest, mountainous or desert areas of Hudaydah, which lack services and provide little for shelter, food or water (Ali, 2021).
fraction_seeking_care_at_hospital	0.15	1	if ORC intervention is switch off, assuming 15% of the individuals who would seek treatment at ORC resort to care at the hospital. MSF (2018) reported that approximately 15-20% of patients will seek medical care

			during the peak week (less for rural settings, more for crowded urban settings). However, if ORC and DTC is unavailable, infected individuals are assumed to seek healthcare services at hospitals. Spiegel et al. (2018) and Qadri, Islam, and Clemens (2017) highlighted that delivery of health care has been limited by the destruction by air strikes of approximately half the health sector facilities, including hospitals and clinics in Yemen. Hence, "seeking care at hospital" uses 0.15.
fraction_severe_infected_seeking_care	0.4	1	Only symptomatic infections are likely to seek treatment and be reported. Camacho et al. (2018) demonstrated that only 32.4% of suspect cholera cases in Yemen visited a DTC on the same day of symptom onset, while for 10.2% of patients it took two or more days to access care (Yemen report). This parameter uses 0.4.
immunity_waning_treated_population	recovered_immune_treated_population/average_symptomatic_infection_acquired_immunity_period	person/day	"immunity waning treated population" flow is the rate at which all recovered immune treated individuals leave the stock after an average symptomatic infection acquired immunity period of 3 years (material delay) and flow back to the susceptible population.
immunity_waning_untreated_population	MAX(recovered_immune_untreated_population/average_symptomatic_infection_acquired_immunity_period, 0)	person/day	All recovered symptomatic individuals leave recovered immune untreated population stock after an average symptomatic infection acquired immunity period of 3 years and flow as "immunity waning untreated population" back to the susceptible population. The MAX function is to ensure the flow is more than 0. The flow also minus the vaccination flow once the intervention is activated.
indicated_ratio_of_severe_disease	normal_ratio_of_severe_disease*effect_of_ORC_strain_on_fraction_of_severe_disease	1	The "indicated ratio of severe disease" shows the value of normal ratio of severe disease under the effect of ORC strain on fraction of severe disease. An increase in ORC health services strain leads to a decrease care quality. Hence, more mildly infected individuals progress to severe infected stage.
indirect_degree_of_infection	connectedness_of_aquifers*smoothed_fraction_of_contaminated_water	1/day	Studies have shown that Cholera is most commonly acquired from drinking water in which V. cholerae is found naturally or that has been contaminated by the faeces of an infected individual (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009). Food may be contaminated when prepared with contaminated water or kitchen utensils, or mixed with other contaminated food, or handled by infected persons in unhygienic conditions. Okoh et al. claimed that V. cholera presence in wastewater, therefore, could be dependent on the number of infected people in the population contributing to the wastewater flow.

			Once these vibrios get into environmental water, they convert to conditionally viable environmental cells within 24 h (Nelson et al. 2008). Such vibrios are infectious on reintroduction into a human body. This becomes a major public health problem in underdeveloped areas like the ECP where, as of 2011, about 36 % of the population still got their drinking water directly from rivers and streams (Okoh, 2015). According to WHO–UNICEF statistics, in 2014 only 55% had access to drinking water from improved water sources (Qadri, Islam, and Clemens, 2017). Therefore, in this model, the "indirect rate of infection" equals the product of following two factors: the smoothed fraction of contaminated water and the connectedness of aquifers (Pruyt, 2013). Although cholera can be transmitted through direct faecal-oral contamination. For example, by eating food that has come into contact with human faeces. This model only incorporates indirect transmission through contaminated water: indirect contamination is assumed to occur much more often than direct contamination (Pruyt, 2013).
Infected_IDP	DELAY (PULSE(data_IDP, "time_IDPs_increase_to_Al-hudaydah", 0), duration_IDPs_movement)*fraction_of_Infected_IDP	person /day	A spike in internal displaced persons (IDPs) from August 2018 due to intensified conflict in Al-hudaydah. Pulse function is used to show the increase of IDP that is DELAY over 5 months: to represent the displacement of IDP over time in Al-Hudaydah.
infections	susceptible_population *indirect_degree_of_infection	person /day	"infections" flow is the product of the susceptible population and the indirect infection rate. When individuals from the susceptible population become infected with cholera, they shift to the recently infected population.
initial_recently_infected_population	500	person	OCHA (2017) recorded 21 suspected and confirmed cases in 2017. The health seeking ratio in the beginning is 10% of the symptomatic individuals, assuming that there is a lack of DTC and ORC, and perceived of threat among the public. Symptomatic is 25% of total infected individuals (MSF, 2018). Hence, the estimated total infected individuals is 840 in April. The calibration of the model to historical data resulted as 500 as initial value of recently infected population, it is within a reasonable range.
mildly_infected	MAX(recently_infected_population*(1-ratio_of_asymptomatic	person /day	"mildly infected" flow is the rate at which recently infected individuals leave the stock through multiplication with (1 minus the ratio of asymptomatic) after an average

	)/average_incubation_time, 0)		incubation time of 1 day (material delay). The MAX function is to ensure the flow is more than 0.
mildly_infected_population(t)	mildly_infected_population(t - dt) + (mildly_infected - rehydration_care - become_severe_infected - remain_untreated_mildly_infected) * dt	person	"midly infected population" are mild cases of V. cholerae infection that may be clinically indistinguishable from other causes of diarrheal illness (LaRocque & Harris, 2020). Mildly infected individuals who shifted to the "mildly infected population" stock then leave after the time progress to next stage - 1 day, and flow to 3 directions: "treated mildly infected population", "untreated mildly infected population" and "severe disease population" stocks. The "asymptomatic population" is assumed to be 0 initially.
normal_ratio_of_severe_disease	0.3	1	The "normal ratio of severe disease" is the ratio of mildly infected population progress into severe disease. Among patients who seek treatment, 25-30% of patients will have severe dehydration, 30-40% some dehydration, and 30-40% no dehydration (Médecins Sans Frontières, 2018). Kaper, Morris, and Levine (1995) report that, among all cholera infection (including asymptomatic), 11% of patients with classical infections develop severe disease while 15% of classical infections result in moderate illness (defined as cases detected and managed in outpatient clinics). Hence, the "normal ratio of severe disease" is 0.3 in this model, from the symptomatic mildly infected population.
ratio_of_asymptomatic	0.75	1	Depending on the strain involved, 75% of infections remain clinically unapparent while the remaining 25% develop mild to severe symptoms. For example, stomach cramps and vomiting followed by diarrhoea, which may progress to fluid losses of up to 1 litre per hour (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018).
recently_infected_population(t)	recently_infected_population(t - dt) + (infections + Infected_IDP - mildly_infected - asymptomatic) * dt	person	Infected individuals who shifted to the "recently infected population" stock then leave after an average incubation time of 1 day and flow towards "mildly infected population" and "asymptomatic population" stocks. The World Health Organization estimates that officially reported cases of cholera represent only 5–10% of the actual number occurring annually worldwide because of inadequate laboratory and epidemiological surveillance systems and economic, social and political disincentives to case reporting (CDC, 2020). Historical data (OCHA, 2017) shows 40 cases in April 2017. Assuming that those are tested symptomatic severe cases and taking into consideration of under-reporting, the "recently infected population" is assumed to be 1000.

recovered_asymptomatic_population(t)	recovered_asymptomatic_population(t - dt) + (recovered_from_asymptomatic - asymptomatic_infection_acquired_immunity_waning - vaccination_recovered_asymptomatic) * dt	person	"recovered asymptomatic population" are asymptomatic individuals who recover and become immune because of natural infection. Asymptomatic individuals who shifted to the "recovered asymptomatic population" stock then leave after mild infection-acquired immunity waning of 6 months and flow back to "susceptible population" stock. The "recovered asymptomatic population" is assumed to be 0 initially.
recovered_from_asymptomatic	MAX(asymptomatic_population/average_duration_of_illness_asymptomatic-vaccination_asymptomatic, 0)	person /day	"recovered from asymptomatic" flow is the rate at which asymptomatic individuals leave the stock after an average duration of illness asymptomatic of 5 days (material delay). The MAX function is to ensure the flow is more than 0. The flow also minus the vaccination flow once the intervention is activated.
recovered_from_treated_mild_infection	treated_mildly_infected_population*(1-indicated_ratio_of_severe_disease)/average_duration_of_illness_symptomatic	person /day	"recovered from treated mild infection" flow is the rate at which part of the treated mildly infected individuals, through multiplication with (1 minus indicated ratio of severe disease), leaves the stock after an average duration of illness asymptomatic of 9 days (material delay).
recovered_from_treated_severely_infection	treated_severe_infected_population/average_duration_of_recovery_under_treatment-treated_death	person /day	"recovered from treated severely infection" flow is the rate at which most of the treated severe disease individuals leave the stock after an average duration of illness asymptomatic of 9 days (material delay) and flow as "recovered from treated severely infection" to the recovered immune treated population after minus the treated death flow.
recovered_from_untreated_mild_infection	untreated_mildly_infected_population/average_duration_of_illness_symptomatic	person /day	"recovered from untreated mild infection" flow is the rate at which all of the untreated mildly infected individuals leaves the stock after an average duration of illness symptomatic of 9 days (material delay).
recovered_from_untreated_severe_disease	untreated_severe_infected_population/average_duration_of_illness_symptomatic-untreated_deaths	person /day	"recovered from untreated severe infection" flow is the rate at which all of the untreated severe infected individuals leaves the stock after an average duration of illness symptomatic of 9 days (material delay). The flow also minus the untreated deaths flow.
recovered_immune_treated_population(t)	recovered_immune_treated_population(t - dt) + (recovered_from_treated_mild_infection + recovered_from_treated_severely_infection -	person	"recovered immune treated population" are symptomatic individuals who recover and become immune because of natural infection with treatment. Treated symptomatic individuals, both mild and severe disease, who shifted to the "recovered a immune treated population" stock then leave after average symptomatic infection acquired immunity period of 3 years and flow back to "susceptible

	immunity_waning_treated_population) * dt		population" stock. The "recovered immune treated population" is assumed to be 0 initially.
recovered_immune_untreated_population(t)	recovered_immune_untreated_population(t - dt) + (recovered_from_untreated_mild_infection + recovered_from_untreated_severe_disease - immunity_waning_untreated_population) * dt	person	"recovered immune untreated population" are symptomatic individuals who recover and become immune because of natural infection without any treatment. Untreated symptomatic individuals, both mild and severe disease, who shifted to the "recovered a immune untreated population" stock then leave after average symptomatic infection acquired immunity period of 3 years and flow back to "susceptible population" stock. The "recovered immune untreated population" is assumed to be 0 initially.
rehydration_care	IF switch_data_collection =0 THEN rehydration_care_at_hospital ELSE MAX(rehydration_care_at_hospital, seeking_care_at_ORC)	person /day	"treatment at ORC" flow is the rate at which mildly infected individuals leave the stock by seeking treatment at ORC. The flow depends on the fraction mildly infected seeking care and it is affected by the ORC strain. If there is no ORC, infected individuals would need to rely on the current health facilities. Hence, a MAX function is used.
rehydration_care_at_hospital	(mildly_infected_population/time_progress_to_next_stage)*fraction_seeking_care_at_hospital	person /day	"rehydration care at hospital" flow is the rate at which mildly infected population seek rehydration care at hospital.
remain_untreated_mildly_infected	mildly_infected_population/time_progress_to_next_stage-rehydration_care-become_severe_infected	person /day	"remain untreated mildly infected" flow is the rate at which mildly infected individuals leave the stock through multiplication with (1 minus the normal ratio of severe disease) after the time progress to next stage - 1 day (material delay). The MAX function is to ensure the flow is more than 0. The flow also minus the treatment at ORC rate once the intervention is activated.
remain_untreated_severe_infected	MAX((severe_infected_population/time_progress_to_next_stage)-emergency_treatment, 0)	person /day	"remain untreated severe infected" flow is the rate at which severe infected individuals leave the stock through multiplication with (1 minus the untreated fatality ratio) after the time progress to next stage - 1 day (material delay). The MAX function is to ensure the flow is more than 0. The flow also minus the treatment at DTC rate once the intervention is activated.
seeking_care_at_DTC	effect_of_DTC_strain_on_seeking_emergency_treatment*fraction_severe_infected_seeking_care*severe_infected_population/time_progress_to_next_stage	person /day	"rehydration care at DTC" flow is the rate at which severe infected population seek emergency care at DTC.

seeking_care_at_ORC	(mildly_infected_population/time_progress_to_next_stage)*fraction_mildly_infected_seeking_care*effect_of_ORC_strain_on_people_seeking_hydration_care	person/day	"seeking care at ORC" flow is the rate at which mildly infected population seek rehydration care at ORC.
severe_infected_population(t)	severe_infected_population(t - dt) + (become_severe_infected - remain_untreated_severe_infected - emergency_treatment) * dt	person	"severe infected population" are severe cases of V. cholerae infection that is characterized by a sudden onset of acute voluminous watery diarrhoea described as 'rice water stools' and vomiting leading to rapid volume depletion and death if left untreated (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018). Mildly infected individuals who shifted to the "severe infected population" stock then leave after the time progress to next stage - 1 day, and flow to 3 directions: "treated severe infected population", "untreated severe infected population" and "untreated cholera death" stocks. The "severe infected population" is assumed to be 0 initially.
smoothed_fraction_of_contaminated_water	(SMTH3(total_bacteria_shedding_from_the_fraction_of_infected,time_to_affect_water_in_aquifers)*effect_of_sanitary_on_contaminated_water)	1	The "smoothed fraction of contaminated water" smoothes the (third order) effect of the fraction of infected on the fraction of contaminated water with a delay of 14 days. This structure is refering to cholera model by Pruyt (2013). A third order delay is used to account for the fact that there are many stages in the process between bacteria shedding by the infected individuals to contaminating the water. (Sterman, Business Dynamics: Systems Thinking and Modeling for a Complex World, 2000) Igbinosa et al. (2011) found that South Africa has been plagued by outbreaks of Vibrio-related waterborne infections that are suspected to be linked to inefficiently treated effluents discharge from wastewater treatment facilities (cited from Okoh et al., 2015). Effluent is sewage that has been treated in a septic tank or sewage treatment plant.
susceptible_population(t)	susceptible_population(t - dt) + (immunity_waning_untreated_population + vaccination_acquired_immunity_waning + immunity_waning_treated_population + asymptomatic_infection_acquired_immunity_waning + stop_receiving_clean_water - infections -	person	Total population in Al Hudaydah governorate, Yemen in 2017 was 3,238,199 (OCHA, 2017). For models that simulate an outbreak within a short period of time (e.g. two years in this model), one can ignore the dynamics of population growth (birth rate and death rate, gray arrows) and assume a constant population. It is assumed the total population as susceptible to cholera as the first cholera case only reported in September 2016.

	vaccination_susceptible - receiving_clean_water) * dt		
"time_IDPs_increase_to_Al-hudaydah"	540	day	The conflict in Al-Hudaydah intensified from June 2018. Hence, the starting day is 540,000. Although IDP present in Al-Hudaydah even before June 2018, the impact from IDP is less compared to the drastic increase of IDP from June 2018. Hence, only IDP from June 2018 is captured in the model.
time_progress_to_next_stage	1	day	The incubation period of cholera can range from several hours to 5 days (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009). Similar to the "average incubation time", "time to progress to next stage" uses 1 day as the symptomatic individuals will then progress to either mild or severe disease stage.
time_to_affect_water_in_aquifers	8	day	The "time to affect water in aquifers" has an assumptive value of 5 days delayed. According to Nevondo and Cloete (2001), survival of vibrios in the aquatic environment relates sharply to various chemical, biological and physical characteristics of the aquatic milieu, with V. cholerae known to remain viable in surface waters for periods ranging from 1 h to 13 days (cited from Okoh, 2015).
total_asymptomatic_shedding	(recently_infected_population+asymptomatic_population)*bacteria_shedding_from_asymptomatic	person	"total asymptomatic shedding" is the total bacteria shed by number of asymptomatic population and recently infected population
total_bacteria_shedding_from_the_fraction_of_infected	(total_asymptomatic_shedding+total_mildly_shedding+total_severe_infected_not_in_DTC_shedding)/Total_Population	1	"fraction of infected" is the fraction of infected individuals who are contributing to the concentration of V. cholerae in the environment. This is a product of the number of infected individuals and the bacteria shedding in the stool over the total population. This compound parameter is depending on severity of infection as the bacteria shedding is different (Kaper, Morris, & Levine, 1995). Okoh et al. claimed that V. cholera presence in wastewater, therefore, could be dependent on the number of infected people in the population contributing to the wastewater flow.
total_mildly_shedding	(mildly_infected_population+untreated_mildly_infected_population+treated_mildly_infected_population)*bacteria_	person	"total mildly shedding" is the total bacteria shed by number of treated mildly infected, mildly infected and untreated mildly infected population.

	shedding_from_mildly_infected		
total_severe_infected_not_in_DTC_shedding	(severe_infected_population+untreated_severe_infected_population)*bacteria_shedding_from_severely_infected	person	Severity affects the intensity of shedding, and so the average contribution of an infectious person to transmission may change systematically with time as the distribution of infectious doses changes (Kaper, Morris, & Levine, 1995; Nelson et al., 2013). The "severe infected not in DTC" excludes treated severe infected population because at DTC, the sewage system is in place with disinfection. Hence, it is assumed that all patients at DTC do not attribute their bacteria shedding back into the environment.
total_symptomatic_bacteria_shedding	total_mildly_shedding+total_severe_infected_not_in_DTC_shedding	person	"total symptomatic bacteria shedding" is a product of both mild and severely infected bacteria shedding.
treated_cholera_death(t)	treated_cholera_death (t - dt) + (treated_death) * dt	person	"treated cholera death" are the deaths result from severe infected individuals who have received treatment.
treated_death	treated_severe_infected_population*fatality_fraction/average_duration_of_illness_symptomatic	person /day	"treated deaths" flow is the rate at which severe infected individuals leave the stock through multiplication with the treated fatality fraction after an average duration of illness symptomatic of 9 days (material delay).
treated_mild_become_severe_infected	treated_mildly_infected_population*indicated_ratio_of_severe_disease/time_progress_to_next_stage	person /day	"treated mild become severe infected" flow is the rate at which treated mildly infected individuals leave the stock after the time to progress to next stage - 1 day (material delay) into treated severe infected population. The flow depends on the indicated ratio of severe disease which is lower if the capacity of the ORC is not strained. The ORC aims to treat mildly infected individuals at an early stage as a prevention from deteriorating into severe infected stage. The strained ORC will affected the quality of treatment among the mildly infected individuals where the rate "treated mild become severe infected" is higher. Médecins Sans Frontières (2018) reports that the initial clinical state can rapidly deteriorate (or not improve) if: – the volume of fluid prescribed on admission is insufficient: degree of dehydration underestimated or error in calculation. The volume is not administered within the correct time frame: rehydration too slow or too fast, interruptions in treatment (empty IV bags or ORS cups). On-going fluid losses (continued diarrhoea) are not adequately compensated by additional ORS or RL. Frequent vomiting persists: IV therapy may be needed for those who systematically vomit all ORS, even in patients with some dehydration.

treated_mildly_infected_population(t)	treated_mildly_infected_population(t - dt) + (rehydration_care - recovered_from_treated_mild_infection - treated_mild_become_severe_infected) * dt	person	"treated mildly infected population" are mild cases of V. cholerae infection that are treated. Mildly infected individuals who shifted to the "treated mildly infected population" stock then leave after an average duration of illness symptomatic 9 days, and flow to "recovered immune treated population" and "treated severe infected population" stocks. The "treated mildly infected population" is assumed to be 0 initially.
treated_severe_infected_population(t)	treated_severe_infected_population(t - dt) + (emergency_treatment + treated_mild_become_severe_infected - recovered_from_treated_severely_infection - treated_death) * dt	person	"treated severe infected population" are severe cases of V. cholerae infection that are treated. Severe infected individuals who shifted to the "treated severe infected population" stock then leave after an average duration of illness symptomatic 9 days, and flow to "recovered immune treated population" and "treated cholera death" stocks. The "treated severe infected population" is assumed to be 0 initially.
untreated_cholera_death(t)	untreated_cholera_death(t - dt) + (untreated_deaths) * dt	person	"untreated cholera death" are the deaths result from severe infected individuals who left untreated.
untreated_deaths	untreated_severe_infected_population*untreated_fatality_fraction/average_duration_of_illness_symptomatic	person/day	"untreated deaths" flow is the rate at which severe infected individuals leave the stock through multiplication with the untreated fatality fraction after an average duration of illness symptomatic of 9 days (material delay).
untreated_fatality_fraction	0.01	1	Case fatality rate is 0.19% in 2017 in Al-hudaydah governorate (OCHA, 2017). "untreated fatality fraction" uses 0.004 assuming that the fatality fraction is higher than the case fatality rate with treated death fraction of 0.0021. McCrickard et al. (2016) reports that more than half of the records of cholera deaths in Dar es Salaam were missing from the existing surveillance system, which only captured patients who arrived at DTCs. Deaths that occurred in other treatment locations or in the community were not reported. Underreporting of deaths during cholera epidemics, a phenomenon not unique to Tanzania poses a threat to global health security.
untreated_mildly_infected_population(t)	untreated_mildly_infected_population(t - dt) + (remain_untreated_mildly_infected - recovered_from_untreated_mild_infection) * dt	person	"untreated mildly infected population" are mild cases of V. cholerae infection that are not treated. Mildly infected individuals who shifted to the "untreated mildly infected population" stock then leave after an average duration of illness symptomatic 9 days, and flow to "recovered immune untreated population" stock. The "untreated mildly infected population" is assumed to be 0 initially.

untreated_severe_infected_population(t)	untreated_severe_infected_population(t - dt) + (remain_untreated_severe_infected - recovered_from_untreated_severe_disease - untreated_deaths) * dt	person	"untreated severe infected population" are severe cases of V. cholerae infection that are not treated. Severe infected individuals who shifted to the "untreated severe infected population" stock then leave after an average duration of illness symptomatic 9 days, and flow to "recovered immune untreated population" stock. The "untreated severe infected population" is assumed to be 0 initially.
vaccinated_population(t)	vaccinated_population(t - dt) + (vaccination_susceptible + vaccination_recovered_asymptomatic + vaccination_asymptomatic - vaccination_acquired_immunity_waning) * dt	person	"vaccinated population" has the vaccinated individuals from recovered asymptomatic population, asymptomatic population, and susceptible population. Since there is no mass screening to filter the indviduals with infection acquired immunity, it is assumed that the health workers vaccinate those who seemed healthy and never been treated for cholera the past 1 year.
vaccination_acquired_immunity_waning	vaccinated_population //average_duration_of_protection	person /day	All vaccinated individuals leave vaccinated population stock after an average duration of protection (depending on 1 or 2 doses of vaccines) and flow as "vaccination acquired immunity waning" back to the susceptible population.
vaccination_asymptomatic	asymptomatic_population*indicated_fractional_vaccination	person /day	"vaccination asymptomatic" flow is the rate at which asymptomatic individuals leave the stock through multiplication with indicated fractional vaccination.
vaccination_recently_infected_population	recently_infected_population*indicated_fractional_vaccination	person /day	Vaccination on recently infected population is assumed to be no impact. Hence, the flow is not attached to any stock. This is used
vaccination_recovered_asymptomatic	recovered_asymptomatic_population*indicated_fractional_vaccination	person /day	"vaccination recovered asymptomatic" flow is the rate at which recovered asymptomatic individuals leave the stock through multiplication with indicated fractional vaccination.
Health_sector:			
beds	50	person /centre	2,531 beds were reported in 54 Diarrhoea treatment centres DTCs (EOC, 2018). "beds" is assumed to have 50 patients capacity in each DTC. MSF (2018) guideline shows that one DTC has the capacity from 50 to 200 beds.
building_DTC_start_time	80	day	"building DTC start time" is the day when DTC started to be built.
building_ORC_start_time	90	day	"building ORC start time" is the day when ORC started to be built.

data_number_of_DTC	18	centre	Emergency Operations Center (2017) reported 18 functioning DTC. The population in Al-hudaydah was in need of 44 ORC.
data_number_of_ORC	144	centre	Emergency Operations Center (2017) reported 142 functioning ORC. The population in Al-hudaydah was in need of 422 ORC.
desired_DTC_capacity	IF switch_data_collection =0 THEN 0 ELSE (IF switch_DTC=1 THEN (0+STEP(data_number_of_DTC*beds, indicated_building_DTC_start_time)) ELSE IF switch_DTC=2 THEN (0+STEP(desired_number_of_DTC*beds, indicated_building_DTC_start_time)) ELSE 0)	person	"desired DTC capacity" is adjusted according to the number of severely infected individuals from the cholera prevalence (simulation). The variable input is a graphical function that has included the intervention historical data in 2017. It can be changed to test the policy impacts when the switch is turned to 2. "desired DTC capacity" also includes the implementation limitation from the effect of new DTC added.
desired_number_of_DTC	18	centre	"desired number of DTC" is adjusted according to the number of severely infected individuals from the cholera prevalence (simulation). It can be changed to test the policy impacts when the switch is turned to 2.
desired_number_of_ORC	144	centre	"desired number of ORC" is adjusted according to the number of severely infected individuals from the cholera prevalence (simulation). It can be changed to test the policy impacts when the switch is turned to 2.
desired_ORC_capacity	IF switch_data_collection =0 THEN 0 ELSE (IF switch_ORC=1 THEN (0+STEP(data_number_of_ORC*patient_treated, indicated_building_ORC_start_time))ELSE IF switch_ORC=2 THEN (0+STEP(desired_number_of_ORC*patient_treated, indicated_building_ORC_start_time)) ELSE 0)	person	"desired ORC capacity" is adjusted according to the number of symptomatic individuals from the cholera prevalence (simulation). The variable input is a graphical function that has included the intervention historical data in 2017. It can be changed to test the policy impacts when the switch is turned to 2. "desired ORC capacity" also includes the implementation limitation from the effect of new ORC added.
DTC_capacity(t)	DTC_capacity(t - dt) + (DTC_capacity_building) * dt	person	People who are severely dehydrated may need intravenous fluids and hospitalisation. In these cases, they should be admitted to a Diarrhoea Treatment Centre (DTC). Without treatment, the mortality rate can reach 50

			per cent; with adequate care, it's less than 2 per cent (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009). A DTC is set up outside of the main hospital to prevent the spread of the disease and is fully autonomous. In open settings, with spread-out populations, treatment needs to be as close as possible to affected populations. "DTC capacity" expressed as number of severely infected individuals that can be treated at ORC in Al-hudaydah. The stock has an initial value of 0.
DTC_capacity_building	(desired_DTC_capacity-DTC_capacity)//time_to_build_DTC	person/day	"DTC capacity building" is a goal seeking function at which the current capacity to treat severely infected individuals is closing the gap with desired DTC capacity over the time to build DTC (first order delay).
DTC_need	people_in_need_DTC//beds	centre	"DTC need" is a demand of beds relative to supply of beds ratio.
DTC_strain	treated_severe_infected_population*ratio_severe_disease_in_DTC//DTC_capacity	1	Strain on DTC services capacity, level of overloading, from ratio of treated severe infected population to DTC capacity.
effect_of_DTC_strain_on_seeking_emergency_treatment	GRAPH(DTC_strain) Points(11): (0.000, 1.296), (0.500, 1.222), (1.000, 1.128), ...	1	The graphical function shows that when the DTC strain is high, it affects the health seeking behavior among the infected individuals. More data/expert input is required for this parameter.
effect_of_ORC_strain_on_fraction_of_severe_disease	GRAPH(ORC_strain) Points(18): (0.000, 0.503346425462), (0.0882352941176, 0.505994142063), (0.176470588235, 0.510691654066), ...	1	By helping to reduce the severity of dehydration of patients who require health facility services, ORCs reduce stress and overcrowding at health facilities (UNICEF, 2013). Besides, when mildly infected individuals receive early treatment, it can help prevent the symptoms deteriorates to severely infected stage that requires DTC treatment. Médecins Sans Frontières (2018) also reports that the initial clinical state can rapidly deteriorate (or not improve) if: The volume of fluid prescribed on admission is insufficient (degree of dehydration underestimated or error in calculation). In addition, when the volume is not administered within the correct time frame (rehydration too slow or too fast, interruptions in treatment). In this model, the graphical function shows that when the ORC strain is high, it affects the quality and availability of care to mildly infected individuals. Hence, the ORC has less effect on preventing individuals flow into "treated severe infected population".
effect_of_ORC_strain_on_people_seeking_hydration_care	GRAPH(ORC_strain) Points(11): (0.000, 1.296), (0.500, 1.222), (1.000, 1.128), ...	1	The graphical function shows that when the ORC strain is high, it affects the health seeking behavior among the infected individuals. More data/expert input is required for this parameter.

fatality_fraction	service_strain_fatality_fraction+(treated_fatality_fraction-service_strain_fatality_fraction)/(1+DTC_strain^service_capacity_sensitivity)	1	According to Médecins Sans Frontières (2018), the case fatality rate (CFR) is is used for assessing the quality of healthcare services (case management) at treatment centres. The standard indicator for adequate case management is a CFR < 1%. In this model, the "fatality fraction" on treated death is affected by the strain on DTC services capacity. The formula includes the sensitivity of care quality to health services strain. The negative exponent indicates an inverse relationship, whereby an increase in health services strain leads to a decrease care quality. Hence, an increase in fatality fraction.
indicated_building_DTC_start_time	IF switch_data_collection =2 THEN building_DTC_start_time + (response_time_to_update_system) ELSE building_DTC_start_time	day	"indicated building DTC start time" includes the delay from surveillance system.
indicated_building_ORC_start_time	IF switch_data_collection =2 THEN building_ORC_start_time + (response_time_to_update_system) ELSE building_ORC_start_time	day	"indicated building ORC start time" includes the delay from surveillance system.
initial_DTC_capacity	50	person	The initial DTC is assumed to be 50 persons. This is an assumption as the cholera cases were reported since September 2016.
initial_ORC_capacity	200	person	The initial ORC is assumed to be 200 persons. This is an assumption as the cholera cases were reported since September 2016.
ORC_capacity(t)	ORC_capacity(t - dt) + (ORC_capacity_building) * dt	person	Cholera is relatively simple to treat in people with mild to moderate forms usually able to recover through treatment with fluids and oral rehydration salts, which are easy to administer (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018; Nelson et al., 2009). Care is decentralised to smaller-scale Oral Rehydration Centres (ORCs) known as cholera treatment units and oral rehydration solution points, supported by mobile teams."ORC capacity" expressed as number of people that can be treated at ORC in Al-hudaydah. The stock has an initial value of 0.

ORC_capacity_building	(desired_ORC_capacity - ORC_capacity)//time_to_build_ORC	person/day	"ORC capacity building" is a goal seeking function at which the current capacity to treat mildly infected individuals is closing the gap with desired ORC capacity over the time to build ORC (first order delay).
ORC_need	(people_in_need_ORC)//patient_treated	centre	"ORC need" is a demand of care relative to supply of care ratio.
ORC_strain	people_in_need_ORC//ORC_capacity	1	Strain on services capacity, level of overloading, from ratio of mildly and severely infected population to ORC capacity.
other_AWD_cases	7000	person	AWD case that is not easy to be differentiated from cholera patients. Most cases of acute, watery diarrhea are caused by viruses (viral gastroenteritis). The most common ones in children are rotavirus and in adults are norovirus (this is sometimes called "cruise ship diarrhea" due to well publicized epidemics) (Ochoa and Surawicz, 2012). This is an assumption number of 7000 persons. More data/expert input is required for this parameter.
patient_treated	50	person/centre	Michas (2020) reports majority physicians see 20 patients per day, only 1.3% of physicians saw between 51 and 60 patients per day. Assuming doctors in an emergency setting can see 50 patients. "patient tested" is assumed to be 50 patients per day.
people_in_need_DTC	treated_severe_infected_population*ratio_severe_disease_in_DTC	person	"people in need DTC" is number of severely infected individuals who need DTC treatment. Some severely infected individuals can be treated at ORC.
people_in_need_ORC	(treated_severe_infected_population*(1-ratio_severe_disease_in_DTC)+treated_mildly_infected_population+other_AWD_cases)	person	"people in need DTC" is number of mildly infected individuals who need ORC treatment. This include other AWD case that is not easy to be differentiated from cholera patients.
ratio_severe_disease_in_DTC	0.7	1	Some severely infected individuals can be treated at ORC while some of them require treatment at DTC. It is assumed that 0.2 of all severely infected individuals need treatment at DTC.
service_capacity_sensitivity	2	1	"service capacity sensitivity" indicates the sensitivity of care quality to health services strain.
service_strain_fatality_fraction	0.01	1	Case fatality rate is 0.19% in 2017 in Al-hudaydah governorate (OCHA, 2017). "treated fatality fraction" uses 0.004 assuming that the fatality fraction is higher than the case fatality rate with treated death fraction of 0.0019 when minimally treated due to overwhelmed, chaotic health care.

switch_DTC	1	1	A switch to activate and deactivate the intervention
switch_ORC	1	1	A switch to activate and deactivate the intervention
time_to_build_DTC	120	day	"time to build DTC" is an assumptive duration (days) needed to increase the current capacity to meet the need from "desired desired DTC capacity".
time_to_build_ORC	30	day	"time to build ORC" is an assumptive duration (days) needed to increase the current capacity to meet the need from "desired desired ORC capacity".
treated_fatality_fraction	0.0021	1	Case fatality rate is 0.21% in 2017 in Al-hudaydah governorate (OCHA, 2017). "treated fatality fraction" uses 0.001 assuming that the fatality fraction is lower than the case fatality rate with treated death fraction of 0.0019 when the quality of healthcare services is good.
National_cholera_surveillance_system:			
data_updated_in_cholera_surveillance_system	IF switch_data_collection =2 THEN SMTH3("recorded_suspected_and_confirmed_cases_(cummulative)", normal_time_to_update_system+response_time_to_update_system) ELSE SMTH3("recorded_suspected_and_confirmed_cases_(cummulative)", normal_time_to_update_system)	person	
including_unreported(t)	including_unreported(t - dt) + (including_unreported_flow) * dt	person	"including unreported" is the stock of all infected individuals.
including_unreported_flow	asymptomatic+mildly_infected*0.8	person /day	"including unreported flow" is the rate of all infected individuals in the model per day.
normal_time_to_update_system	14	day	"normal time to update system" is a desired duration (days) needed to collect and update data of the surveillance system.
"recorded_suspected_and_confirmed_cases_(	"recorded_suspected_and_confirmed_cases_(cummulative)"(t - dt) + ("recorded_suspected_	person	In areas where an epidemic is under way, a suspected case of cholera is defined as acute watery diarrhea, with or without vomiting, in a patient over 5 years of age. According the study by Camacho (2018), Yemen Health

cummulative)"(t)	and_confirmed_cases_(rate)") * dt		Authorities set up a national cholera surveillance system to collect information on suspected cholera cases presenting at health facilities (no mass screening, the data depends on the availability of ORC, DTC, and health seeking ratio). Individual variables included symptom onset date, age, severity of dehydration, and rapid diagnostic test result. Suspected cholera cases were confirmed by culture, and a subset of samples had additional phenotypic and genotypic analysis. "cumulative cholera cases (suspected and confirmed cases)" is a stock with recorded cases from ORC and DTC.
"recorded_suspected_and_confirmed_cases_(rate)"	rehydration_care+emergency_treatment	person/day	According the study by Camacho (2018), Yemen Health Authorities set up a national cholera surveillance system to collect information on suspected cholera cases presenting at health facilities. Individual variables included symptom onset date, age, severity of dehydration, and rapid diagnostic test result. Suspected cholera cases were confirmed by culture, and a subset of samples had additional phenotypic and genotypic analysis. "recorded cholera cases" flow is the rate of individuals seeking treatment at ORC and DTC.
response_time_to_update_system	0	day	"normal time to update system" is an assumptive duration (days) needed to collect and update data of the surveillance system.
switch_data_collection	1	1	A switch to activate and deactivate the intervention
Sanitation_condition:			
added_latrine_capacity(t)	added_latrine_capacity(t - dt) + (latrine_construction) * dt	person	"added latrine capacity" is expressed as number of people that can be provided with latrine facility.
average_sewered_population	Total_Population*ratio_sewered_population	person	"average sewered population" is the product of total population multiply with ratio sewered population.
building_capacity_to_do_treatment	((desired_sewage_plant_treatment-capacity_to_treat_sewage_plant)/time_to_increase_treatment_capacity)*effect_of_maximum_support_on_building_capacity	person/day/day	"building capacity to do treatment" is a goal seeking function at which the current capacity to treat sewage plant is closing the gap with desired desired sewage plant treatment over the time to increase treatment capacity (first order delay).
building_latrine_start_time	0	day	"building latrine start time" is the day when latrines started to be built.

capacity_to_treat_sewage_plant(t)	capacity_to_treat_sewage_plant(t - dt) + (building_capacity_to_do_treatment) * dt	person/day	Taking into the implementation challenges such as delay in building capacity in treating and maintaining sewage plants, "capacity to treat sewage plant" expressed as number of people that can be covered by the treated sewage plant.
current_max_latrine_need	Total_Population*current_ratio_open_defecation	person	"current max latrine need" is the maximum capacity reduces with the additional capacity (and likewise) overtime.
current_ratio_open_defecation	ratio_open_defecation-(added_latrine_capacity/Total_Population)	1	Ratio of people practicing open defecation in urban area of Yemen after the intervention.
data_sewage_treatment_plant_support	GRAPH(TIME) Points(728): (0.0, 0), (1.00412654746, 0), (2.00825309491, 0), ...	person/day	Data from the implemented intervention (OCHA, 2017).
degradation	sewage_treatment_plant_supported/degradation_time	person/day	"degradation' flow is the rate that describes how quickly the sewage treatment plant are in need of treatment and maintenance again.
degradation_time	30	day	"degradation time" is assumed to be 30 days, assuming a sewage treatment plant needs maintenance after 30 days. More data/expert input is required for this parameter.
desired_latrine_construction	IF switch_data_collection=0 THEN 0 ELSE (IF switch_latrine=2 THEN STEP(desired_number_of_new_latrine, indicated_building_latrine_start_time)*people_per_latrine*effect_of_maximum_new_latrine ELSE 0)	person	Once the switch is changed to value 2, "desired latrine construction" has a pulse function of the product of desired number of new latrine, people per latrine, and building latrine start time. It also includes the effect of maximum new latrine as the implementation limitation.
desired_number_of_new_latrine	0	latrine	"desired number of new latrine" is adjusted according to the maximum new latrine capacity needed. It can be changed to test the policy impacts when the switch is turned to 2.
desired_sewage_plant_treatment	GRAPH(IF switch_data_collection=2 THEN TIME + (response_time_to_update_system) ELSE TIME) Points(730): (0.0,	person/day	"desired sewage plant treatment" is adjusted according to the number of individuals covered by treated sewage plant. The variable input is a graphical function that has included the intervention historical data in 2017. It can be changed to test the policy impacts. The intervention start time include response time (delay) from the surveillance system.

	0), (1.00137174211, 0), (2.00274348422, 0), ...		
effect_from_latrine_intervention	normal_sanitary_condition*weight_of_latrine_use*effect_of_additional_latrine_on_sanitary_condition	1	effect of additional latrine on sanitary condition is the product of the effect of additional latrine on sanitary condition based on the assigned weight.
effect_from_other_infrastructure_conditions	normal_sanitary_condition*weight_of_other_sanitary_interventions*Other_infrastructure_states	1	effect from other infrastructure conditions is the product of other infrastructure states on sanitary condition based on the assigned weight.
effect_from_sewage_plant_intervention	normal_sanitary_condition*weight_of_sewage_plant_support*effect_of_sewage_plant_treatment_on_sanitary_condition	1	effect from sewage plant intervention is the product of effect of sewage plant treatment on sanitary condition based on the assigned weight
effect_of_additional_latrine_on_sanitary_condition	GRAPH(latrine_need) Points(20): (0.000, 2.000), (0.0526315789474, 1.978), (0.105263157895, 1.949), ...	1	Latrine intervention includes additional latrine and maintenance during the epidemic. The "effect of additional latrine on sanitary condition" has a graphical function of S-shape decay.When the latrine need is value 1 (no intervention), the effect is 1 (no effect to the normal sanitary condition). The maximum effect is limited at 2 in order to constrain the sanitary condition at its maximum at 100%.
effect_of_maximum_new_latrine	GRAPH(latrine_need) Points(11): (0.0000, 0.000), (0.0300, 0.237185670755), (0.0600, 0.423017710815), ...	1	The "effect of maximum new latrine" has a graphical function of logarithmic growth. Assuming that when the latrine need is closer to 0, the effect decreases increasingly towards 0 because there is a lack of need to add more latrine.
effect_of_maximum_support_on_building_capacity	GRAPH(sewage_treatment_plant_need) Points(11): (0.0000, 0.000), (0.0300, 0.212119217174), (0.0600, 0.385094456986), ...	1	The "effect of maximum support on building capacity" has a graphical function of logarithmic growth. Assuming that when the sewage treatment plant need is closer to 0, the effect decreases increasingly towards 0 because there is a lack of need to support the sewage plant treatment.
effect_of_sanitary_on_contaminated_water	GRAPH(indicated_sanitary_conditions) Points(13): (0.000, 0.7503), (0.0833333333333, 0.7144),	1	"effect of sanitary on contaminated water" represents the sanitation states that impact the population in accessing clean water. When the indicated sanitary conditions is close to 1, from the range of 0 to 1, (poor to good sanitary condition), the effect (values) on the contaminated water decreases decreasingly towards zero: It reduces the water

	(0.166666666667, 0.6755), ...		contamination level. The maximum effect (minimum value) is limited at 0.2 as good infrastructure cannot promise 0 water contamination. There are other factors on the water contamination.
effect_of_sewage_plant_treatment_on_sanitary_condition	GRAPH(sewage_treatment_plant_need) Points(20): (0.000, 2.000), (0.0526315789474, 1.967), (0.105263157895, 1.929), ...	1	Sewage plant support intervention includes additional treatment and maintenance to the sewage plants during the epidemic. Hence, this is additional treatment to the usual maintenance routines in the governorate. The "effect of sewage plant treatment on sanitary condition" has a graphical function of S-shape decay.When the sewage treatment plant need is value 1 (no intervention), the effect is 1 (no effect to the normal sanitary condition). The maximum effect is limited at 2 in order to constrain the sanitary condition at its maximum at 100%.
indicated_building_latrine_start_time	IF switch_data_collection =2 THEN building_latrine_start_time + (response_time_to_update_system) ELSE building_latrine_start_time	day	"building latrine start time" includes the delay from surveillance system.
indicated_sanitary_conditions	effect_from_sewage_plant_intervention+effect_from_other_infrastructure_conditions+effect_from_latrine_intervention	1	"indicated sanitary conditions" represents the sanitation states that impact the population in accessing clean water. It multiplies the effect of sewage plant treatment on sanitary, effect of additional latrine on sanitary condition, and effect of other infrastructure states on the indicated sanitary conditions. Most of Yemen's major water and sanitation systems have sustained damage, and refuse collection services have been severely impaired. That there has not been a complete collapse is down to the resourcefulness of the population. “In some of the large cities, it is the business community that has come together, raised funds, and arranged solid waste collection campaigns that have been very successful” (Burki, 2016).
initial_latrine_capacity_needed	(Total_Population*ratio_open_defecation)	person	"initial latrine capacity needed" is the initial need of latrine capacity by looking at the current number of population who are openly defecating.
latrine_construction	MAX((desired_latrine_construction-added_latrine_capacity)/time_to_build_latrine, 0)	person /day	"latrine construction" is a goal seeking function at which the added latrine capacity is closing the gap with desired latrine construction over the time to build latrine (first order delay).

latrine_need	current_max_latrine_need/INIT(current_max_latrine_need)	1	"latrine need" is the current ratio open defecation relative to the initial ratio open defecation. If the value is 1, it indicates 100% need. If there is intervention, the need of latrine reduces, causes the value to be less than 1; hence, a reduced need and an effect of intervention on sanitary conditions.
normal_sanitary_condition	0.5	1	Under conflict affected context, the value of "normal sanitary condition" is assumed to be 0.5 functioning. According to WHO–UNICEF statistics, in 2014 only 53% of the population used improved sanitation facilities (cited from (Qadri, Islam, and Clemens, 2017).
number_of_latrine_constructed	added_latrine_capacity/people_per_latrine	latrine	"number of latrine constructed" is obtained from dividing added latrine capacity with people per latrine.
Other_infrastructure_states	1	1	"Other infrastructure states" are represented by household and personal level sanitation that is different than community level interventions on sewage treatment plant and latrines. Under conflict affected context, the value of other infrastructures is assumed to be 0.5 functioning. Therefore, the value for this parameter is 1. No intervention means no effect to the normal sanitary condition. Personal and household sanitation conditions play an important role on fecal-oral cholera transmission that is not within the boundary of this model. Hence, it is represented as constant values in this model.
people_per_latrine	20	person/latrine	Gunther (2012) research findings recommend that not more than four households (or 20 individuals) should share a toilet stance to ensure long-term hygienic and sustainable use. MSF (2018) and Spiegel et al. (2018) also report a minimum of one latrine for 20 people. Hence, the value 20 is used for each latrine.
ratio_open_defecation	0.01	1	Worldbank (2021) reports 1% of people practicing open defecation in urban area of Yemen in 2017. Open defecation included cases where feces are disposed in fields, water, and other open spaces and unimproved sanitation includes disposing feces in latrines without a platform, hanging latrines, or bucket latrines.
ratio_sewered_population	0.693	1	Average sewered population in Al-hudaydah is 69.3% (Ministry of Electricity and Water, 2003).
sewage_treatment_plant(t)	sewage_treatment_plant(t - dt) + (degradation - treatment) * dt	person	Sewage plant treatment removes contaminants from sewage to produce an effluent that is suitable for discharge to the surrounding environment or an intended reuse application. Non-functional sewage plants leads to contamination of the shallow aquifers and wells, where local civilians and private tankers collect drinking water.

			Sewage plant support intervention includes additional treatment and maintenance to the sewage plants during the epidemic (UNICEF, 2018). Initial value of the stock is "average sewered population" in Al-hudaydah.
sewage_treatment_plant_need	sewage_treatment_plant/INIT(sewage_treatment_plant)	1	"sewage treatment plant need" is the stock sewage plant treatment relative to the initial sewage plant treatment. If the value is 1, it indicates 100% need. If there is intervention, the stock reduces, causes the value to be less than 1; hence, a reduced need and an effect of intervention on sanitary conditions.
sewage_treatment_plant_supported(t)	sewage_treatment_plant_supported(t - dt) + (treatment - degradation) * dt	person	"sewage treatment plant supported" is the stock where the number of individuals covered by treatment and maintenance of the sewage plants.
switch_latrine	0	1	A switch to activate and deactivate the intervention
switch_treatment	1	1	A switch to activate and deactivate the intervention
time_to_build_latrine	30	day	"time to build latrine" is an assumptive duration (days) needed to increase the current capacity to meet the need from "desired latrine construction".
time_to_increase_treatment_capacity	14	day	"time to increase treatment capacity" is an assumptive duration (days) needed to increase the current capacity to meet the need from "sewage treatment plant". More data/expert input is required for this parameter.
treatment	IF switch_data_collection =0 THEN 0 ELSE (IF switch_treatment=1 THEN data_sewage_treatment_plant_support ELSE IF switch_treatment=2 THEN capacity_to_treat_sewage_plant ELSE 0)	person /day	Sewage treatment is a type of wastewater treatment which aims to remove contaminants from sewage to produce an effluent that is suitable for discharge to the surrounding environment or an intended reuse application, thereby preventing water pollution from raw sewage discharges. "treatment' flow is the rate at which individuals who leave sewage treatment plant stock to sewage treatment plant supported stock.
weight_of_latrine_use	0.15	1	"weight of latrine use" assigns the weight of latrine state in influencing the indicated sanitary condition. It is assumed to be 0.2 of the sanitary condition as open defecation can lead to contamination of the shallow aquifers and wells. Hence, the effect of functioning latrine intervention is assumed to be 0.2. More data/expert input is required for this parameter.

weight_of_other_sanitary_interventions	0.45	1	"weight of other sanitary interventions" assigns the weight of other sanitation state in influencing the indicated sanitary condition. It is assumed to be 0.45 because this parameter sanitary conditions include household and personal level sanitation that is different than community level interventions on sewage treatment plant and latrines. Although personal and household sanitation conditions play an important role on fecal-oral cholera direct transmission, this is not within the boundary of this model.
weight_of_sewage_plant_support	0.4	1	"weight of sewage plant support" assigns the weight of sewage plant state in influencing the indicated sanitary condition. It is assumed to be 0.4 of the sanitary condition as the highest numbers of cholera cases have been reported in places where sewage treatment plants are non-functional. Without working sewage treatment plants, raw sewage is often diverted to poor neighborhoods and agricultural lands (leads to contamination of the shallow aquifers and wells) where local civilians and private tankers collect drinking water. Hence, the value is conceptualised with a higher weight than latrine use and other infrastructure states. More data/expert input is required for this parameter.
Vaccination:			
"1_dose"	1	vaccine/person	1 dose of vaccine per person
"1_dose_protection"	180	day	Although OCV currently used in mass campaigns are administered according to a two-dose regimen 14 days apart, a single dose provides short-term protection, with a pooled effectiveness of 69% (95% CI 35–85%) within the first year, which has important implications for outbreak management (Pezzoli, 2020) MSF (2018) reports that immunity develops one week after administration and lasts up to 6 months after a single dose and at least 3 years after 2 doses.
"2_doses"	2	vaccine/person	2 doses of vaccines per person
"2_doses_protection"	365*3	day	Potentially facing annual epidemics, it may be necessary to revaccinate at-risk populations every 2 y given that the duration of vaccine protection is about 2.5 to 3 years (Durham el at., 1998; UNICEF, 2018) They have an average two-dose efficacy of 58% (95% confidence interval [CI], 42–69%) and effectiveness of 76%

			(95% CI, 62–85%) for at least 3 years, with one study showing efficacy for up to 5 years. Although OCV currently used in mass campaigns are administered according to a two-dose regimen 14 days apart, a single dose provides short-term protection, with a pooled effectiveness of 69% (95% CI 35–85%) within the first year, which has important implications for outbreak management (Pezzoli, 2019).
average_duration_of_protection	IF switch_vaccine_dose=0 THEN "1_dose_protection" ELSE IF switch_vaccine_dose=1 THEN "2_doses_protection" ELSE 0	day	"average duration of protection" depends on 1 or 2 doses vaccination.
data_vaccines	260000	person	According to UNICEF (2018) situation report, WHO and UNICEF Yemen have supported the first round of an oral cholera vaccination campaign in five districts in the northern governorates of Al-hudaydah and Ibb to protect an additional 540,595 people (over 1 years of age) against Cholera. In total 387,390 (69 per cent) persons have been vaccinated (first dose) against the total target of 561,002 people. There is no data on dis-aggregation of Al-hudaydah and Ibb governorates. Hence, among the 3 districts, 2 are withing Al-hudaydah, it is assumed that 260,000 first dose OCV distributed in Al-hudaydah with the total target of 370,000 people (from the total of 561,002 people).
desired_number_of_vaccines	260000	vaccine	"desired number of vaccines" is initiated with the value 260000 from the historical data. The value can be changed to test the policy.
fractional_vaccination	IF switch_data_collection =0 THEN 0 ELSE (IF switch_vaccination=1 THEN data_vaccines/potential_vaccine_recipients/length_of_vaccination_campaign ELSE IF switch_vaccination=2 THEN number_of_vaccinated_people /potential_vaccine_recipients/length_of_vaccination_campaign ELSE 0)	1/day	"fractional vaccination" is rate that derived from dividing the number of vaccinated people over the campaign period (either from data or policy test input) with total population. This fraction draws number of person from the targeted stocks of sub-population into the vaccinated population stock.

indicated_fractional_vaccination	(STEP(fractional_vaccination*vaccine_effectiveness, indicated_vaccination_start_time+time_to_procure_vaccines) + STEP(-fractional_vaccination*vaccine_effectiveness, vaccination_stop_time+time_to_procure_vaccines)) +(interval_for_second_round_of_vaccination//interval_for_second_round_of_vaccination)*(STEP(fractional_vaccination*vaccine_effectiveness, indicated_vaccination_start_time+time_to_procure_vaccines+interval_for_second_round_of_vaccination) + STEP(-fractional_vaccination*vaccine_effectiveness, vaccination_stop_time+time_to_procure_vaccines+interval_for_second_round_of_vaccination))	1/day	"indicated fractional vaccination" is a rate that depends on both the vaccination start time (policy initiation) and the time to procure vaccines (delay). Step function is used to enable the flows of individuals from the targeted stocks of sub-population into the vaccinated population stock.
indicated_vaccination_start_time	IF switch_data_collection =2 THEN vaccination_start_time + (response_time_to_update_system) ELSE vaccination_start_time	day	"vaccination start time" is the day when the campaign starts.
interval_for_second_round_of_vaccination	0	day	for interface.
length_of_vaccination_campaign	6	day	"length of vaccination campaign" can be adjusted according to the health workers capacity. The value is set at a 6 days campaign in Al-hudaydah (UNICEF, 2018).
number_of_vaccinated_people	IF switch_vaccine_dose=0 THEN	person	Number of people vaccinated depends on the vaccine dose policy (switch)

	desired_number_of_vaccines/"1_dose" ELSE IF switch_vaccine_dose=1 THEN desired_number_of_vaccines/"2_doses" ELSE 0		
potential_vaccine_recipients	recovered_asymptomatic_population + asymptomatic_population + susceptible_population + recently_infected_population	person	Individuals who are perceived as potential recipients of vaccines are individuals who were not previously infected with cholera. Besides susceptible individuals, this population includes asymptomatic individuals (both currently infected and recovered) and recently infected individuals because they cannot be differentiated by healthcare providers since there is no test before inoculation.
switch_vaccination	1	1	A switch to activate and deactivate the intervention
switch_vaccine_dose	0	1	A switch for 1 or 2 doses OCV policy. 1 as 1 dose; 2 as 2 doses
time_to_procure_vaccines	26	day	"time to procure vaccines" is the delay from the day to request vaccines from global vaccine stockpile, to the day the vaccines delivered to the health workers before the vaccination campaigns. According to Pezzoli (2020), in emergency settings, the longest delay was from the occurrence of the emergency to requesting OCV (median: 26 days). The parameter uses 26 days.
vaccination_start_time	600	day	"vaccination start time" is the day when the campaign starts.
vaccination_stop_time	indicated_vaccination_start_time+length_of_vaccination_campaign	day	"vaccination stop time" is the day after the campaign ends.
vaccination_susceptible	susceptible_population*indicated_fractional_vaccination/1	person/day	"vaccination susceptible" flow is the rate at which susceptible individuals leave the stock through multiplication with indicated fractional vaccination.
vaccine_effectiveness	0.76	1	Not everyone vaccinated will be immune to infection. A recent meta-analysis of seven randomized trials and six observational studies estimates the mean effectiveness of standard two-dose killed oral cholera vaccination at 76% with protection lasting for at least 3 years (Shim and Galvani, 2012). Also, Fung (2014) summarized five models on the Haitian cholera epidemic model parameters in Table (Appendix).
Water_provision:			

building_capacity_to_distribute_water	(desired_water_distribution_capacity-capacity_to_distribute_water)/time_to_increase_distribution_capacity	person/day/day	"building capacity to distribute water" is a goal seeking function at which the current capacity to distribute water is closing the gap with desired water distribution capacity over the time to increase distribution capacity (first order delay).
capacity_to_distribute_water(t)	capacity_to_distribute_water(t - dt) + (building_capacity_to_distribute_water) * dt	person/day	Taking into the implementation challenges such as delay in building capacity in supply side limitations, "capacity to distribute water" is expressed as number of people that can be provided with clean water.
Data_clean_water_provision	GRAPH(TIME) Points(364): (0.0, 0), (1.00550964187, 0), (2.01101928375, 0), ...	person/day	Clean water provision intervention data were derived from OCHA (2017). The overtime data only available for 2017.
day	1	day	1 day is used because water is daily essential need for human survival.
desired_water_distribution_capacity	GRAPH(IF switch_data_collection =2 THEN TIME + (response_time_to_update_system) ELSE TIME) Points(728): (0.0, 0), (1.00412654746, 0), (2.00825309491, 0), ...	person/day	"desired water distribution capacity" is adjusted according to the number of susceptible individuals requiring clean water. The variable input is a graphical function that has included the intervention historical data in 2017. It can be changed to test the policy impacts. The intervention start time include response time (delay) from the surveillance system.
fractional_susceptible_population	susceptible_population/Total_Population	1	Fraction of population remaining susceptible to cholera.
population_with_clean_water(t)	population_with_clean_water(t - dt) + (receiving_clean_water - stop_receiving_clean_water) * dt	person	Cholera occurs in areas with poor access to sanitation and unsafe drinking water - so providing people with clean drinking water is vital to preventing and curbing any outbreaks. Clean Water Provision Intervention provides people with sachets to purify water, truck clean water in, and install, fix and clean out sanitation facilities such as toilets in affected areas. The epidemiology model by Tuite et al. (2010) simplified the cholera water provision intervention with an assumption at which 100% reduction of “contact” rate if covered by clean water provision. Hence, in this model, a similar assumption is made to represent the population with clean water. The initial value is 0. However, people who have clean water are still vulnerable to infection through other routes, such fecal-oral transmission (which is not within the boundary of this model).
ratio_of_clean_water_in_reduc	0.7	1	Compared to Tuite et al. (2011) model on 100% reduction of "contact" rate if covered by clean water provision, this

ing_susceptibility			model assumes only 70% of individuals who receive clean water shift into the population with clean water stock. Figure 3 below illustrates the different pathways of cholera transmission. Having clean water does not ensure a 100% reduction in susceptibility (Wolfe et al., 2018). In addition, not all the water provision goes directly to the susceptibility population. The water provision is shared among all SIR sub-populations since there is no disaggregation among the recipients in this model. Hence, only a fraction of individuals from the susceptible population stock receives clean water.
receiving_clean_water	IF switch_data_collection=0 THEN 0 ELSE (IF switch_water_provision=1 THEN Data_clean_water_provision*susceptible_population_receiving_water*ratio_of_clean_water_in_reducing_susceptibility ELSE IF switch_water_provision=2 THEN capacity_to_distribute_water*susceptible_population_receiving_water*ratio_of_clean_water_in_reducing_susceptibility ELSE 0)	person/day	"receiving clean water' flow is the rate at which a fraction of susceptible population is receiving water based on the capacity to distribute water (supply). IF switch_water_provision=1 THEN "WASH_support_(data)"*susceptible_population_receiving_water ELSE IF switch_water_provision=2 THEN capacity_to_distribute_water*susceptible_population_receiving_water ELSE 0
stop_receiving_clean_water	population_with_clean_water/day	person/day	"stop receiving clean water" flow is the rate at which individuals who had received clean water leave the stock after one day (material delay) once they no longer provided with water. They become susceptible to cholera again.
susceptible_population_receiving_water	fractional_susceptible_population	1	"susceptible population receiving water" is the fractional susceptible population. This is an assumption of water is provided to the population without knowing who are the receivers. It is unrealistic to model all water provision goes to the susceptible population. Hence, only a fraction of the intervention is able to impact the population by reducing their susceptibility to cholera.
switch_water_provision	1	1	A switch to activate and deactivate the intervention
time_to_increase_distribution_capacity	14	day	"time to increase distribution capacity" is an assumptive duration (days) needed to increase the current capacity to meet the need from "desired water distribution capacity".

6.3 Appendix C: Sensitivity Analysis and Calibration

This appendix shows the sensitivity analysis (Monte Carlo analysis) run on all exogenous parameters and initial values using Sobol Sequence and Random Sampling. A base case run is given below, and each sensitivity run utilizes these values and changes one of the values in normal and incremental distribution within a preset range. The appendix is structured with two parts: SIR and intervention structures. A brief discussion about the insights of the sensitivity analysis follows the results for each tested parameter. For calibration, an example is shown on the last page.

Table 7. Summary of sensitivity test. (Click the parameters for further analysis results)

No	Parameters	Numerical	Behavioral	Interventions
1	connectedness of aquifers			
2	time to affect water in aquifers			
3	ratio of asymptomatic			
4	average incubation time			
5	average duration of illness asymptomatic			
6	susceptible population			
7	recently infected population			
8	asymptomatic population			
9	recovered asymptomatic population			
10	severe infected population			
11	normal ratio of severe disease			
12	time progress to next stage			
13	average duration of illness symptomatic			
14	average asymptomatic infection acquired immunity period			
15	fraction mildly infected seeking care			
16	fraction severe infected seeking care			
17	treated fatality fraction			
18	bacteria shedding from asymptomatic			
19	bacteria shedding from mildly infected			
20	bacteria shedding from severely infected			
21	effect of the fraction of infected on the fraction of contaminated water			

Indicators:

	Sensitive		Highly sensitive

No	Parameters	Numerical	Behavioral	Interventions
22	time to increase distribution capacity			
23	desired water distribution capacity			
24	vaccination start time			
25	desired number of vaccines			
26	time to procure vaccines			
27	desired sewage plant treatment			
28	degradation time			
29	effect of sewage plant treatment on sanitary condition			
30	time to increase treatment capacity			
31	weight of sewage plant support			
32	weight of latrine use			
33	ratio sewered population			
34	ratio open defecation			
35	building latrine start time			
36	time to build latrine			
37	people per latrine			
38	desired number of new latrine			
39	effect of sanitary on contaminated water			
40	building ORC start time			
41	time to build ORC			
42	desired number of ORC			
43	effect of ORC strain on fraction of severe disease			
44	desired number of DTC			
45	building DTC start time			
46	desired time to update system			

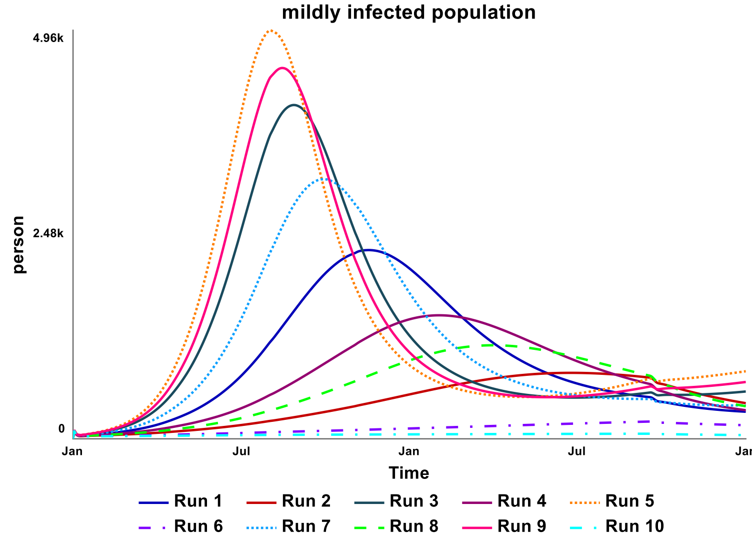
Indicators:

	Sensitive		Highly sensitive

1. SIR Model Component Structures: [Back to summary]

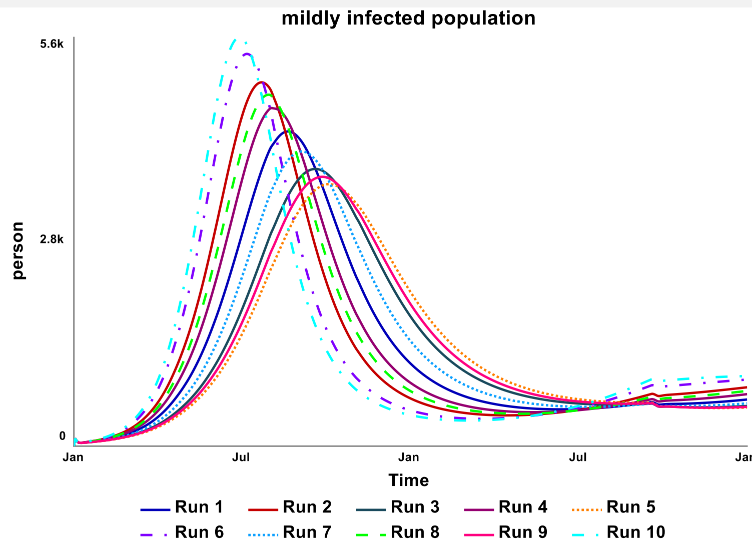
Sensi parameter	connectedness of aquifers
Run 1	0.12
Run 2	0.10
Run 3	0.13
Run 4	0.11
Run 5	0.14
Run 6	0.09
Run 7	0.12
Run 8	0.10
Run 9	0.14
Run 10	0.08

Result: Behavior over time graphs



The model is strongly (numerically and behaviourally) sensitive to changes in the value of "connectedness of aquifers" as expected. According to Pruyt's (2013) cholera model, this is an abstract concept related to the amount of reservoir water consumed. Adapting from Pryut's cholera model, this variable is a simplified and uncertain factor indicating the contact rate (susceptible population) with contaminated water. Higher connectedness values, higher impact on the infection rate (likewise). The variable is calibrated to the historical data, amounting to 13% in the base model.

	time to affect water in aquifers
Run 1	14
Run 2	11
Run 3	17
Run 4	12.5
Run 5	18.5
Run 6	9.5
Run 7	15.5
Run 8	11.75
Run 9	17.75
Run 10	8.75



The model is numerically sensitive to changes in the value of "time to affect water in aquifers" as expected. The variable controls the delay in "smoothed fraction of contaminated water". Hence, if the delay is short, the contaminated water reached or used by the susceptible population faster through the "indirect degree of infection" variable.

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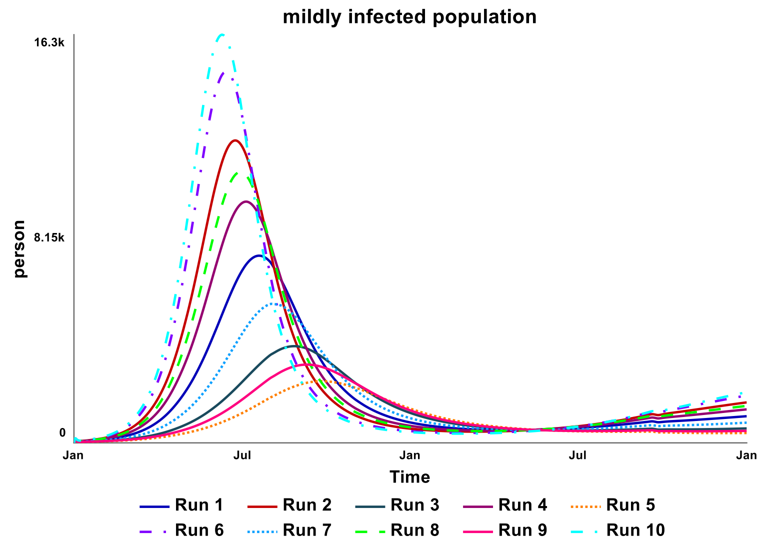
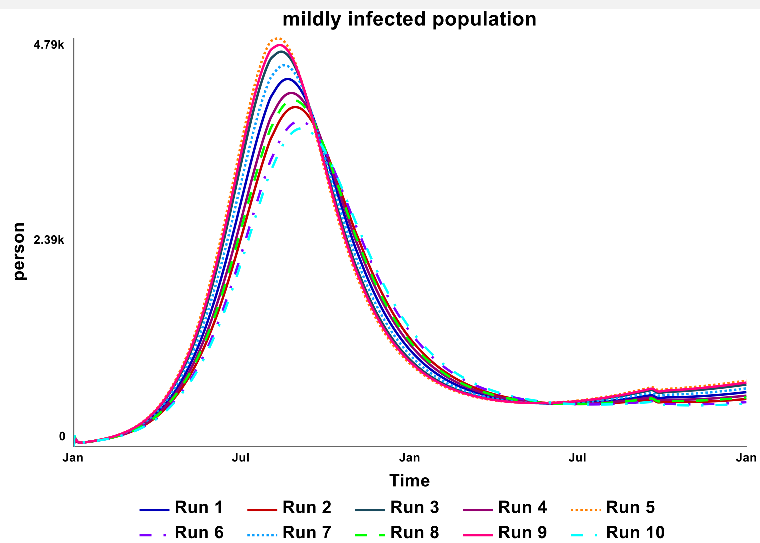
	ratio of asymptomatic
Run 1	0.68
Run 2	0.59
Run 3	0.76
Run 4	0.63
Run 5	0.81
Run 6	0.54
Run 7	0.72
Run 8	0.61
Run 9	0.78
Run 10	0.52



The model is strongly (numerically and behaviourally) sensitive to changes in the value of "ratio of asymptomatic" as expected. Since 75% of infections remain clinically unapparent, they are the 'silent spreader' in the communities.

	average incubation time
Run 1	1.00
Run 2	0.75
Run 3	1.25
Run 4	0.88
Run 5	1.38
Run 6	0.63
Run 7	1.13
Run 8	0.81
Run 9	1.31
Run 10	0.56



The model is numerically sensitive to changes in the value of "average incubation time" as expected. The value determines the infection progression rate to different stages of the disease; hence, it determines the differences of bacteria sheddings on the water contamination rate. The longer the incubation time, the longer the individuals stay in the recently infected population stock instead of moving on the severely infected population stock with higher bacteria shedding rate.

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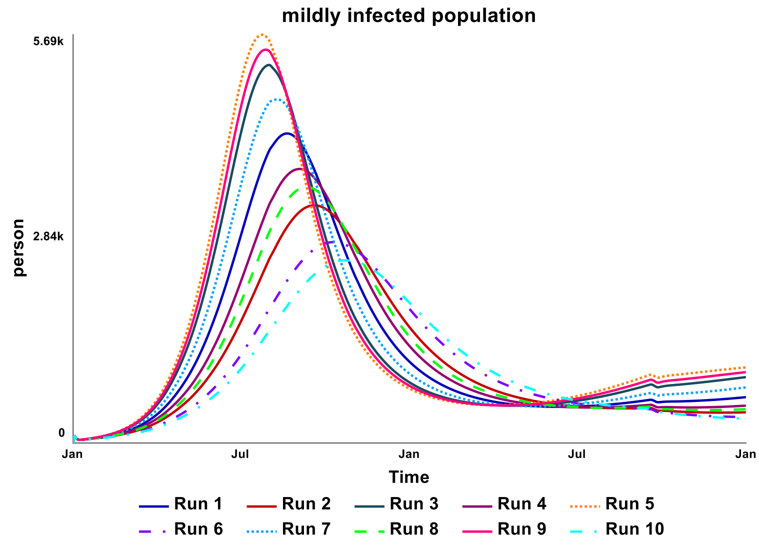
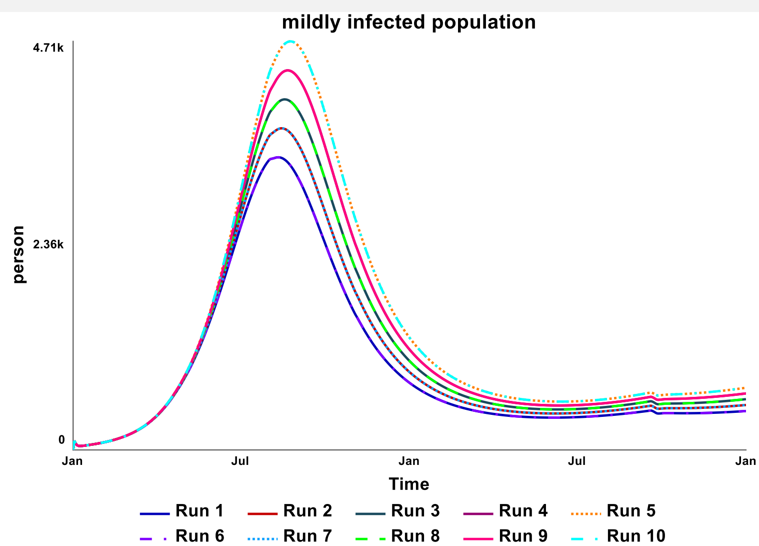
	average duration of illness asymptomatic
Run 1	5
Run 2	4
Run 3	6
Run 4	4.5
Run 5	6.5
Run 6	3.5
Run 7	5.5
Run 8	4.25
Run 9	6.25
Run 10	3.25



The model is strongly (numerically and behaviourally) sensitive to changes in the value of "average duration of illness asymptomatic" as expected. Since 75% of infections remain clinically unapparent, they are the 'silent spreader' in the communities. The faster the silent spreaders recovered, the lesser the bacteria shedding in contaminating the water source.

	susceptible population
Run 1	2500000
Run 2	2750000
Run 3	3000000
Run 4	3250000
Run 5	3500000
Run 6	2500000
Run 7	2750000
Run 8	3000000
Run 9	3250000
Run 10	3500000



The model is numerically sensitive to changes in the value of "susceptible population" (initial value) as expected. The infection rate depends on the number of susceptible individuals. If the initial population value is lower, the scale of the infected population is smaller. On the other hand, the sensitivity of the susceptible population stock also indicated a leverage point for interventions. Interventions targeting to reduce the susceptibility can strengthen the balancing feedback loop and flatten the infection curve.

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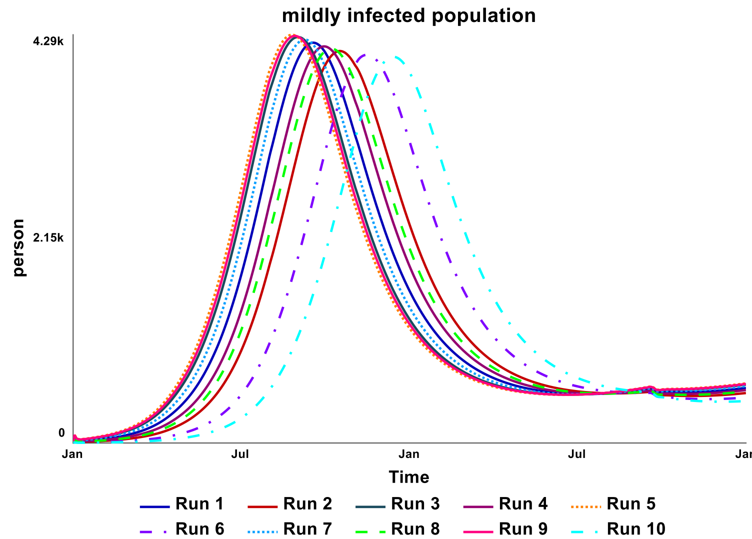
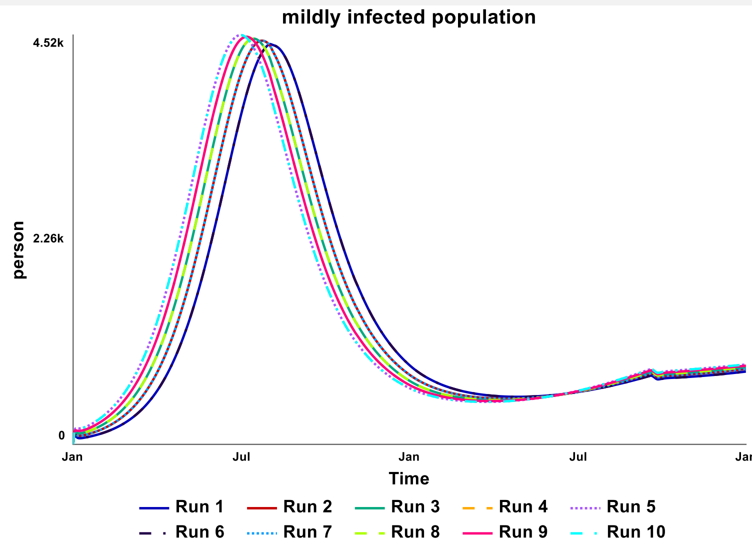
	recently infected population
Run 1	500.50
Run 2	250.75
Run 3	750.25
Run 4	375.63
Run 5	875.13
Run 6	125.88
Run 7	625.38
Run 8	313.19
Run 9	812.69
Run 10	63.44



The model is numerically sensitive to changes in the value of "recently infected population" (initial value) as expected. A higher number of infected individuals in the population increases the strength of the infection reinforcing feedback loop. Hence, one of the leverage points is to prevent people from getting infected in the first place.

	asymptomatic population
Run 1	500
Run 2	778
Run 3	1056
Run 4	1333
Run 5	1611
Run 6	1889
Run 7	2167
Run 8	2444
Run 9	2722
Run 10	3000



The model is numerically sensitive to changes in the value of "asymptomatic population" (initial value) as expected. Similar results were found with tests on "mildly infected population", "untreated mildly infected population", and "treated mildly infected population". A higher number of asymptomatic and mild infected individuals in the population increases the strength of the infection reinforcing feedback loop. Among the infected individuals, 75% are asymptomatic, and 15% are mildly symptomatic (Kaper, Morris, & Levine, 1995; Médecins Sans Frontières, 2018). This underscores a key challenge in stopping the epidemic: If people do not know they are infected, they are probably not taking steps to prevent transmitting it (treated mildly infected population might not be identified as cholera patients because it is clinically indistinguishable from other causes of diarrheal illness). To prevent bacteria shedding from silent spreaders in contaminating water sources, policies must focus on improving sanitary conditions (infrastructures) and preventing people from getting infected in the first place.

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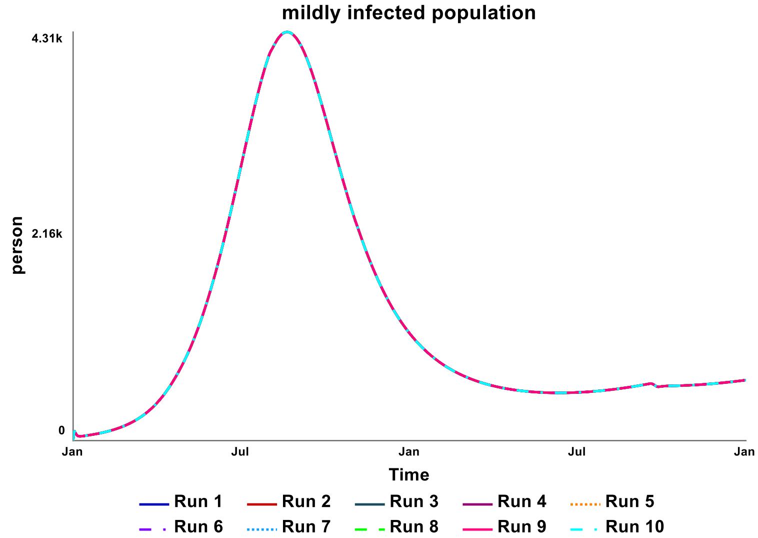
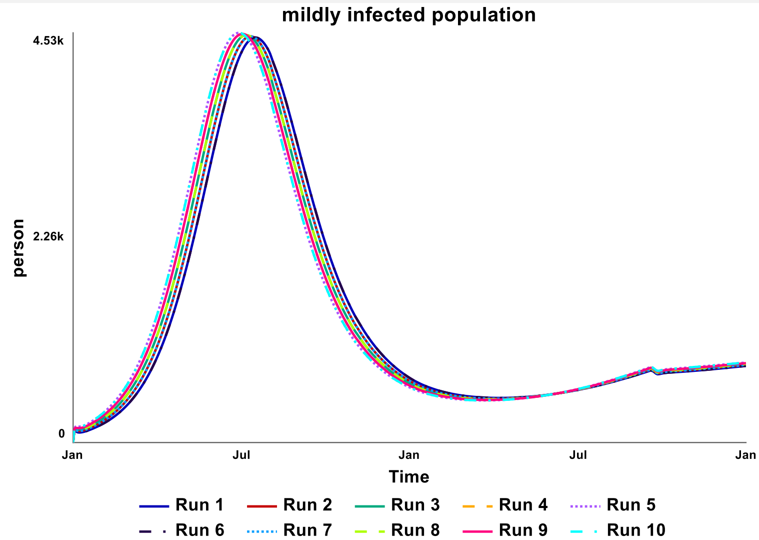
	recovered asymptomatic population
Run 1	500.50
Run 2	250.75
Run 3	750.25
Run 4	375.63
Run 5	875.13
Run 6	125.88
Run 7	625.38
Run 8	313.19
Run 9	812.69
Run 10	63.44



The model is insensitive to changes in the value of "recovered asymptomatic population" (initial value) as expected. Similar results were found with tests on "recovered immune untreated population", "treated severe population", "recovered immune treated population". These sub-population are part of the balancing feedback loops in the model.

	severe infected population
Run 1	500.50
Run 2	250.75
Run 3	750.25
Run 4	375.63
Run 5	875.13
Run 6	125.88
Run 7	625.38
Run 8	313.19
Run 9	812.69
Run 10	63.44



The model is slight numerically sensitive to changes in the value of "severe infected population" (initial value) as expected. A similar result was found with a test on "untreated severe population". Although only 10% of all infected individuals progress into a severe disease state, bacteria shedding is highest among the severely infected individuals (Kaper, Morris, & Levine, 1995). Hence, it is crucial to treat these individuals, prevent deaths, and prevent them from contaminating water sources.

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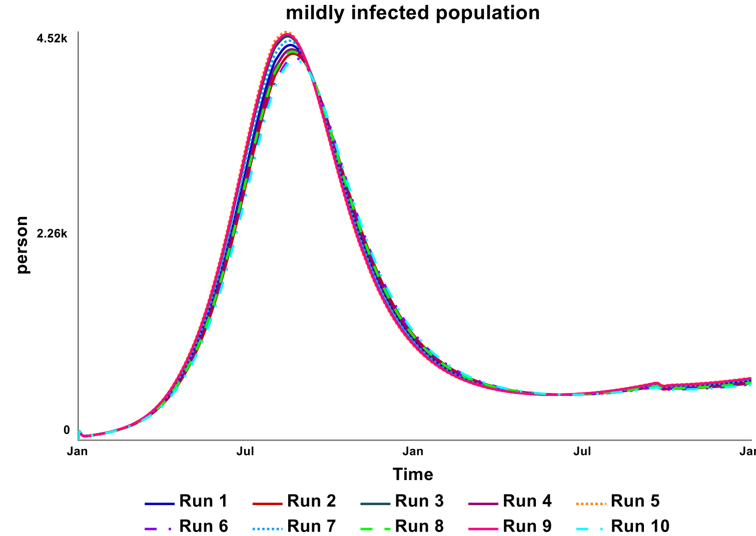
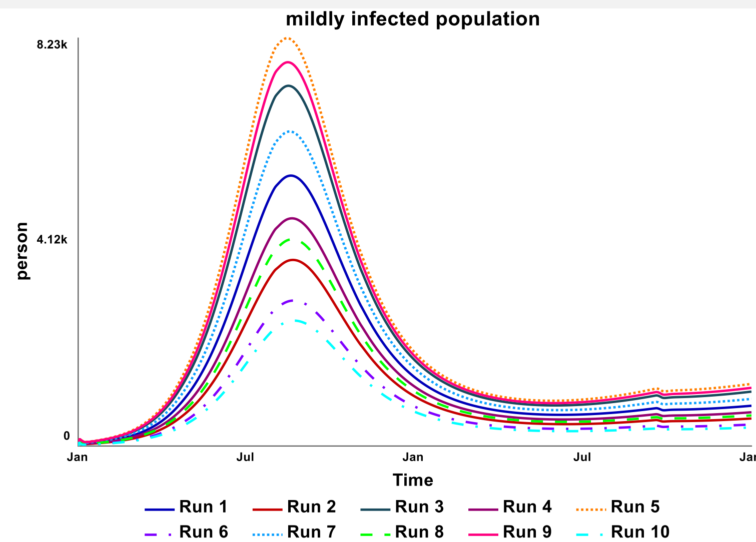
	normal ratio of severe disease
Run 1	0.35
Run 2	0.28
Run 3	0.43
Run 4	0.31
Run 5	0.46
Run 6	0.24
Run 7	0.39
Run 8	0.29
Run 9	0.44
Run 10	0.22



The model is slight numerically sensitive to changes in the value of "normal ratio of severe disease" as expected. The testing range is small, between 9-11% of all infected individual because this parameter is determining the flow from mild infection to severe infection. Hence, 0.4 (40%) of the mild infected population progresses into severe infected population. If this ratio were increased from 10% of all infected populations, it gives numerical and behavioral sensitivity results.

	time progress to next stage
Run 1	1.25
Run 2	0.88
Run 3	1.63
Run 4	1.06
Run 5	1.81
Run 6	0.69
Run 7	1.44
Run 8	0.97
Run 9	1.72
Run 10	0.59



The model is strongly (numerically) sensitive to changes in the value of "time progress to next stage" as expected. The faster the infected individuals leave the mild and severe infected stocks, the faster they move to the recovery state, attributing to the balancing feedback loops.

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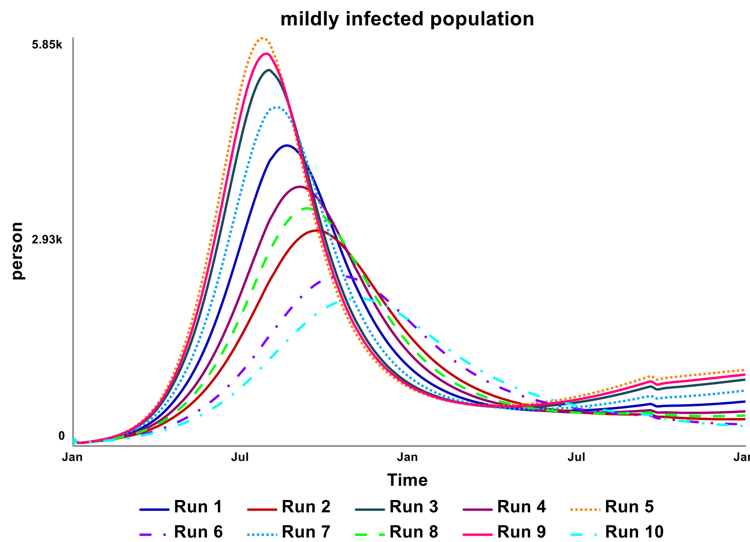
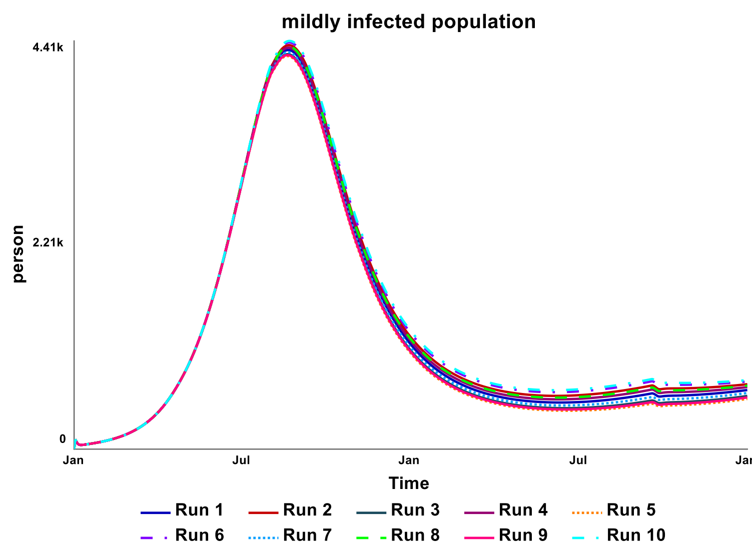
	average duration of illness symptomatic
Run 1	9
Run 2	7
Run 3	11
Run 4	8
Run 5	12
Run 6	6
Run 7	10
Run 8	7.5
Run 9	11.5
Run 10	5.5



The model is strongly (numerically and behaviourally) sensitive to changes in the value of "average duration of illness symptomatic" as expected. The faster the infected individuals leave the infectious stocks into the recovery stocks, the stronger the strength of the balancing feedback loops.

	average asymptomatic infection acquired immunity period
Run 1	180
Run 2	165
Run 3	195
Run 4	172.5
Run 5	202.5
Run 6	157.5
Run 7	187.5
Run 8	168.75
Run 9	198.75
Run 10	153.75



The model is numerically sensitive to changes in the value of "average asymptomatic infection acquired immunity period" as expected. A similar result was found with a test on "average symptomatic infection acquired immunity period. When individuals stay in the recovered stocks longer, more individuals are accumulated in the recovered stocks, strengthening the balancing feedback loops.

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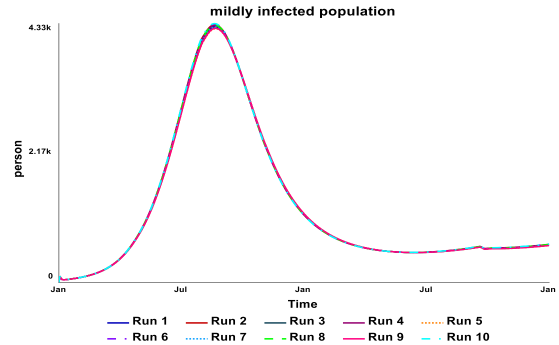
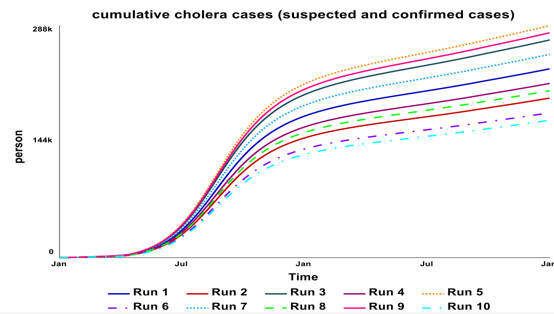
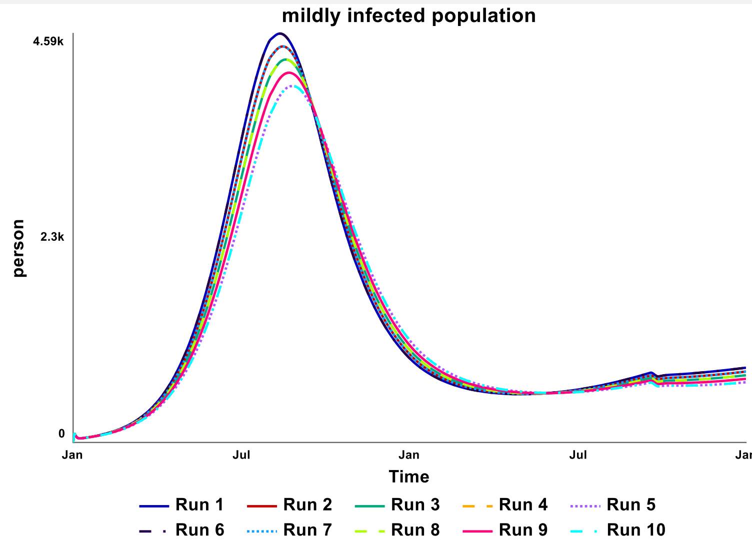
	fraction mildly infected seeking care
Run 1	0.20
Run 2	0.15
Run 3	0.25
Run 4	0.18
Run 5	0.28
Run 6	0.13
Run 7	0.23
Run 8	0.16
Run 9	0.26
Run 10	0.11





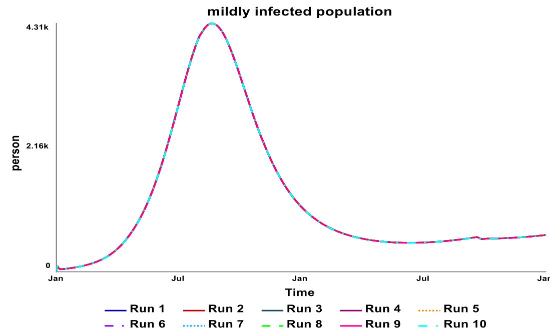
The model is insensitive to changes in the value of "fraction mildly infected seeking care" as expected. For mildly infected cases, individuals are provided with oral rehydration treatment that is not helping to prevent bacteria shedding into the environment. On the other hand, the reported cholera cases are numerically sensitive to this parameter change. The surveillance system relies on reported cases from ORC and DTC in Yemen. Hence, if more people seek treatment (demand) and more treatment centers are available (supply), the reported cholera cases are higher.

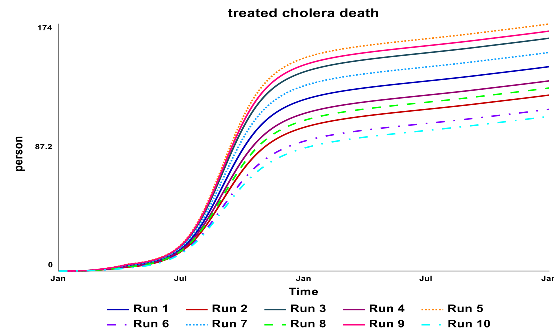
	fraction severe infected seeking care
Run 1	0.20
Run 2	0.23
Run 3	0.27
Run 4	0.30
Run 5	0.33
Run 6	0.37
Run 7	0.40
Run 8	0.43
Run 9	0.47
Run 10	0.50



The model is numerically sensitive to changes in the value of "fraction severe infected seeking care" as expected. A ratio of severely infected individuals required emergency treatment at DTC, where the excretion of the individuals at the centers is treated before entering the sewage system. Hence, reducing the risk of water contamination by cholera bacteria shedding.

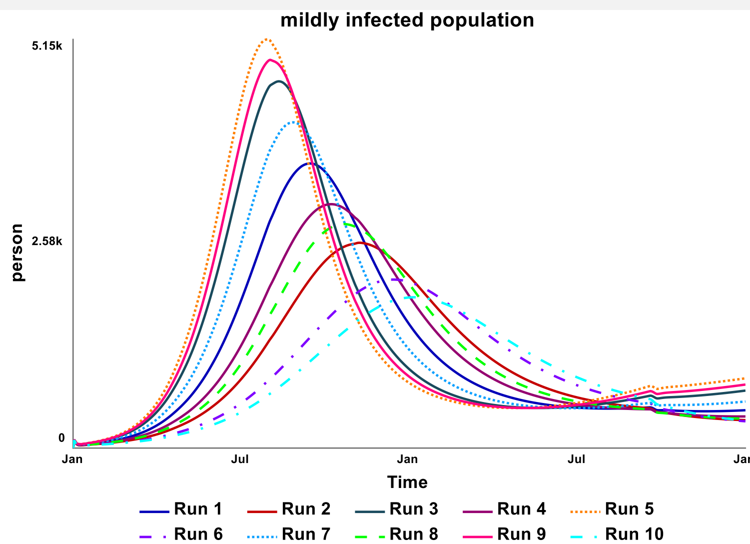
	treated fatality fraction
Run 1	0.0013
Run 2	0.0009
Run 3	0.0016
Run 4	0.0011
Run 5	0.0018
Run 6	0.0007
Run 7	0.0014
Run 8	0.0010
Run 9	0.0017
Run 10	0.0006





The model is insensitive to changes in the value of "treated fatality fraction" as expected. Similar results were found with tests on "untreated fatality fraction", "treated fatality fraction", "service capacity sensitivity", and "service strain fatality fraction". All these parameters are sensitive to the cholera deaths.

	bacteria shedding from asymptomatic
Run 1	0.60
Run 2	0.50
Run 3	0.70
Run 4	0.55
Run 5	0.75
Run 6	0.45
Run 7	0.65
Run 8	0.53
Run 9	0.73
Run 10	0.43



The model is strongly (numerically and behaviourally) sensitive to changes in the value of "bacteria shedding from asymptomatic" as expected. Although the tested values are the lowest among the three infectious levels of bacteria sheddings, the highest number of asymptomatic individuals (75%) attribute to the high sensitivity of this parameter value.

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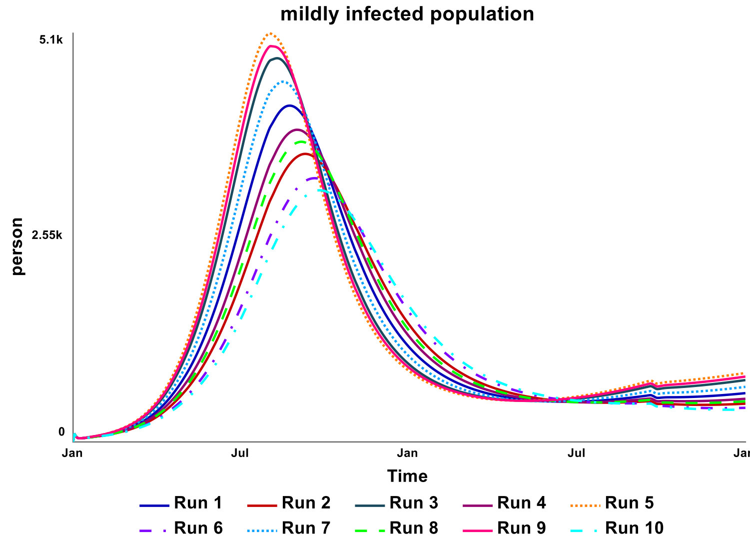
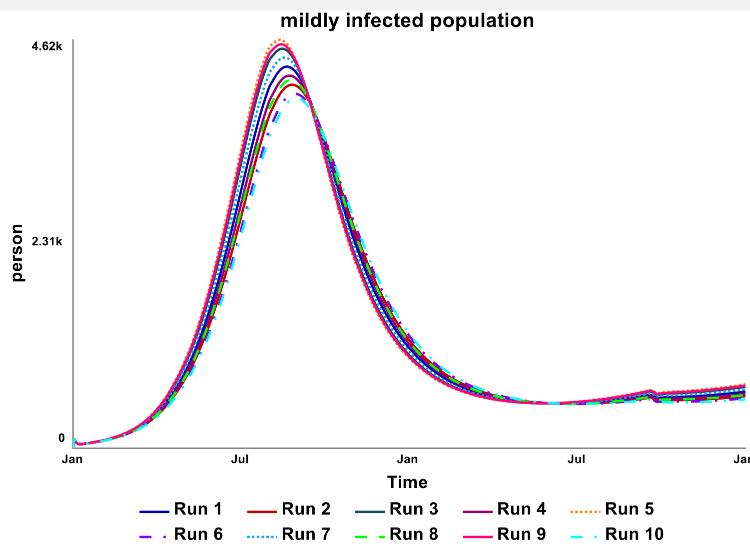
	bacteria shedding from mildly infected
Run 1	1.30
Run 2	1.15
Run 3	1.45
Run 4	1.23
Run 5	1.53
Run 6	1.08
Run 7	1.38
Run 8	1.19
Run 9	1.49
Run 10	1.04



The model is numerically sensitive to changes in the value of "bacteria shedding from mildly infected" as expected. For mildly infected cases, they shed bacteria into the environment with and without treatment.

	bacteria shedding from severely infected
Run 1	2.00
Run 2	1.75
Run 3	2.25
Run 4	1.88
Run 5	2.38
Run 6	1.63
Run 7	2.13
Run 8	1.81
Run 9	2.31
Run 10	1.56



The model is numerically sensitive to changes in the value of "bacteria shedding from severely infected", and least sensitive compared to the other two infectious level of bacteria shedding, as expected. First, the number of severely infected individuals is only account for 10% of the total infected population. Second, among this 10% severely infected individuals, those who received treatment at DTC are assumed to not contribute to the bacteria shedding into the environment as the excretion of the individuals at the centers is treated before entering the sewage system.

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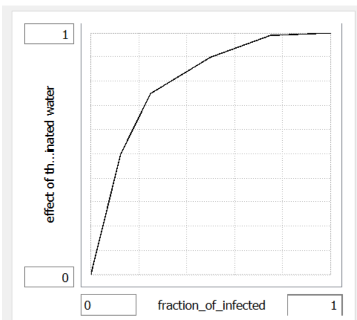
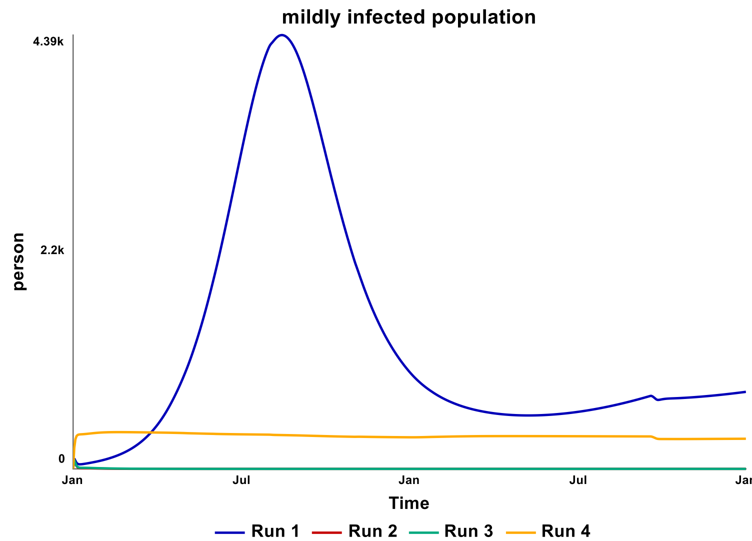
effect of the fraction of infected on the fraction of contaminated water

Run 1 – logarithmic growth
Run 2 – exponential growth
Run 3 – linear growth
Run 4 – S-shape growth





The model is strongly (numerically and behaviourally) sensitive to changes in the graphical function shape of "effect of the fraction of infected on the fraction of contaminated water", as expected. This effect refers to Pryut's cholera model (2013). The effect of the fraction of infected on the fraction of contaminated water is a graphical function: if the fraction of infected is 0% then the fraction of contaminated water is assumed to be 0%, if it is 12.5% then the fraction of contaminated water is assumed to be 5%, if it is 25% then the fraction of contaminated water is assumed to be 75%, if it is 50% then the fraction of contaminated water is assumed to be 90%, if it is 75% then the fraction of contaminated water is assumed to be 99%, and if it is 100% then the fraction of contaminated water is assumed to be 100%. This relationship is also an assumption in Pryut's cholera model. Compared to other curves in the graphical function, the assumption from Pryut's model shows a behavior that is expected from the model.

2. Intervention Component Structures:

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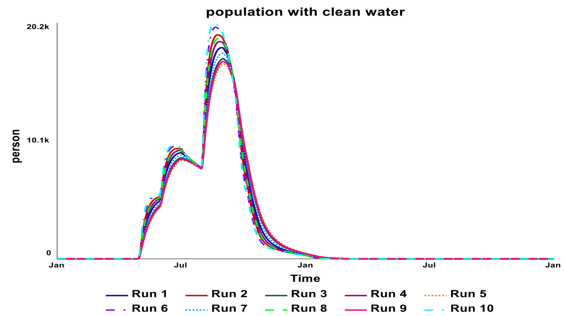
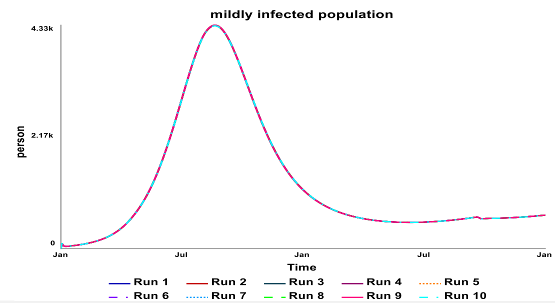
Clean water provision

	time to increase distribution capacity
Run 1	13
Run 2	9
Run 3	17
Run 4	11
Run 5	19
Run 6	7
Run 7	15
Run 8	10
Run 9	18
Run 10	6

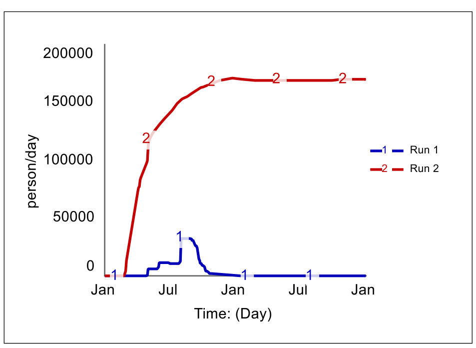


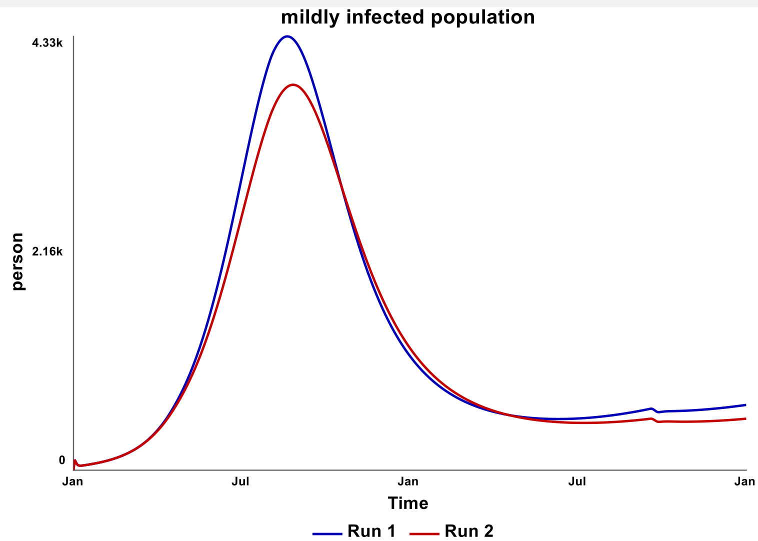


The model is insensitive to changes in the value of "time to increase distribution capacity" as expected because the model is simulated on the historical data of intervention. The intervention barely showed an impact because the resources were limited. However, the population with clean water is numerically sensitive to the delay of this parameter. If the supply of water is provided faster, more individuals move from the susceptible stock into the population with clean water stock faster, increasing the strength of the balancing feedback loop.

desired water distribution capacity

Run 1 - historical data in 2017
Run 2 – test

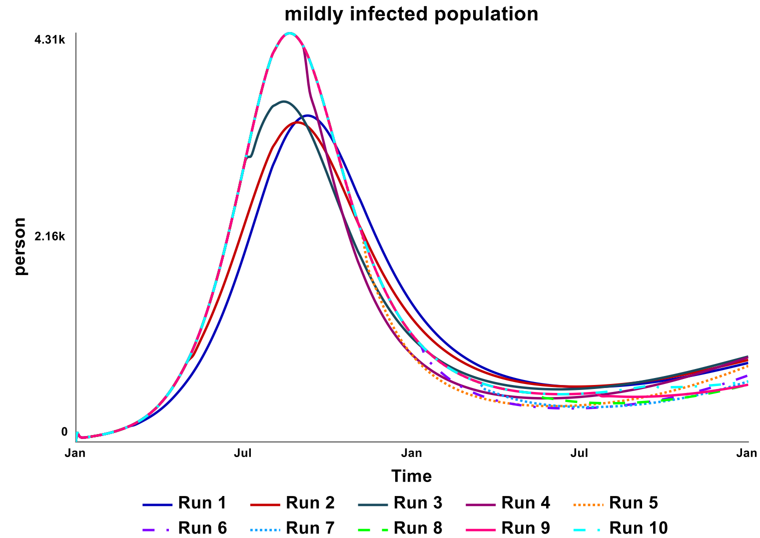




The model is numerically sensitive to changes in the value of "desired water distribution capacity" as expected. When more individuals move from the susceptible stock into the population with clean water stock, the strength of the balancing feedback loop increases.

Vaccination [Back to summary]

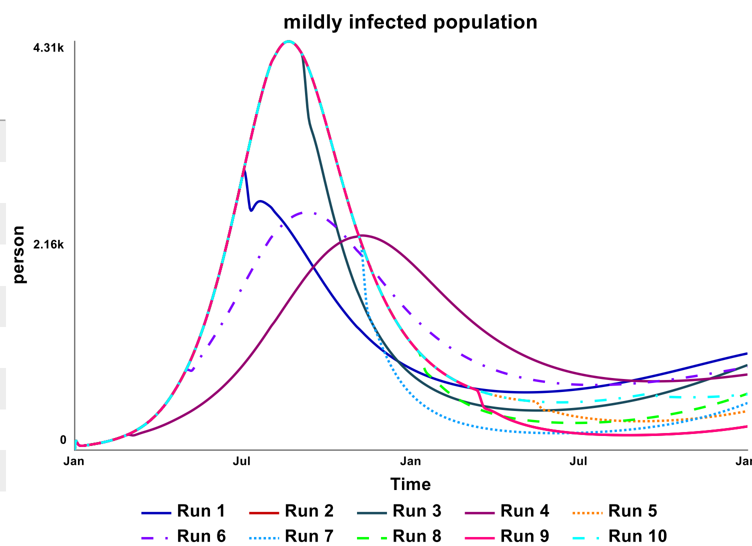
	vaccination start time
Run 1	30
Run 2	93
Run 3	157
Run 4	220
Run 5	283
Run 6	347
Run 7	410
Run 8	473
Run 9	537
Run 10	600



The model is numerically sensitive to changes in the value of "vaccination start time" as expected. With the same amount of vaccine provision in Al-hudaydah (260,000 vaccines - intervention historical data), an earlier vaccine campaign shows a significant reduction of infected population.

	vaccination start time	desired number of vaccines
Run 1	156	890000
Run 2	410	1000000
Run 3	220	450000
Run 4	30	780000
Run 5	473	560000
Run 6	93	560000
Run 7	283	1000000
Run 8	346	450000
Run 9	410	1000000
Run 10	600	340000

One vaccine dose policy



The model is strongly (numerically and behaviourally) sensitive to changes in the values of "vaccination start time" and "desired number of vaccines". For example, Run 4 (780,000 vaccines on day 30) shows the most promising outcome. However, it is unrealistic to implement such vaccine procurement in such a short amount of time. Run 6 (560,000 vaccines on day 93) shows a more realistic approach, with a low number of vaccines but earlier vaccine provision to the population reduces the mildly infected population profoundly. Run 9 (1,000,000 vaccines on day 410) shows the least favorable impact. Even though there are one million vaccines, providing vaccines very late in the epidemic gives minimal impact.

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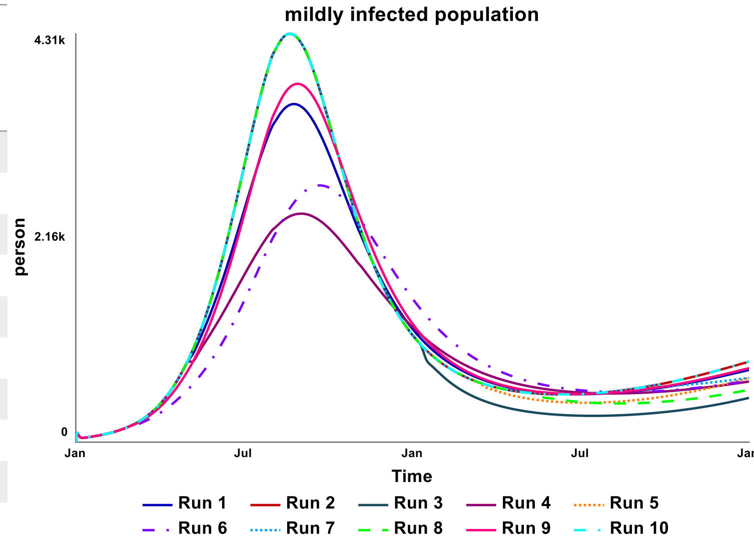
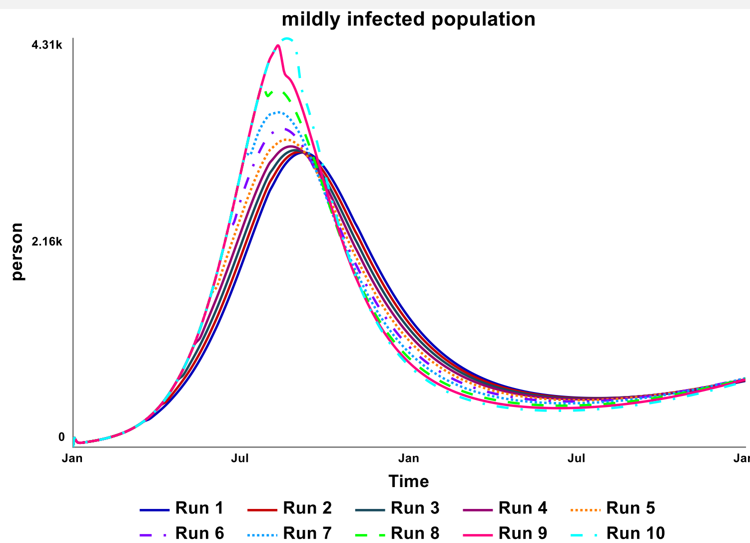
	vaccination start time	desired number of vaccines
Run 1	93	340000
Run 2	537	10000
Run 3	347	670000
Run 4	93	1000000
Run 5	410	230000
Run 6	30	780000
Run 7	600	340000
Run 8	473	450000
Run 9	30	230000
Run 10	537	10000



Two vaccine dose policy

The model is strongly (numerically and behavioral) sensitive to changes from one-dose to a two-dose policy with the same testing range in the one-dose policy. The two-dose policy provides three years of protection compared to one year in one dose vaccination. When the individuals are protected longer, it contributes to the balancing feedback loops. The oscillation in late 2018 is dampened more in two dose policy compared to one dose policy.

	time to procure vaccines
Run 1	15
Run 2	33
Run 3	52
Run 4	70
Run 5	88
Run 6	107
Run 7	125
Run 8	143
Run 9	162
Run 10	180



By setting the model at two doses policy, 560,000 vaccines, and starting on day 60: the model is numerically sensitive to changes in the value of "time to procure vaccines" as expected. This delay takes into consideration of implementation challenges of capacity building. The delay attributes to the delay in providing vaccines to the population. Hence, the sooner the vaccine provision starts in an epidemic, the faster the balancing feedback loop is strengthened, reducing the infected population.

Sanitation infrastructure conditions

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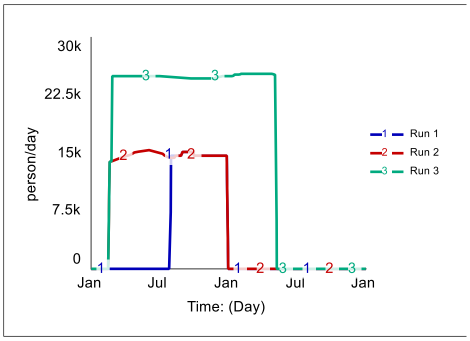
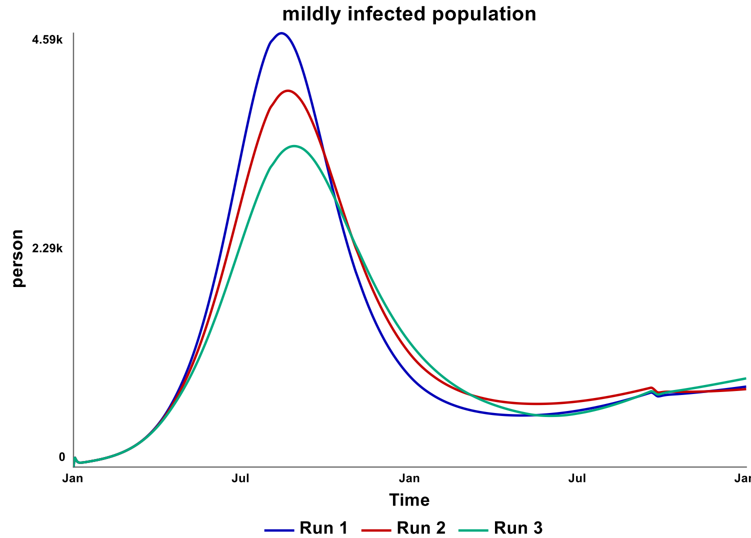
desired sewage plant treatment

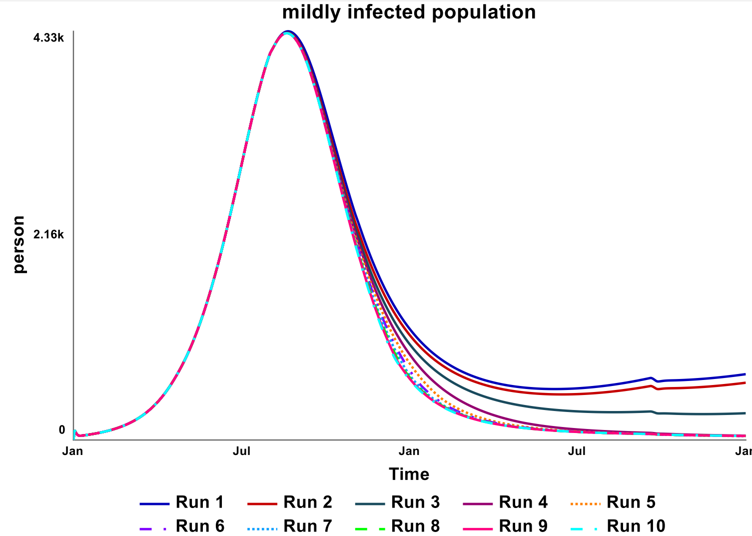
Run 1 – historical data
Run 2 – earlier intervention
Run 3 – double the intervention





The model is strongly (numerically) sensitive to changes in the values of "desired sewage plant treatment" as expected. The infection reinforcing feedback loop is affected by the water source contamination by the infected individuals. If the current sewage plant treatment is well supported, there is less water contamination by cholera.

	degradation time
Run 1	10
Run 2	49
Run 3	89
Run 4	128
Run 5	168
Run 6	207
Run 7	247
Run 8	286
Run 9	326
Run 10	365



The model is numerically sensitive to changes in the value of "degradation time" as expected. Assuming a sewage treatment plant needs maintenance after a certain period (degradation time). If the degradation time is longer, the resources (intervention historical data) to support the treatment plant could have reached more treatment plants. As a result, there is a reduction in water contamination by cholera.

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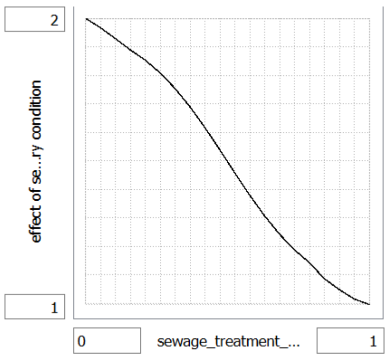
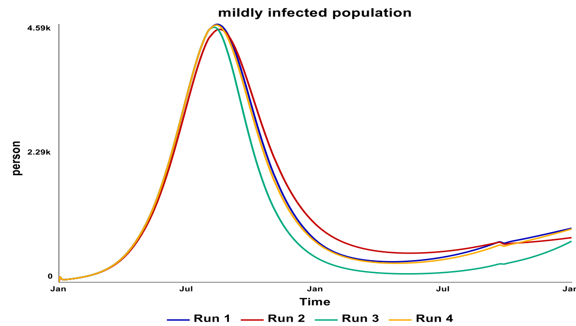
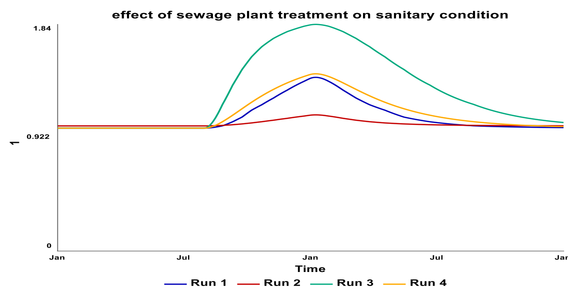
effect of sewage plant treatment on sanitary condition

Run 1 – S-shape decay
Run 2 – exponential decay
Run 3 – logarithmic decay
Run 4 – linear decay

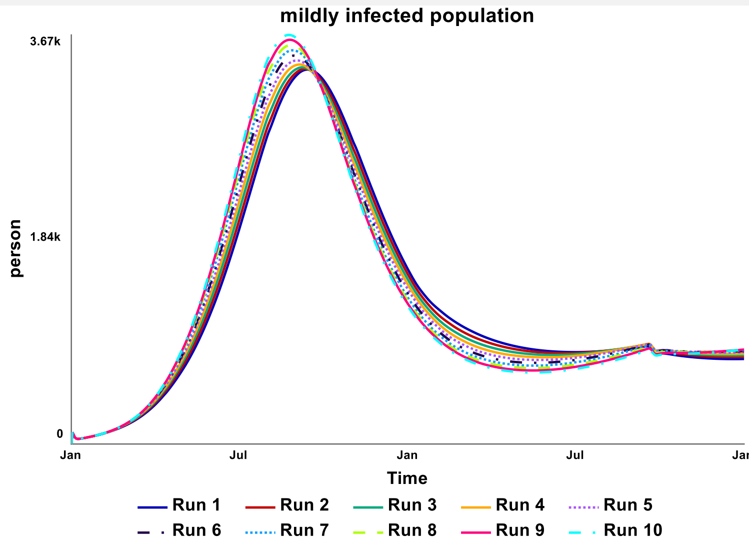






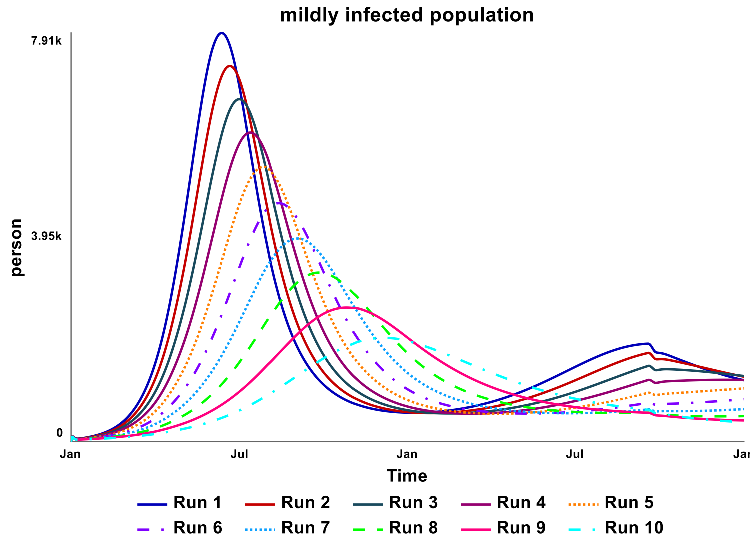
The model is numerically sensitive to changes in the graphical function shape of "effect of sewage plant treatment on sanitary condition", as expected. Run 1 (S-shape decay) and Run 4 (linear decay) show similar behavior. However, very few relationships are linear due to the problem's complexity. Hence, non-linear S-shape decay is assumed to represent the effect of sewage plant treatment on sanitary conditions.

	time to increase treatment capacity
Run 1	10
Run 2	20
Run 3	30
Run 4	40
Run 5	50
Run 6	60
Run 7	70
Run 8	80
Run 9	90
Run 10	100



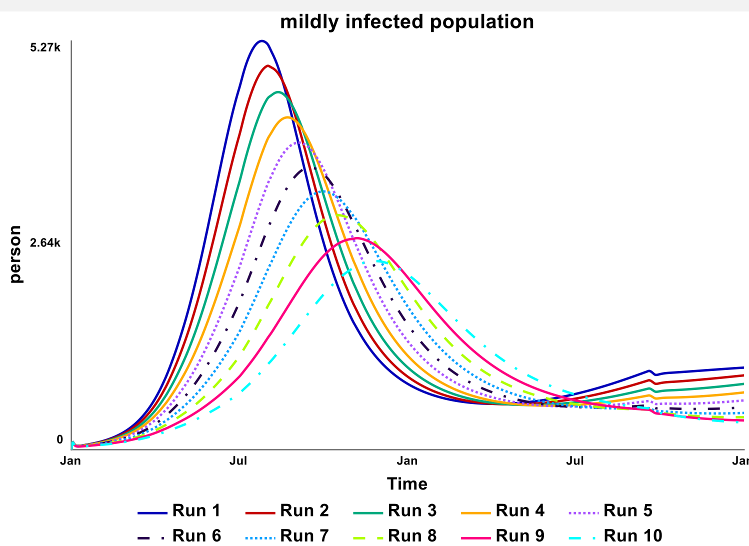
The model is numerically sensitive to changes in the value of "time to incrase treatment capacity" as expected. This delay takes into consideration of implementation challenges of capacity building. Hence, the faster the intervention begins, the sooner the balancing feedback loop being strengthened (reducing water contamination), decreasing the infected population.

	weight of sewage plant support
Run 1	0.20
Run 2	0.26
Run 3	0.31
Run 4	0.37
Run 5	0.42
Run 6	0.48
Run 7	0.53
Run 8	0.59
Run 9	0.64
Run 10	0.70



The model is strongly (numerically and behavioral) sensitive to changes in the values of "weight of sewage plant support" as expected. This is one of the crucial leverage points on the sanitary condition as the highest numbers of cholera cases have been reported in places where sewage treatment plants are non-functional. Without working sewage treatment plants, raw sewage is often diverted to poor neighborhoods and agricultural lands (leads to contamination of the shallow aquifers and wells) where local civilians and private tankers collect drinking water. The value is conceptualized with a higher weight than "latrine use" and "other infrastructure states" on the highly sensitive effect of sanitary on contaminated water (strong leverage point).

	weight of latrine use
Run 1	0.10
Run 2	0.13
Run 3	0.17
Run 4	0.20
Run 5	0.23
Run 6	0.27
Run 7	0.30
Run 8	0.33
Run 9	0.37
Run 10	0.40



By setting the model at 500 additonal latrines, and starting on day 100: the model is strongly (numerically and behavioral) sensitive to changes in the value of "weight of latrine use" as expected. This intervention affects the sanitary condition substantially as open defecation can lead to contamination of the shallow aquifers and wells.

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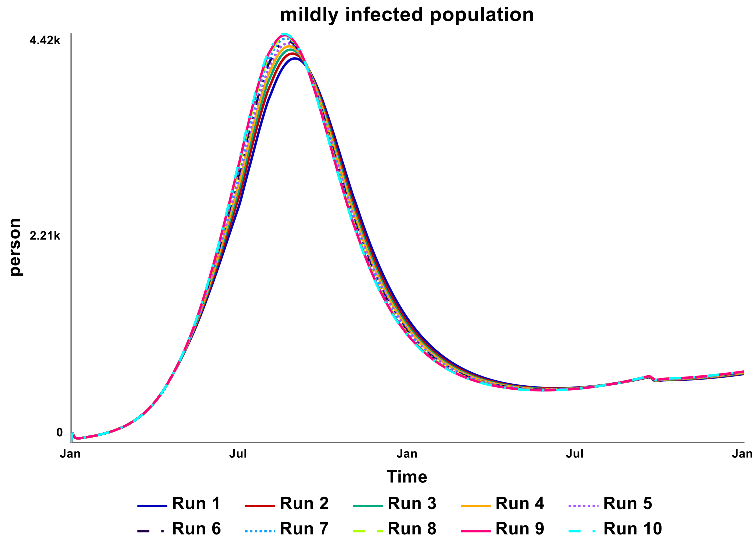
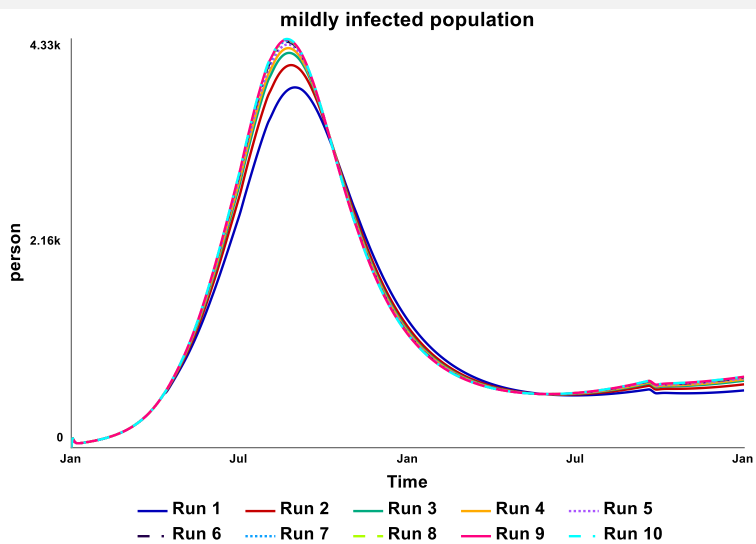
	ratio sewered population
Run 1	0.4
Run 2	0.45
Run 3	0.5
Run 4	0.55
Run 5	0.6
Run 6	0.65
Run 7	0.7
Run 8	0.75
Run 9	0.8
Run 10	0.85



The model is numerically sensitive to changes in the value of "ratio sewered population" as expected. Assuming that the sewage treatment plant intervention (historical data) remains the same but the ratio value differs, the impact would also differ following the changing needs for sewage plant treatment.

	ratio open defecation
Run 1	0.005
Run 2	0.006
Run 3	0.007
Run 4	0.008
Run 5	0.009
Run 6	0.011
Run 7	0.012
Run 8	0.013
Run 9	0.014
Run 10	0.015



The model is numerically sensitive to changes in the value of "ratio open defecation" as expected. Assuming that the number of latrine building remains the same but the ratio of open defecation differs, the impact would also differ following the changing needs for latrines.

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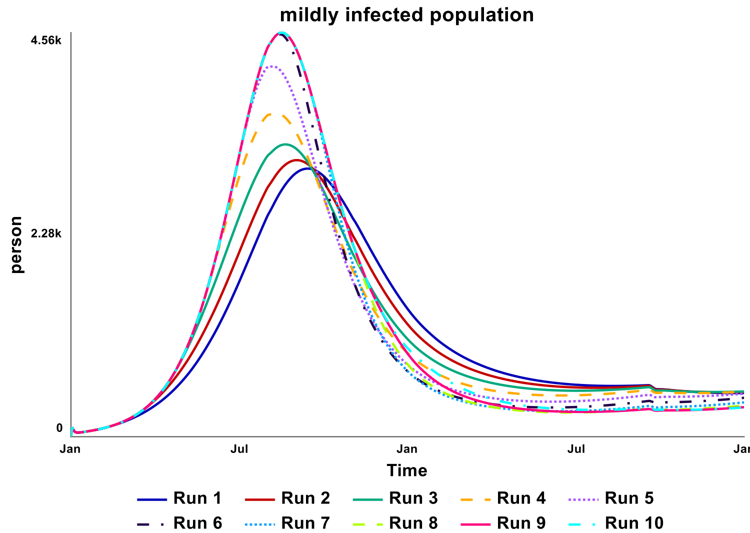
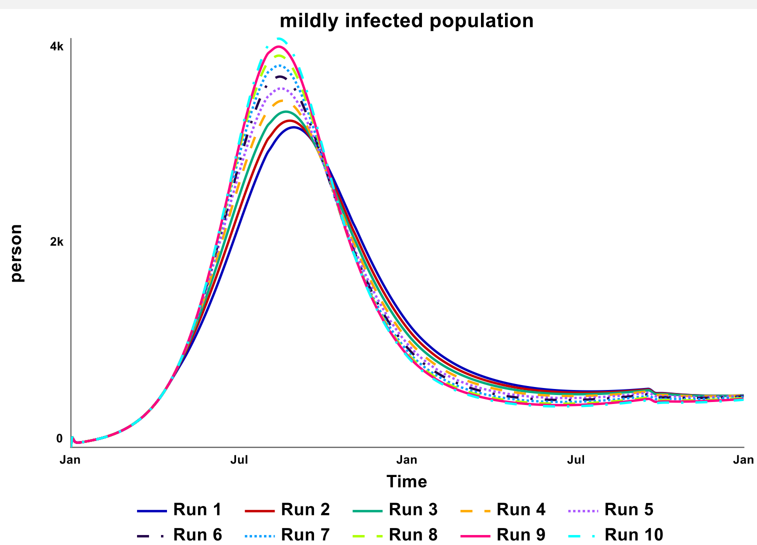
	building latrine start time
Run 1	30
Run 2	67
Run 3	104
Run 4	142
Run 5	179
Run 6	216
Run 7	253
Run 8	291
Run 9	328
Run 10	365



By setting the model at 1000 additional latrines: the model is numerically sensitive to changes in the value of "building latrine start time" as expected. With the same amount of latrine provision in Al-hudaydah, an earlier vaccine campaign shows a significant reduction of infected population.

	time to build latrine
Run 1	15
Run 2	23
Run 3	32
Run 4	40
Run 5	48
Run 6	57
Run 7	65
Run 8	73
Run 9	82
Run 10	90



By setting the model at 1000 additional latrines, and starting on day 100: the model is numerically sensitive to changes in the value of "time to build latrine" as expected. This delay takes into consideration of implementation challenges of capacity building. Hence, the faster the intervention begins, the sooner the balancing feedback loop being strengthened (reducing water contamination), decreasing the infected population.

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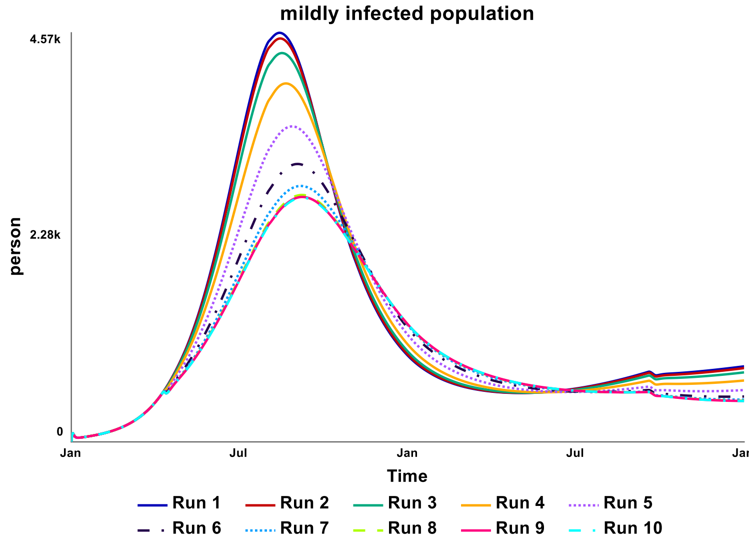
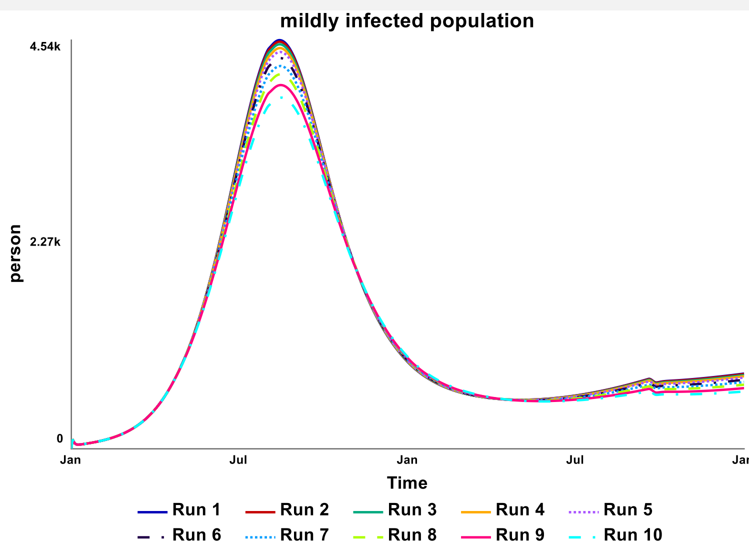
	people per latrine
Run 1	10
Run 2	20
Run 3	30
Run 4	40
Run 5	50
Run 6	60
Run 7	70
Run 8	80
Run 9	90
Run 10	100



By setting the model at 500 additional latrines, and starting on day 100: the model is numerically sensitive to changes in the value of "people per latrine" as expected. The higher the value, the more Al-hudaydah population would be covered by latrine and sewage system (assuming the latrines are well maintained).

	desired number of new latrine
Run 1	250
Run 2	306
Run 3	361
Run 4	417
Run 5	472
Run 6	528
Run 7	583
Run 8	639
Run 9	694
Run 10	750



By setting the model at 500 additional latrines, people per latrine at 20, and starting on day 100: the model is numerically sensitive to changes in the value of "desired number of new latrine" as expected. The higher the value, the more Al-hudaydah population would be covered by latrine and sewage system (assuming the latrines are well maintained).

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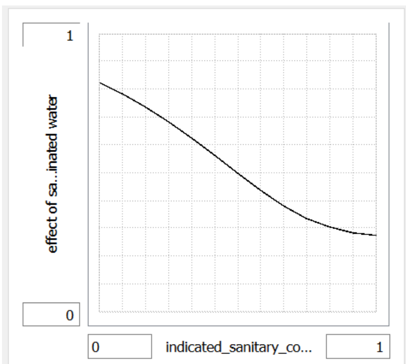
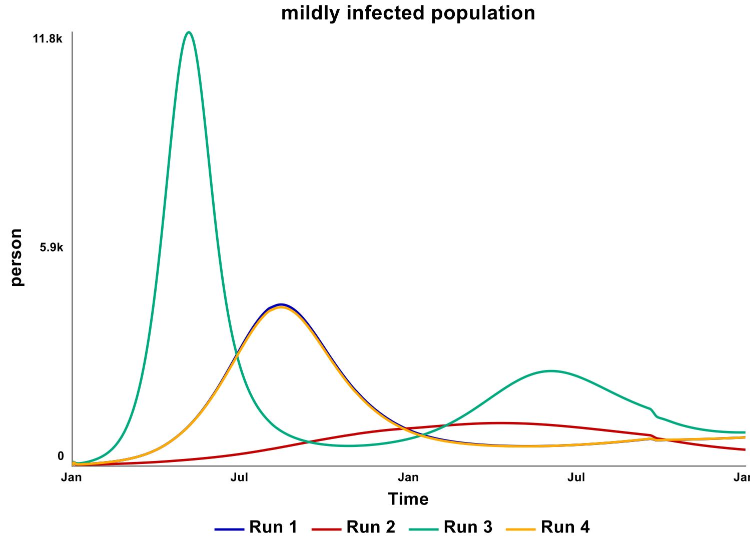
effect of sanitary on contaminated water

Run 1 – S-shape decay
Run 2 – exponential decay
Run 3 – logarithmic decay
Run 4 – linear decay





The model is strongly (numerically and behavior) sensitive to changes in the graphical function shape of "effect of sanitary on contaminated water", as expected. Run 1 (S-shape decay) and Run 4 (linear decay) show similar behavior. However, very few relationships are linear due to the problem's complexity. Hence, a non-linear S-shap decay is assumed to represent a sanitary effect on contaminated water.

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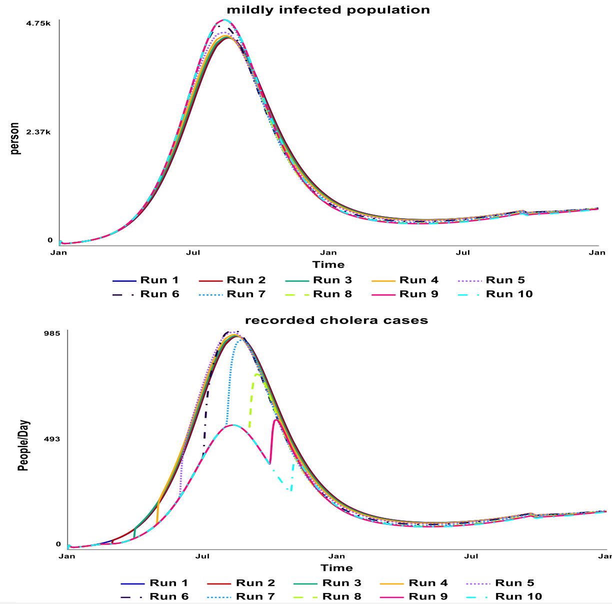
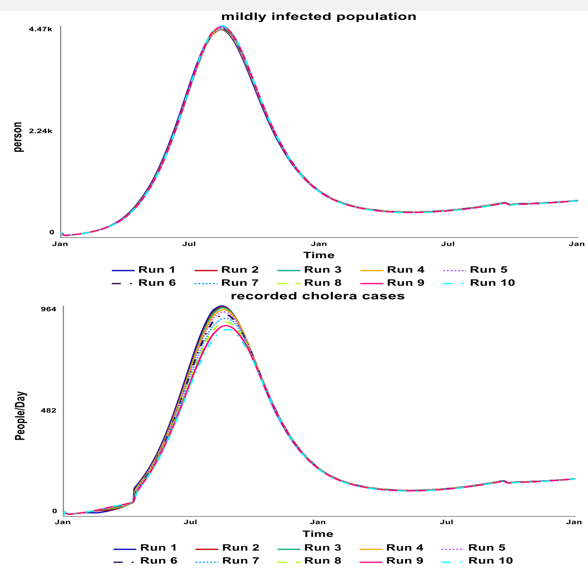
	building ORC start time
Run 1	30
Run 2	60
Run 3	90
Run 4	120
Run 5	150
Run 6	180
Run 7	210
Run 8	240
Run 9	270
Run 10	300



The model is slight numerical sensitive to changes in the value of "building ORC start time" as expected because the model is simulated on the historical data of intervention. The intervention showed minimal impact because the resources were limited to accommodate the need of Al-hudaydah infected individuals and mildly infected individuals might not be aware they are infected. However, the recorded cholera cases are highly (numerically) sensitive to the values. If the ORC service starts earlier, more individuals receive treatment earlier (prevention on progressing to severe state), so does the surveillance system can function earlier to provide crucial information for cholera emergency response.

	time to build ORC
Run 1	30
Run 2	67
Run 3	104
Run 4	142
Run 5	179
Run 6	216
Run 7	253
Run 8	291
Run 9	328
Run 10	365



The model is insensitive to changes in the value of "time to build ORC" as expected with the historical data as the intervention was not sufficient to meet the population need (supply and demand issues). This delay takes into consideration of implementation challenges of building ORC. Hence, the faster the intervention begins, the sooner the infected individuals receive treatment (prevention on progressing to severe state), and the surveillance system can function earlier to provide crucial information for cholera emergency response.

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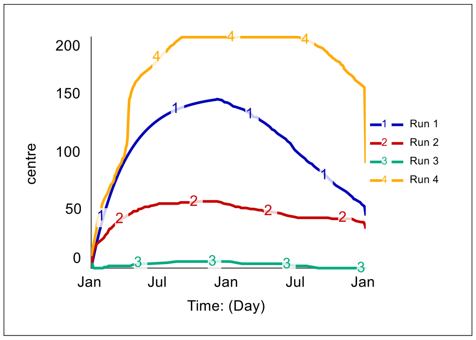
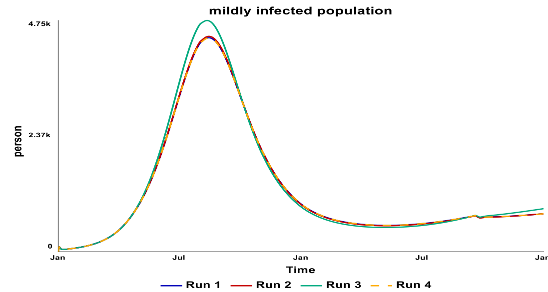
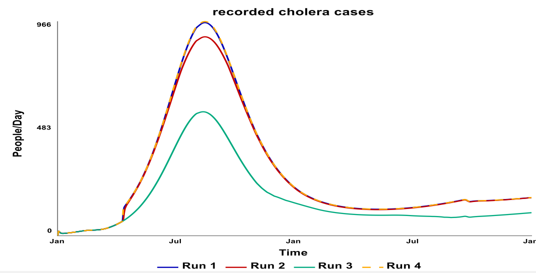
desired number of ORC



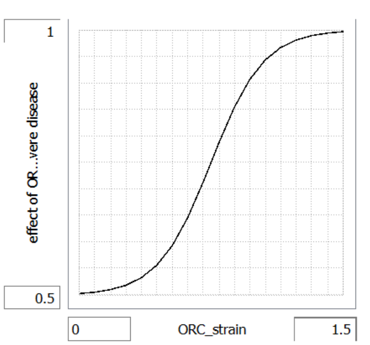


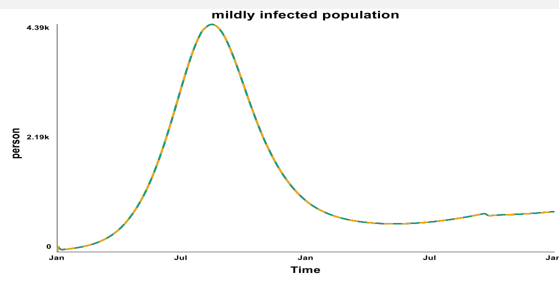


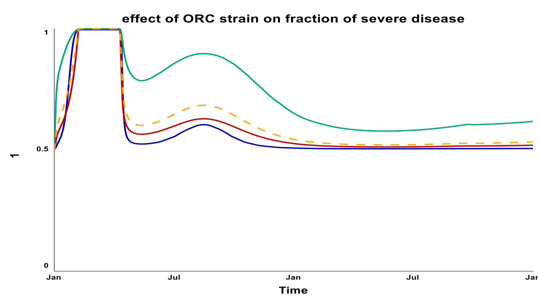
The model is numerically sensitive to changes in the value of "desired number of ORC" as expected. A similar result was found on "patient treated". Run 1, 2, and 4 show similar results, indicating a lack of need (or demand) from the infected individuals. Increasing the demand (health-seeking behavior) among the mildly infected individuals is one of the leverage points and should be further explored as the next steps.

effect of ORC strain on fraction of severe disease

Run 1 – S-shape growth
Run 2 – exponential growth
Run 3 – logarithmic growth
Run 4 – linear growth







The model is insensitive to changes in the graphical function shape of "effect of ORC strain on fraction of severe disease", as expected. Based on the historical data of ORC, the impact is minimal towards the overall infection reinforcing feedback loop. However, the effect impacts the number of progressing into severe disease states as mildly infected individuals receive early treatment helps to prevent progressing to a severe state. When the severely infected increases (only during the initial months before the ORC were built), cholera deaths slightly increase.

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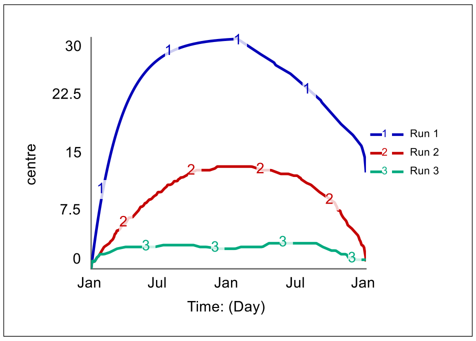
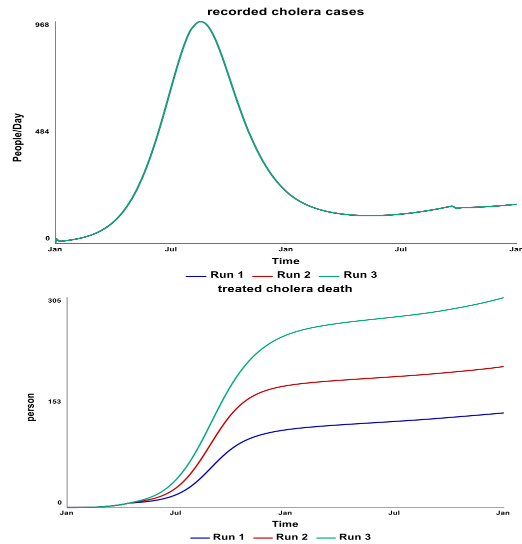
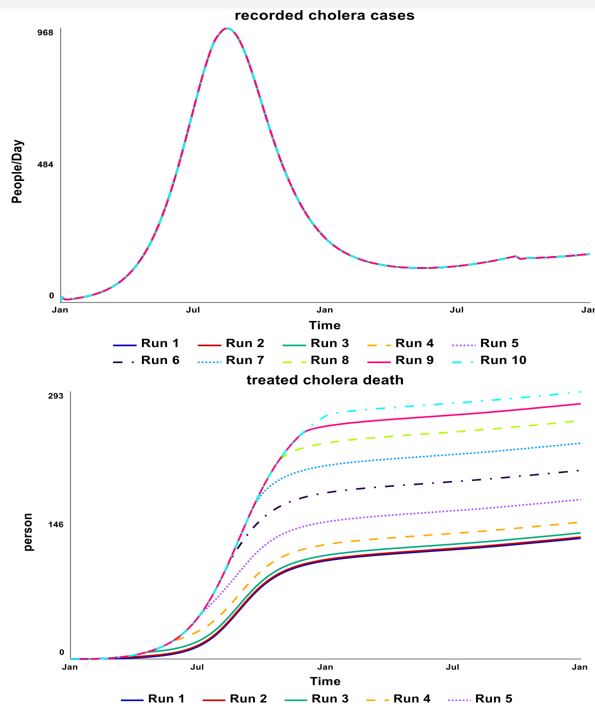
desired number of DTC





The model is insensitive to changes in the value of "desired number of DTC" as expected. A similar result was found on "bed". Severely infected individuals seeking treatment are very low relative to the total infected population. Even though the DTC treats the human waste before releasing it into the sewage system as the desired action to decrease water contamination, the impact is minimal. However, the teated cholera death is highly (numerically) sensitive to treatment at DTC.

	building DTC start time
Run 1	30
Run 2	67
Run 3	104
Run 4	142
Run 5	179
Run 6	216
Run 7	253
Run 8	291
Run 9	328
Run 10	365



The model is insensitive to changes in the value of "building DTC start time" as expected. A similar result was found with "time to build DTC". However, the teated cholera death is highly (numerically) sensitive to both parameters.

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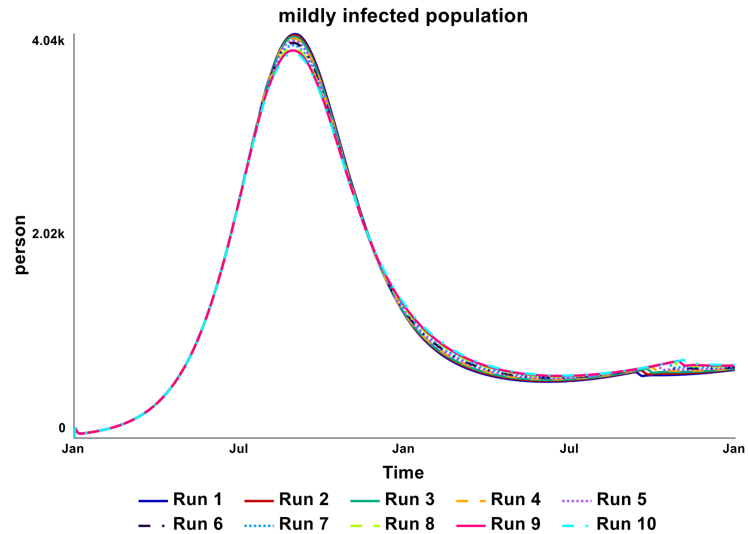
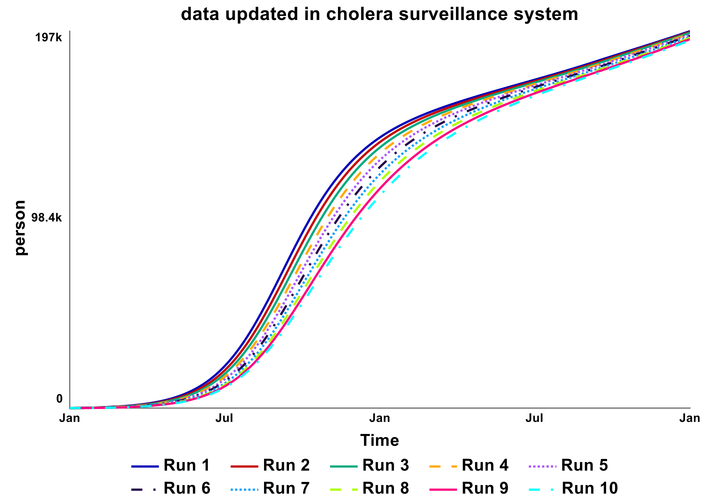
	desired time to update system
Run 1	7
Run 2	13
Run 3	19
Run 4	25
Run 5	31
Run 6	36
Run 7	42
Run 8	48
Run 9	54
Run 10	60





The model is numerical sensitive to changes in the value of "desired time to update system" as expected in the scenario based on historical intervention data. It assumes that if the surveillance system is delayed, the emergency response based on the collected cholera prevalence data experiences a delay in the start time (policy structures). Likewise, if the surveillance system is highly responsive, the start time of the intervention will be earlier.

Calibration Example using Stella Architect

Starting optimization "Optimization" at 2022-May-25 16:35:33

Method	maxiter	init_step	tolerance
Powell	5000	1	0.00001

Payoff:	**Payoff**
Action	minimize
Kind	Calibration
Element	data suspected and confirmed cases (cummulative)
Weight	auto
Comparison Variable	recorded suspected and confirmed cases (cummulative)
Comparison Run	-2
Comparison Type	Squared Error
Comparison Tolerance	0

Parameter:	connectedness of aquifers	time to affect water in aquifers
min_value	0	1
max_value	1	14
scaling	1	1

	connectedness of aquifers	time to affect water in aquifers	**Payoff**
Starting at	0.5	8	
After 76 runs	0.500262792	7.50549131	1,586.61825

Finishing optimization at 2022-May-25 16:35:38