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A cost-benefit analysis of using wastewater monitoring to guide typhoid vaccine campaigns

Aparna Keshaviah[1*], Agha Ali Akram[1], Dheeya Rizmie[1], Ian Raxter[1], Rezaul Hasan[2], Ziaur Rahman[2,3], Afroza Jannat Suchana[2], Farjana Jahan[2], Aninda Rahman[4], Mahbubur Rahman[5], Mahbubur Rahman[2], Megan B. Diamond[6] and Anthony Louis D'Agostino[1]

Abstract

Introduction Enteric diseases are a leading cause of mortality in developing countries, yet are highly preventable. Typhoid vaccines remain underutilized, and diagnostic capacity constraints impede treatment and prevention. Wastewater monitoring could provide a more accurate picture of disease burden if detection and quantification of *Salmonella* Typhi in wastewater are advanced. To motivate why countries should invest to improve wastewater testing methods, we conducted a cost-benefit analysis, quantifying the value this approach could yield.

Methods We estimated benefits that could accrue if wastewater data informed the early launch of a theoretical typhoid vaccine campaign in Cox's Bazar, Bangladesh. After empirically estimating the lead-time advantage of wastewater data over clinical data to flag case upticks, we simulated changes in case counts from a 1- to 14-day early campaign launch, using ordinary differential equation modeling. We quantified benefits resulting from averted cases (from preserved caregiver time, school days, and wages), hospitalizations (from savings to public funds), and deaths (using the value of statistical life). We then calculated how cumulative benefits, costs, and the ratio of the two varied by campaign launch timing scenario over a five-year period.

Results Wastewater concentrations of *Salmonella* Typhi upticked up to 13 days before case counts. Cumulative benefits varied by year and launch timing. With a 13-day early launch, every $100 spent on wastewater monitoring could yield $295 in societal benefits by year 5. Cumulative benefits roughly equaled cumulative costs with a 5-day early launch and outweighed costs when the campaign was launched even earlier.

Conclusion If wastewater data can be advanced to reliably provide early warnings of new typhoid outbreaks, governments could reap large benefits that more than justify spending on program implementation. Our findings could generalize to other high-aid countries that, like Bangladesh, experience routine enteric disease outbreaks and have strong operational networks.

Keywords Wastewater surveillance, Diarrheal disease, Cost-benefit analysis, Typhoid fever, Vaccination, Bangladesh

*Correspondence:
Aparna Keshaviah
akeshaviah@mathematica-mpr.com
Full list of author information is available at the end of the article

Background

Enteric infections are a leading cause of mortality in developing countries [1], responsible for 1.34 million deaths in 2021 worldwide. Such infections—which include diarrheal diseases and acute febrile illnesses—are also highly preventable [2]. Thanks to efforts by the World Health Organization (WHO) over the past decade, countries in which diarrheal diseases are endemic have improved access to the oral cholera vaccine and rotavirus vaccine [3]. However, typhoid vaccines remain underutilized, and with rising rates of anti-microbial resistant *Salmonella* Typhi (*S.* Typhi) [4], expanded distribution of typhoid conjugate vaccines (TCVs) could reduce death and suffering [5].

Beyond vaccination, timely treatment can reduce mortality from enteric. With typhoid fever, the case fatality rate decreases from 30% if left untreated to under 1%, when treated [6]. But because typhoid fever is difficult to distinguish clinically from other febrile illnesses, diagnostic capacity constraints can impede treatment and prevention. For example, in the Cox's Bazar region of Bangladesh—a country with one of the highest rates of typhoid fever worldwide [4]—almost all suspected cases of typhoid fever lack confirmatory testing via blood or stool cultures; instead, physicians often base diagnoses on symptoms, complete blood count tests, and the unreliable Widal test [7].

Wastewater monitoring for *S.* Typhi offers the potential to gain a more accurate picture of disease burden and transmission, particularly in regions where typhoid is endemic [8]. Like SARS-CoV-2, *S.* Typhi is shed in the stools of people who are infected, including those without symptoms. Operationally, several countries have used wastewater monitoring to identify the presence of asymptomatic carriers, and thereby stem outbreaks [9, 10]. Wastewater data is also a prime candidate to guide vaccine deployment [9], since the approach can provide information on large swaths of a population—including those without a health care visit, who may seek care at a pharmacy—at a fraction of the cost of individual testing [11]. This inclusive, minimally invasive approach to data collection is particularly well-suited to monitor the health of displaced populations, as it can be adapted to improve the deployment of public health interventions [12].

Despite the opportunities, more work is needed to improve the lab testing methods used to detect and quantify *S.* Typhi in wastewater. *S.* Typhi can be difficult to isolate in wastewater because other bacteria may inhibit its signal, leading to inconsistent results [9]. Recent research into the use of bacteriophages has shown promise in typhoid-endemic communities, but improved detection is needed in communities with a low typhoid burden [13]. The lack of robust clinical and serological surveillance has also posed challenges to validating wastewater concentrations of *S.* Typhi. [10].

With many competing public health demands and reductions in pandemic relief funding for wastewater monitoring, officials need information on the potential benefits they could reap if they invested to improve wastewater testing. Specifically, economic analyses that quantify how monetary benefits compare to implementation costs can motivate why governments and health authorities should allocate sustained resources for wastewater monitoring. To this end, we conducted a cost-benefit analysis (CBA) of wastewater monitoring for typhoid fever in Cox's Bazar, focusing on hypothetical impacts in the Rohingya refugee community. While there are several ways wastewater data can be used to improve community health and well-being, we quantified long-term potential benefits from just one theoretical use case: informing the early launch of a typhoid vaccine campaign. We compared projected cumulative wastewater monitoring costs to modeled benefits and calculated cost-benefit ratios (CBRs) under different lead-time scenarios over a five-year period spanning 2023 to 2027.

Methods

Bangladesh hosts nearly 1 million Forcibly Displaced Myanmar Nationals in Cox's Bazar—an insular geographic region that is among the most climate vulnerable districts in the country [14]. As the world's largest displaced vulnerable population, the community has received relief aid from the United Nations High Commissioner for Refugees (UNHCR), International Organization for Migration, and partners, who work with the Government of Bangladesh's Office of the Refugee Relief and Repatriation Commissioner and Ministry of Disaster Management and Relief to provide emergency shelter, clean drinking water, food supplies and access to health and sanitation facilities.

The Rohingya refugee population (of whom 51% are female, and 49% under age 18) [15] has been stable in size in recent years, though as of October 2023, roughly 3% had been relocated to the island of Bhasan Char. Across Cox's Bazar, the community lives in 31 campsites [14] and has access to 56 health facilities [16]. Since 2016, icddr, b (the International Centre for Diarrhoeal Disease Research, Bangladesh) has provided technical support to the Institute of Epidemiology, Disease Control and Research (IEDCR) in implementing nationwide enteric disease surveillance, which includes surveillance across 22 sentinel sites (health facilities) in the Rohingya camps [17].

Wastewater sampling and testing

In August 2020, icddr, b began a pilot study of wastewater monitoring, focusing on the SARS-CoV-2 virus in Dhaka.

Since the influx of the Rohingya refugees, roughly 26,000 temporary emergency latrines have been installed in 34 camps in the Cox's Bazar District, and sanitation systems consist mostly of pit latrines (80%), septic tanks (10%), biogas reactors, and anaerobic baffled reactors (10%) [18]. Enteric disease threats, including cholera outbreaks and other waterborne diseases, have been an ongoing challenge in some camps. Accordingly, in October 2022, icddr, b partnered with IEDCR and the Civil Surgeon's Office in Cox's Bazar to expand the program to include routine monitoring in Dhaka as well as Cox's Bazar, for SARS-CoV-2 along with three vaccine-preventable pathogens: *S.* Typhi, *Vibrio cholerae*, and Rotavirus.

We analyzed wastewater data collected from October 2022 through May 2023. At the time of our analysis, icddr, b was sampling wastewater weekly from 12 sites, collecting an average of 47 grab samples monthly that cover 125,653 people in the municipality and another 24,469 refugees in the camps (Fig. 1). Using comprehensive information on geographic coverage, population size, and the prevalence of acute watery diarrhea, icddr, b strategically selected the 12 sampling sites to ensure that they provided a representative picture of both the refugee camp and local municipal populations. In the Cox's Bazar municipality, sampling occurred at three open drain sites that are the main drainage points responsible for wastewater discharge. These points were chosen through scoping visits and transect walks to ensure that samples primarily represented the resident population, avoiding the inclusion of wastewater from the large numbers of tourists. In the refugee camps, sampling occurred at nine open drains across three camps. The three refugee camps were carefully selected after conducting stakeholder meetings, map analysis, and transect walks to understand the sanitation and drainage systems. Sampling was done at the ends of drains, and within each catchment area, field assistants conducted household surveys to gather information on population size and demographics. Samples from the 12 representative sites across the municipality and camps were collected over a three-day period.

The sample collection process involved strict safety protocols to protect individuals and mitigate contamination risks. All personnel involved in sample collection wore appropriate personal protective equipment, including gloves, face masks, and full-body protective suits. All equipment was thoroughly cleaned and sanitized before and after each sample collection. Once collected, the environmental samples were transported to the icddr, b One Health Laboratory in a cold chain (2–8 °C) to maintain sample integrity and reliability and minimize the risk of degradation prior to laboratory analysis.

To capture and trap microbes from 10 mL samples of wastewater, the lab used "Nanotrap® Microbiome A Particles (Ceres Nanosciences; SKU# 44202), followed by nucleic acid extraction using MagMAX Microbiome Ultra Nucleic Acid Isolation Kit (Thermo Fisher Scientific™; Cat# A42357) [19]. *S.* Typhi (specifically, the TviB gene target) was quantified using real-time qPCR methods with sequence-specific primer and probes from 5 µL of nucleic acid [20]. The theoretical limit of detection (LOD) for *S.* Typhi, calculated based on serial dilution standards and using the standard curve, was 49,000 gene copies per liter (gc/L) of wastewater [21]. The actual LOD varied over time, and for some samples, signals below this theoretical LOD could still be quantified.

Clinical case count data

We analyzed clinical case count data from the WHO's Early Warning, Alert and Response System (EWARS) from July 2022 through May 2023. EWARS data, which are further described in the EWARS report from the WHO [22], include weekly counts of patients with acute watery diarrhea, as reported by the health facilities established in the refugee camps [23]. Given resource limitations in the camps, health facilities did not administer

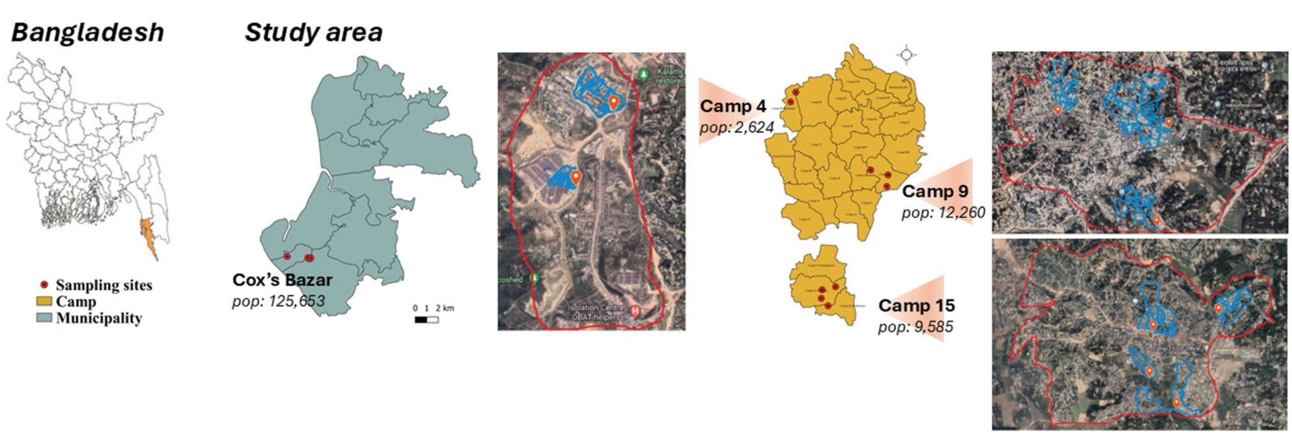

Fig. 1 Wastewater sampling sites in Bangladesh. The map shows the locations and population coverage of 12 representative wastewater sampling sites in Cox's Bazar and the Rohingya refugee camps

rapid tests to all patients. Instead, health facility personnel followed strict criteria for rapid testing, whereby they typically first treated all symptomatic clinical cases, and only administered a rapid test if further treatment was required. They used the results of the rapid tests (reported as positive or negative) to guide such treatment decisions.

Given the imperfect assessment of typhoid fever case status, and the known underreporting of cases [24], we applied three different approaches to counting cases. Specifically, we analyzed EWARS counts of: (1) all symptomatic cases of acute watery diarrhea, (2) the subset of symptomatic cases with a rapid test done, and (3) the subset of symptomatic cases with a positive rapid test for *S.* Typhi. Previous research has estimated that diarrhea (with or without fever) occurs in 8% of typhoid fever cases in Bangladesh among children under five have diarrhea [25].

Theoretical intervention scenarios

Because icddr, b began testing wastewater for enteric diseases relatively recently, the resulting data have yet to be used to inform public health practice. While there are several ways wastewater data on *S.* Typhi concentrations could be used (Supplemental Appendix Figure A), we took a conservative approach and analyzed just one potential use case—to inform the early launch of a typhoid vaccine campaign.

Our analyses imagined the launch of the first widespread, government-led typhoid vaccine campaign in Cox's Bazar, and how wastewater data could inform the timing of such. In the baseline scenario, the campaign is launched on an arbitrary day (Day 0) in Year 1, based on upticks in symptomatic clinical case data. Intervention scenarios initiate the Year 1 campaign 1 to 14 days earlier, based on upticks in *S.* Typhi wastewater concentrations, with no further intervention thereafter. We assumed that wastewater data would impact only the *timing* of a vaccine campaign, and not whether the campaign is launched. Importantly, this assumption keeps the costs of the campaign and accompanying public health actions unchanged between the baseline and intervention scenarios (and thus excluded from our analyses).

The vaccine campaign would take place over the span of one month. At present, the typhoid polysaccharide vaccine is only available through a private pharmaceutical company, and uptake has been low, with $< 0.01\%$ of people getting vaccinated each month, based on our analysis of unpublished vaccine data. However, because vaccine uptake has been high in past government-led campaigns in Cox's Bazar, ranging from 85% to 98% for oral cholera vaccine campaigns [26], we assumed an uptake rate of 85% for our theoretical intervention. We also assumed that a government-led campaign would distribute the pre-approved TCV (following current WHO recommendations), which requires only one dose, has higher efficacy and longer protection than older polysaccharide vaccines, and is safe and effective even in younger children [27–29]. Since 2018, several countries have introduced TCVs into routine immunization programs, with financial support from the Gavi Vaccine Alliance. Drawing on the literature, we assumed a vaccine efficacy rate of 85% for children ages 15 and under [30] and 67% for those 16 and older [31], and we assumed an average duration of efficacy of 19.2 years [27].

Observed early warnings from wastewater data

To estimate the potential lead-time advantage of wastewater data over clinical data (that is, the plausible number of days of early warning), we compared trends in log-transformed wastewater concentrations with trends in clinical case counts in Cox's Bazar. We applied a lag of -14 to 14 days to the clinical case data, comparing wastewater concentrations on day x with case counts on day $x + lag$). The range of lags we examined was consistent with lags estimated during the COVID-19 pandemic [32], but we also allowed the case data to lead the wastewater data. For each lag time and each method of counting clinical cases, we calculated the Spearman rank correlation (r) between the wastewater and case data, both overall and after individually controlling for the rainfall, maximum temperature, or humidity on wastewater sampling days (using partial correlations). We then identified what lag maximized the correlation between the two sources [24].

Typhoid incidence modeling

To quantify the benefits from a wastewater-informed early campaign launch, we simulated the number of averted typhoid fever cases over a five-year period following the intervention. To do so, we implemented an ordinary differential equation (ODE) model to simulate how many cases would occur in Cox's Bazar under the baseline and intervention scenarios and took the difference between the two. We adapted the compartmental ODE model used by Lo et al. [27] in their study of the cost effectiveness of TCVs in South Asia.

The simulation model has compartments for susceptible, infected, recovered, and vaccinated individuals; chronic carriers; and the water-borne concentration of *S.* Typhi (Supplemental Appendix Figure B). Each compartment of disease status is modeled separately, with continuous terms that govern how their counts increase and decrease over time. For example, the susceptible population count increases each month by a constant birth rate, coupled with a waning immunity rate from the naturally recovered population and a vaccine immunity waning rate from the vaccinated population. The population decreases by a natural death rate and long and short cycle vaccination terms. We parameterized our simulation using values from the literature, data from icddr, b and UN Reports specific to Cox's Bazaar, and Markov Chain Monte Carlo values fitted to achieve a target annual disease incidence (Supplemental Appendix Table A). Outside of these continuous model terms, the other way the disease compartments change is based on simulated vaccinations. Only susceptible individuals are vaccinated, and the model simulates case counts for 16 different age groups, using a monthly time step. While other economic evaluations of TCV have used a 10-year time horizon [27], we chose an abbreviated time horizon of five years, since our focus was on modeling the costs and benefits of a single, short-lived vaccination campaign.

To obtain the theoretical incidence associated with 1- to 14-day early vaccine campaign launch (which represents a slightly expanded lead-time range from what we empirically observed, for completeness), we used Eqs. 7 and 8 in the Supplemental Appendix, accounting for a changing susceptible population, daily vaccination coverage rate, and expected vaccination coverage. Lastly, we combined our simulated estimates of averted cases with estimates from the literature of case-hospitalization and case-fatality rates to calculate what share of cases would be hospitalized and fatal, respectively (Supplemental Appendix Table A). Together, these averted counts formed the basis of the benefits we derived in our CBA.

Quantifying costs and benefits

We used realized costs of wastewater monitoring for enteric disease targets for Year 1 costs. For context, prior research assessing the costs of wastewater monitoring for SARS-CoV-2 showed that Bangladesh faced costs that were only slightly higher than the median cost calculated across twelve low- or middle-income countries [11]. We also projected how costs would change over the next 4 years, accounting for potential reductions after excluding one-time fixed costs (such as the cost of digital PCR machines purchased for laboratory testing). In our analysis, wastewater data informed the launch of just a single vaccine campaign in Year 1. However, we assumed that other uses of the data would justify continued monitoring over time (Supplemental Appendix Figure A).

We valued societal benefits separately for averted non-hospitalized cases, averted hospitalizations, and averted deaths, using information from the literature (Supplemental Appendix Table B). For non-hospitalized and hospitalized cases, we quantified the value of preserved caregiver time, preserved school days, and preserved wages. We aggregated results for the 16 age groups output by the ODE model into three buckets: 0–4 years (non-school-going), 5–19 years (school-age children), and 20 years or older (a proxy for working-age adults). We assumed a similar duration of illness for hospitalized and non-hospitalized cases across all three age groups [33], which we conservatively estimated to be 6 days, taking the lower bound of values reported in the literature [33–35]. For hospitalized cases, we also quantified savings to public funds. For deaths averted, all monetary benefits stemmed from the value of a statistical life (VSL)—a widely accepted method to help policymakers assess the value of life-saving policy actions [36]. We adjusted the VSL by considering the difference between the estimated age of deaths averted (based on our model) and the average life expectancy in Bangladesh.

We calculated cumulative benefits and costs annually over a five-year horizon and converted these to the net present value of benefits and costs (i.e., 2023 values) using a 10% discount rate, which is commonly used by multilateral institutions such as the World Bank and the United Nations Development Programme (UNDP). We used current Bangladesh prices and converted them to United States Dollars (USD), assuming no inflation in our analysis (that is, all prices are real prices over the course of the analysis). We assumed mid-year discounting, as is recommended practice [37]. Dividing the present value of cumulative benefits by the present value of cumulative costs yields the CBR, which we calculated at the end of the five-year period for each launch timing scenario. We examined how results varied by scenario and identified the break-even point—that is, the launch timing for which the CBR roughly equaled 1.0.

To examine the robustness of our findings, we conducted sensitivity analyses examining how findings changed when we varied a few key model parameters, including the VSL (looking at moderate and low values that represent 75% and 50%, respectively, of the base-model value of $5,458 per life year); vaccine uptake rate (looking at moderate and low values of 75% and 65%, respectively, compared to the base-model value of 85%); and case-fatality rate (looking at a high of 2% and low of 0.1% [27], compared to the base-model value of 0.5%). We examined how the break-even point for each sensitivity analysis compared to the base model, and how benefits for each sensitivity analysis compared to the base model under a 1-day and 14-day early campaign launch (i.e., the extremes).

Results

Table 1 summarizes the monthly counts of symptomatic cases of acute watery diarrhea, along with detection rates and average concentrations of *S.* Typhi in wastewater. Detection was more likely in the winter and during the rainy seasons. Of the 605 symptomatic acute watery diarrhea cases reported in EWARS during the study period, only 313 (52%) had results from a rapid test reported, and

Table 1 Monthly summaries of clinical case counts and wastewater measures of S. Typhi

Month	Symptomatic clinical cases of AWD	Wastewater samples collected	Samples with *S.* Typhi detected: *N* (%)	Median *S.* Typhi gene copies per liter (gc/L)
July 2022	37	NA	NA	NA
August 2022	24	NA	NA	NA
September 2022	52	NA	NA	NA
October 2022	27	24	0	n.d.
November 2022	21	48	0	n.d.
December 2022	50	48	8 (17%)	85,591
January 2023	95	60	5 (8%)	197,396
February 2023	67	48	2 (4%)	92,027
March 2023	114	48	0	n.d.
April 2023	95	36	0	n.d.
May 2023	23	60	0	n.d.

AWD = acute watery diarrhea; NA = Not available (since wastewater testing for *S.* Typhi began only in October 2022); n.d. = Non−detectable (values were below the limit of detection)

102 cases (17%) had confirmatory pathogen-specific test results reported. Positive pathogen-specific test results indicated a total of 51 cases of cholera, 2 cases of shigella, and 1 case of dengue. Notably, there were no confirmed cases of either typhoid or rotavirus, even in weeks when wastewater testing detected the presence of *S.* Typhi.

Lead-time advantage of wastewater data

The estimated correlation between log-transformed wastewater concentrations of *S.* Typhi and typhoid case counts was at most $r = 0.15$ when based on all cases of acute watery diarrhea, $r = 0.21$ when based on cases with a rapid test conducted, and $r = 0.07$ when based on cases with a positive rapid test (Supplemental Appendix Figure C). Partial correlations with the count of all cases were slightly strengthened after controlling for rainfall ($r = 0.17$), maximum temperature ($r = 0.17$), and humidity ($r = 0.18$) individually, but correlations with other case definitions were diminished after controlling for these environmental variables.

The relatively weak correlations we found may be due to incomplete diagnosis and reporting of clinical case data, which was confirmed during site visits to Cox's Bazar (when icddr, b staff learned that some who experienced diarrhea sought treatment from the nearby store rather than the hospital). However, it is also possible that the weak correlations indicate a need for improved wastewater lab methods, in which case the analyses we present here can motivate why countries should invest to advance wastewater testing.

Our empirical correlation analyses also indicate that wastewater concentrations of *S.* Typhi may uptick anywhere from 1 to 13 days before upticks in case counts, depending on which types of cases we analyzed, with an estimated 8-day lead time compared to cases with a positive rapid test (Supplemental Appendix Figure C). Given the uncertainty in the true lead-time advantage of wastewater data over case data, we explored a slightly wider range of early campaign launch times than we empirically estimated.

Averted cases, hospitalizations, and deaths

Under the baseline scenario, we estimated that 4,338 cases would emerge in the Rohingya refugee community over five years, of which 439 would be hospitalized, and 21 fatal. While monthly differences in modeled case counts across scenarios were small early on, they added up over the five-year period (Supplemental Appendix Figure D). If the vaccine campaign were launched 1 day earlier, the population could see 112 averted cases—including 12 averted hospitalizations, and 1 averted death), whereas a 14-day early launch yields 1,623 cases averted—including 172 averted hospitalizations and 8 averted deaths (Table 2). Across these intervention scenarios, benefits concentrated in younger individuals.

Monetary gains from a wastewater-informed campaign

Converting estimates of averted cases, hospitalizations, and deaths into monetary terms, we calculated that societal benefits would average $1,177 per averted case, an additional $23 per averted hospitalization, and an additional $146,693 per averted death (Supplemental Appendix Table B). As expected, most (78%) of the cumulative benefits stemmed from the deaths averted. Costs of wastewater monitoring in Cox's Bazar totaled $237,141 in Year 1 (Supplemental Appendix Table C). Roughly 46% of costs were recurring, 36% were for labor, and 18% were fixed or capital costs. Lab analysis was the single largest source of costs, accounting for 38% of the total. Over time, icddr, b projected that annual program costs would decrease from an average of $207,202 in Years 1–2 to $126,877 thereafter.

Cumulative net benefits varied by year and launch timing scenario (Fig. 2). The break-even point (where CBR ≈ 1.0) occurred with a 5-day early launch (Fig. 3); with an early campaign launch of at most 4 days or less, the economic benefits that accrue would not outweigh the costs of wastewater monitoring (CBR < 1.0). With an early launch of 8 days (the lead time estimated when comparing wastewater data to cases with a positive rapid test), cumulative societal net benefits to the Rohingya community would outweigh costs even in Year 1, and by

Table 2 Averted cases, hospitalizations, and deaths by year 5, by vaccination campaign launch time

Vaccine campaign launch	Total cases of typhoid fever	Averted cases (vs. Baseline)				Averted hospitalizations (vs. Baseline)	Averted deaths (vs. Baseline)
		Overall	Ages 0–19	Ages 20–49	Ages 50+		
Day – 1	4,226	112	78	26	8	12	1
Day – 2	4,111	227	157	53	16	24	1
Day – 3	3,995	343	237	81	25	37	2
Day – 4	3,878	459	318	108	34	49	2
Day – 5	3,762	575	400	135	41	62	3
Day – 6	3,643	695	483	162	50	74	3
Day – 7	3,526	812	565	189	58	87	4
Day – 8	3,408	930	647	217	66	99	5
Day – 9	3,290	1,047	731	243	73	112	5
Day – 10	3,174	1,164	813	270	81	124	6
Day – 11	3,056	1,281	895	297	89	136	6
Day – 12	2,942	1,396	977	323	97	148	7
Day – 13	2,827	1,511	1,058	348	105	161	8
Day – 14	2,714	1,623	1,138	372	113	172	8

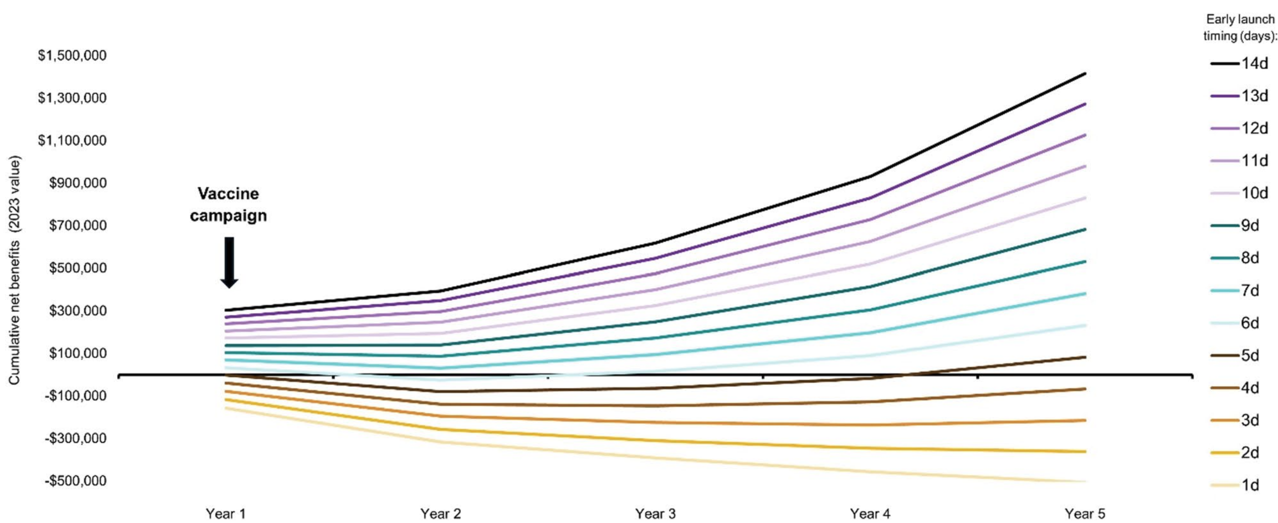

Fig. 2 Cumulative net benefits by year and vaccination campaign launch time. The line graph shows how the cumulative net benefits of launching a typhoid vaccination campaign early increase from years 1 through 5. Each line represents a different campaign launch timing scenarios, ranging from a 1- to 14-day early launch. Cumulative net benefits were calculated as summed benefits minus summed costs and were converted to present values (that is, 2023 dollars) using a 10% discount rate. Negative values indicate that cumulative costs were higher than cumulative benefits by the end of the year shown. See Supplemental Appendix Table D for the values shown in the figure

Year 5, would amount to $530,000. If the campaign were launched 14 days early, the CBR could be as high as 3.2, with cumulative net benefits amounting to $1.4 million by Year 5.

In sensitivity analyses, we found that reducing the VSL led to the need for an even earlier campaign launch (of 6 to 8 days) to break even by Year 5, compared to the base model break-even point (5 days). By contrast, reducing the vaccine uptake rate resulted in a two- to three-day early launch being sufficient to break even (Fig. 4A). Increasing the case-fatality rate also reduced the early launch time needed to break even (to 2 days), while decreasing the case-fatality rate led to a lengthy break-even point (12 days). With respect to benefits, the greatest change from base-model estimates resulted from increasing the case-fatality rate (Fig. 4B). A higher case-fatality rate greatly reduced the estimated losses for a 1-day early launch (to -$172,577) and greatly increased estimated benefits for a 14-day early launch (to $6.24 million), compared to base-model estimates (-$507,418 for a 1-day early launch, $1.42 million for a 14-day early launch). Reducing the vaccine uptake rate also led to reduced losses for a 1-day early launch and heightened gains for a 14-day early launch. By contrast, decreasing the VSL led to slightly higher losses for a 1-day early launch and lower gains for a 14-day early launch. Taken together, these findings suggest that our base model results represent a robust middle ground.

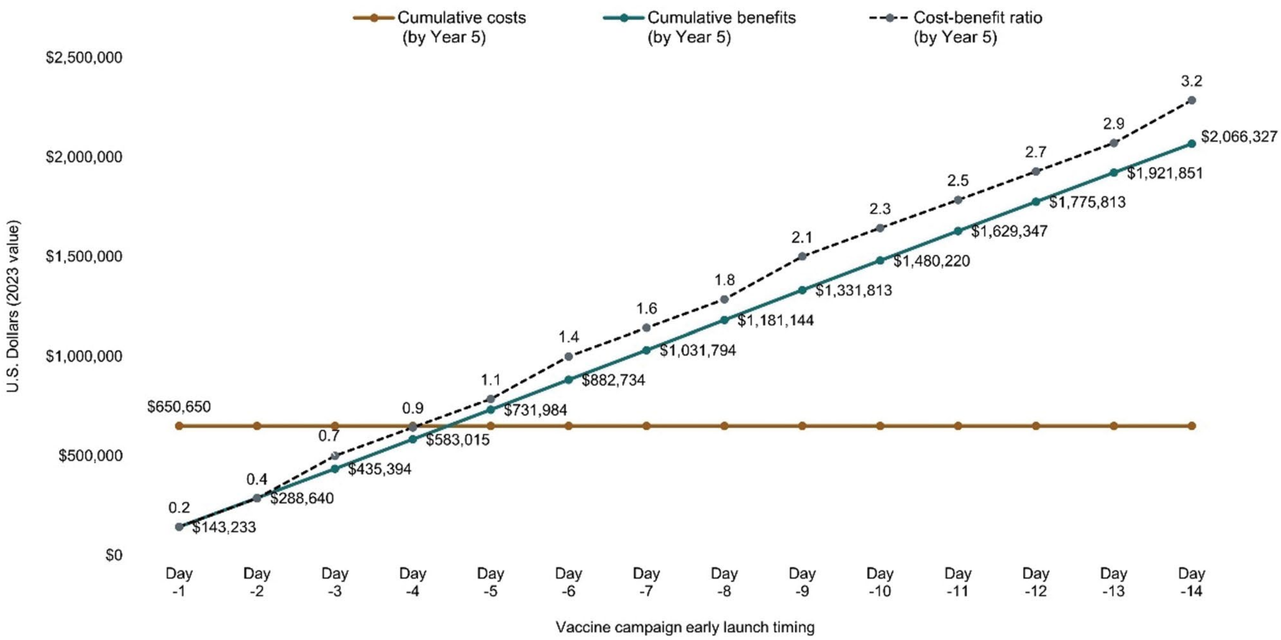

Fig. 3 Year 5 cumulative costs, benefits, and CBRs, by campaign launch timing scenario. The line graph shows how year 5 cumulative costs, benefits, and the cost-benefit ratio vary by campaign launch timing scenario. Cumulative costs and benefits were converted to present values (that is, 2023 dollars) using a 10% discount rate

Discussion

Data on the health status of refugee communities during times of active migration is limited, and researchers have called for improved surveillance of infectious diseases and antimicrobial resistance in such communities [38]. Wastewater monitoring is a prime candidate for monitoring a range of health biomarkers in refugee communities, to inform tailored and timely public health interventions. Our study also clarifies the added value of wastewater data to track endemic infectious diseases, given the sizeable gaps in the diagnosis of typhoid fever and rotavirus.

Considering just a single use case of wastewater data, we found that the benefits of wastewater monitoring can outweigh costs over a short timeframe, so long as wastewater concentrations of *S.* Typhi uptick at least 5 days before case increases. As the early launch timing increases, so too does the CBR. With a 7-day early launch, benefits sustainably outweigh costs even by the end of Year 1 (Supplemental Appendix Table D).

Although no government-supported typhoid vaccination currently exists in Bangladesh, such a campaign is feasible. The country has made significant progress on Sustainable Development Goals in almost all sectors, including improving immunization coverage and reducing the incidence of communicable diseases [39]. In the five-year period from September 2017 to September 2022, icddr, b collaborated with the Government of Bangladesh to successfully launch 25 vaccine campaigns in Cox's Bazar, administering polio, measles and rubella, cholera, pneumococcal, pentavalent, and COVID-19 vaccines [40].

An important note is that, for benefits to accrue from wastewater monitoring, wastewater testing methods must be sensitive, with low limits of detection, and yield reliable results even in periods of heavy rainfall or high temperatures. Further, it is not enough to simply improve lab testing methods. The resulting data and reporting metrics must be timely and easily interpretable, given research showing that many public health officials do not know how to interpret wastewater data [41]. Accordingly, officials should pair investments to improve lab methods with investments in wastewater analytics that empower officials to act on the data. For example, the creation of a typhoid analogue to the Covid-SURGE alert algorithm could increase the chances that early warnings from wastewater data lead to action [42]. Indeed, research by icddr, b and partners showed that providing households in Bangladesh with early warnings of increases in cholera risk, using an intuitive smartphone application, can successfully increase preventive practices that reduce exposure in a timely manner [43]. If efforts to improve lab testing methods are coupled with analytics that make the resulting data more actionable [42], wastewater monitoring can be an effective tool to track *S.* Typhi [44].

Limitations

Our analyses were limited in a few ways. First, correlations between wastewater and case data were based on symptomatic cases only, which may have yielded a longer

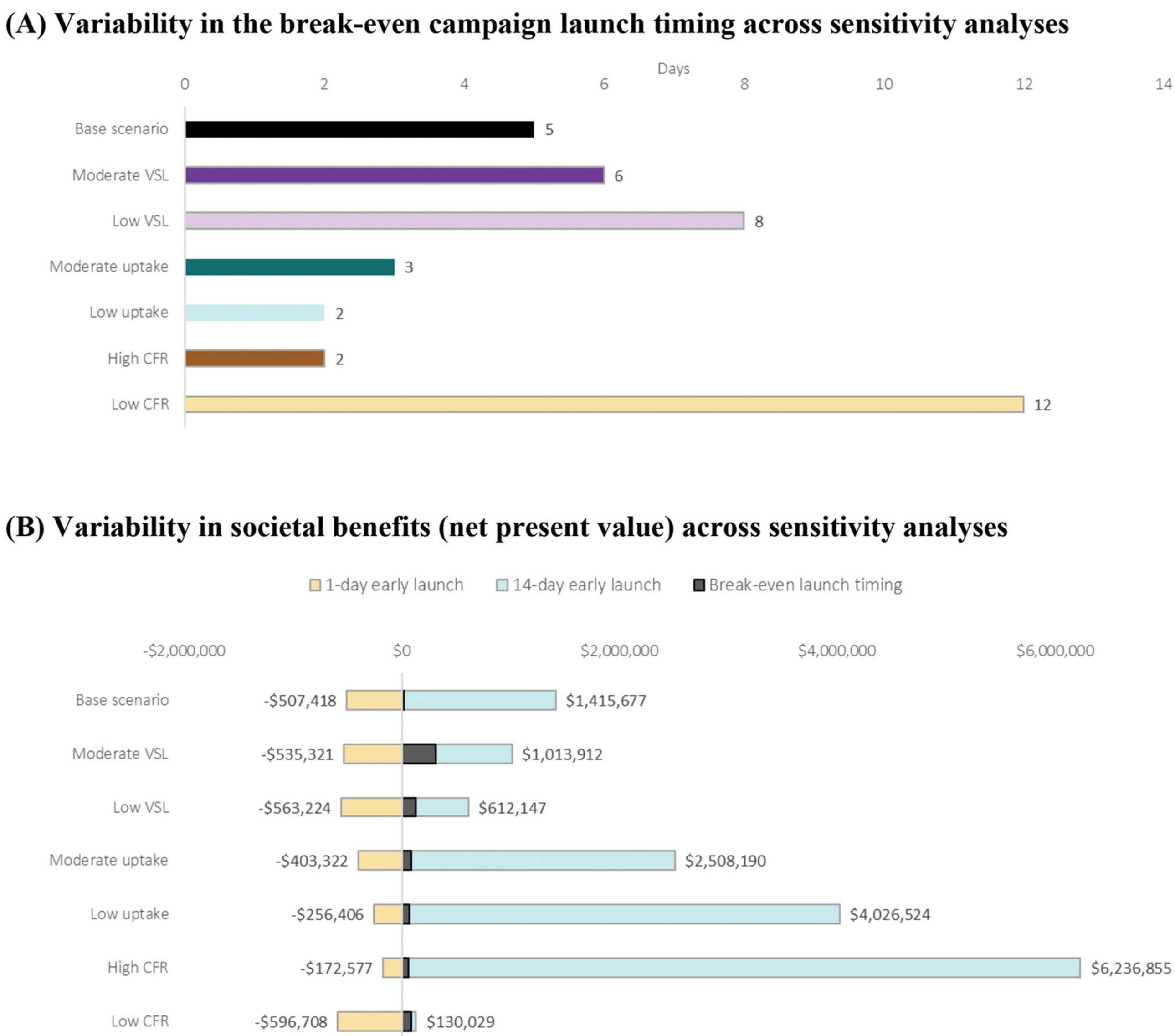

Fig. 4 Results from sensitivity analyses varying key model parameters. The bar graphs show results from sensitivity analyses that individually varied the values of the three key model parameters from the base-model scenario: the VSL ($5,458 per life year in the base model), vaccine uptake rate (85%), and case-fatality rate (0.5%). A total of six variations were generated, based on using a moderate (75% of base model) and low (50% of base model) VSL; moderate (75%) and low (65%) vaccine uptake rate; and high (2%) and low (0.1%) case-fatality rate. Panel **A** shows how sensitivity analyses influenced the break-even launch timing (that is, the days of early launch needed for benefits to roughly equal the costs of monitoring by year 5). Panel **B** shows how sensitivity analyses influenced the net present value of benefits for a 1-day early launch, the break-even launch time from panel A, and a 14-day early launch. In both panels, the top bar shows results from the base scenario

lead-time estimate. Also, in practice, the campaign early launch time may be something less than the estimated lead time advantage of wastewater data, given that it can take several days for the lab data to be generated, reported, interpreted, and acted on. Second, we simplified our model in several ways due to feasibility constraints. We assumed that vaccination would confer full immunity immediately (versus taking time to develop), leading to potential overestimates of cases averted. Also, our accounting of the impacts of a 1- to 14-day early launch was imperfect because we used monthly rather than daily timesteps, which also may have overestimated the number of cases averted. We also recognize that, because we assumed a high vaccine uptake rate, coupled with a long duration of vaccine efficacy, the benefits from launching a vaccine campaign early would be greatest for the first vaccine campaign, with diminishing returns for campaigns launched thereafter. Conversely, we assumed that only susceptible individuals would be vaccinated (as opposed to recovered individuals and chronic carriers too), which likely protracted the return to a steady state of endemic incidence, thus underestimating the effect of the intervention. Further, we expect that intervention impacts were diminished by our assumption of steady-state typhoid incidence over time. If, instead, our model allowed for varying incidence due to seasonal fluctuations or travel, for example, the impacts of early vaccination could be higher. Third, we could not validate our model against historic trends because diagnostic constraints hamper accurate typhoid case counts. Lastly, we made some simplifying assumptions when monetizing benefits. We assumed a linear accumulation of lifetime benefits from school years preserved, as opposed to stepwise benefits that accrue after a certain threshold is reached, which may not be realistic. We also did not account for all possible expenditures incurred by households during the care of a sick individual—for example, increased spending on transportation, food, investigations, and medication. Nor did we include future costs to develop wastewater analytics that facilitate action. While some of these limitations may have inflated the CBRs, we are confident that our results remain conservative, since we did not account for many other potential benefits from using wastewater data to protect public health.

Conclusion

The benefits we derived in this cost-benefit analysis are driven largely by disease transmission dynamics, vaccine campaign delivery, and uptake success. Accordingly, our findings could generalize to other high-aid countries that, like Bangladesh, experience routine enteric disease outbreaks and have strong operational networks across international development organizations such as the WHO and UNHCR. As one of the ten most climate vulnerable countries [45], Bangladesh is likely to see cases rise due to warming temperatures and natural disasters, which can contaminate or destroy clean water supplies [46]. But if wastewater testing methods can be advanced to reliably yield early warnings for new disease outbreaks, and if those warnings are heeded and acted upon, governments can reap large benefits that more than justify spending on program implementation.

Supplementary Information

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Supplementary Material 1

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Author contributions

AK and MBD conceptualized the study, secured funding, and led project administration. DR, ZR, AJS, RH, MR [icddr, b], FJ, MR [IEDCR], and AR curated and validated data from the literature and reports for the analysis, while RH, ZR, and MR [icddr, b] generated the wastewaterdata. All authors had access to the underlying data used in the study. Methodology, code, and calculations were developed by IR for case modeling, AAA for cost-benefit analyses, and DR and AK for correlation analyses. ALD and DR verified the case modeling and cost-benefit analysis code and results. DR and AK directly accessed and visualized the modeling outputs, and together with AAA, interpreted the findings. AK wrote the manuscript, with contributions from AAA, DR, IR, and AJS. All authors contributed equally to reviewing and editing the manuscript.

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The Rockefeller Foundation's project officer helped conceptualize the study, led communication and coordination across the organizational partners contributing to the analyses, and reviewed the manuscript, but was not involved in study design, data collection, analysis, or data interpretation.

Data availability

Upon publication, the data that support the findings of this Article will be made available for academic purposes upon written request to the corresponding author. Most data used in this study are retrievable from publicly available sources that have been cited. The ODE source code and CBA models can be downloaded for academic or non-commercial purposes from: https://github.com/iraxter/typhoid_ww_bangladesh.

Declarations

Ethical approval

Ethical approval is not required for this study because the data analyzed cannot be linked to any specific person or a group of people. Historic wastewater samples were collected through environmental monitoring and not from human patients, while clinical data were deidentified and/or aggregated. Accordingly, there is no possibility of linking a given environmental sample to identifiable human data.

Competing interests

AK, AA, IR, ALD, DR, ZR, AJS, RH, MR [icddr, b], FJ, MR [IEDCR], and AR received grantsfor research to institutions from The Rockefeller Foundation. MDB is employed by The Rockefeller Foundation. AK, DR, AA, IR, and ALD are employee-owners of Mathematica, own stock options at Mathematica, and shares in mutual funds that include health care firms. AK has received grants or contracts for research (through institution) from The World Bank, The RockefellerFoundation, North Carolina Department of Health and Human Services, Dogwood Health Trust(through the Jackson County Department of Public Health and Haywood County Health and Human Services Agency), and the Massachusetts Department of Public Health; has received honoraria for educational events for Genome Canada; has participated on the World Bank's Advisory Board of the Heatwave Data Collaborative (unpaid service); and has served as an unpaid board member to the town of Waynesville's Environmental Sustainability Board. ALD has received grants or contracts for research to institution from the US Department of Health and Human Services, National Science Foundation, and the University of Chicago; and has been financially supported by the Bill and Melinda Gates Foundation for conference attendance (GeoField). DR has received grants or contracts for research to institution from the US Department of Health and Human Services, The Rockefeller Foundation, The Global Center on Adaptation, and the Massachusetts Department of Public Health; has received consulting fees from Imperial College London for research activities; has received payment for lecturing activities at Imperial College London; and has been financially supported by Mathematica to attend health- and economics-related conferences. IR has received grants or contracts for research (through institution) from The Rockefeller Foundation, the World Bank, North CarolinaDepartment of Health and Human Service, the US Centers for Medicare and Medicaid Services, the US Center for Medicare and Medicaid Innovation, and Rural Health RedesignCenter Organization, Inc. AA has received grants or contracts for research (through institution) from United States Agency for International Development, the Bill and Melinda GatesFoundation, AGRA, Agency Fund, and the World Bank Strategic Impact Evaluation Fund; and has received consultancy fees from the World

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Author details
[1]Mathematica, Inc. Princeton, P.O. Box 2393, Princeton, NJ 08543-2393, USA
[2]Environmental Health and WASH, Health Systems and Population Studies Division, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh
[3]University of California, Santa Cruz, CA, USA
[4]Communicable Disease Control (CDC) Program, Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare, Dhaka, Bangladesh
[5]Institute of Epidemiology, Disease Control and Research (IEDCR), Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare, Dhaka, Bangladesh
[6]The Rockefeller Foundation, New York, NY, USA

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References

1. Wang B, et al. Global, regional, and National incidence and mortality for enteric infections from 1990 to 2019. BMC Public Health. 2025;25:100.
2. Institute for Health Metrics and Evaluation. Enteric infections - Level 2 cause| Institute for Health Metrics and Evaluation. https://www.healthdata.org/research-analysis/diseases-injuries-risks/factsheets/2021-enteric-infections-level-2-disease (2021).
3. WHO. Diarrhoeal Disease. https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease (2024).
4. Hancuh M, et al. Typhoid fever surveillance, incidence estimates, and progress toward typhoid conjugate vaccine Introduction - Worldwide, 2018–2022. MMWR Morb Mortal Wkly Rep. 2023;72:171–6.
5. Marks F, et al. Incidence of typhoid fever in Burkina Faso, Democratic Republic of the congo, Ethiopia, Ghana, Madagascar, and Nigeria (the severe typhoid in Africa programme): a population-based study. Lancet Glob Health. 2024;12:e599–610.
6. CDC, Typhoid. & Paratyphoid Fever| CDC Yellow Book 2024. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/typhoid-and-paratyphoid-fever (2024).
7. Mawazo A, Bwire GM, Matee MIN. Performance of Widal test and stool culture in the diagnosis of typhoid fever among suspected patients in Dar Es Salaam, Tanzania. BMC Res Notes. 2019;12:316.
8. Andrews JR, et al. Environmental surveillance as a tool for identifying High-risk settings for typhoid transmission. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020;71:S71–8.
9. Matrajt G, Lillis L, Meschke JS. Review of methods suitable for environmental surveillance of Salmonella Typhi and paratyphi. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020;71:S79–83.
10. Uzzell CB, et al. Environmental surveillance for Salmonella Typhi and its association with typhoid fever incidence in India and Malawi. J Infect Dis. 2024;229:979–87.
11. Hu X, Keshaviah A, Harrison E. The Costs of Wastewater Monitoring in Low-and Middle-Income Countries. https://www.mathematica.org/publications/the-costs-of-wastewater-monitoring-in-low-and-middle-income-countries (2023).
12. Bowes DA, Zaman MH. Considerations for conducting wastewater-based public health assessments in migrant populations. J Environ Expo Assess. 2023;2.
13. Shrestha S, et al. Detection of Salmonella Typhi bacteriophages in surface waters as a scalable approach to environmental surveillance. PLoS Negl Trop Dis. 2024;18:e0011912.
14. UNDP. Climate Vulnerability Index (Draft). https://www.undp.org/bangladesh/publications/climate-vulnerability-index-draft (2023).
15. UNHCR. Joint Government of Bangladesh– UNHCR Population Factsheet as of Feb 2023. https://data.unhcr.org/en/documents/details/99389 (2023).
16. WHO, Bangladesh. Health Sector Cox's Bazar - Monthly Bulletin (March 2023) - Bangladesh. https://reliefweb.int/report/bangladesh/bangladesh-health-sector-coxs-bazar-monthly-bulletin-march-2023 (2023).
17. Islam MT, et al. Field evaluation of a locally produced rapid diagnostic test for early detection of cholera in Bangladesh. PLoS Negl Trop Dis. 2019;13:e0007124.
18. Ali M, et al. Functionality Analysis of Sanitation Options in Rohingya Camps in Cox's Bazar of Bangladesh. 2018.
19. Liu P, et al. Comparison of Nanotrap® Microbiome A particles, membrane filtration, and skim milk workflows for SARS-CoV-2 concentration in wastewater. Front Microbiol. 2023;14:1215311.
20. Nair S, et al. Real-Time PCR assay for differentiation of typhoidal and nontyphoidal Salmonella. J Clin Microbiol. 2019;57:e00167–19.
21. Forootan A, et al. Methods to determine limit of detection and limit of quantification in quantitative real-time PCR (qPCR). Biomol Detect Quantif. 2017;12:1–6.
22. WHO, Bangladesh - Rohinya Crisis EWARS, Week. 47 2024. https://cdn.who.int/media/docs/default-source/searo/bangladesh/bangladesh---rohingya-crisis---pdf-reports/ewars/2024/ewars-w47-2024.pdf (2024).
23. Karo B, et al. World health organization early warning, alert and response system in the Rohingya crisis. Emerg Infect Dis. 2018;24:2017–8.
24. Garrett DO, et al. Incidence of typhoid and paratyphoid fever in Bangladesh, Nepal, and Pakistan: results of the surveillance for enteric fever in Asia project. Lancet Glob Health. 2022;10:e978–88.
25. Islam MS, et al. Prevalence and determinants of diarrhea, fever, and coexistence of diarrhea and fever in children Under-Five in Bangladesh. Children. 2023;10:1829.
26. Qayum MO, et al. Oral cholera vaccine coverage evaluation survey: forcibly displaced Myanmar nationals and host community in Cox's Bazar, Bangladesh. Front Public Health. 2023;11:1147563.
27. Lo NC, et al. Comparison of strategies and incidence thresholds for Vi conjugate vaccines against typhoid fever: A Cost-effectiveness modeling study. J Infect Dis. 2018;218:S232–42.
28. Burrows H, et al. Comparison of model predictions of typhoid conjugate vaccine public health impact and cost-effectiveness. Vaccine. 2023;41:965–75.
29. Koesnoe S, et al. A phase II clinical trial of a Vi-DT typhoid conjugate vaccine in healthy Indonesian adolescents and adults: one-month evaluation of safety and immunogenicity. Trop Dis Travel Med Vaccines. 2024;10:3.
30. Qadri F, et al. Protection by vaccination of children against typhoid fever with a Vi-tetanus toxoid conjugate vaccine in urban Bangladesh: a cluster-randomised trial. Lancet. 2021;398:675–84.
31. Lightowler MS, et al. Effectiveness of typhoid conjugate vaccine in Zimbabwe used in response to an outbreak among children and young adults: A matched case control study. Vaccine. 2022;40:4199–210.
32. Olesen SW, Imakaev M, Duvallet C. Making waves: defining the lead time of wastewater-based epidemiology for COVID-19. Water Res. 2021;202:117433.
33. Saha S, et al. Epidemiology of typhoid and paratyphoid: implications for vaccine policy. Clin Infect Dis Off Publ Infect Dis Soc Am. 2019;68:S117–23.
34. Poulos C, et al. Cost of illness due to typhoid fever in five Asian countries. Trop Med Int Health TM IH. 2011;16:314–23.
35. Khanam F, et al. Typhoid fever in young children in Bangladesh: clinical findings, antibiotic susceptibility pattern and immune responses. PLoS Negl Trop Dis. 2015;9:e0003619.
36. Robinson LA, Hammitt JK, O'Keeffe L. Valuing mortality risk reductions in global Benefit-Cost analysis. J Benefit-Cost Anal. 2019;10:15–50.
37. Sanders GD, et al. Recommendations for conduct, methodological practices, and reporting of Cost-effectiveness analyses: second panel on Cost-Effectiveness in health and medicine. JAMA. 2016;316:1093–103.
38. Saleh M, Farah Z, Howard N. Infectious disease surveillance for refugees at borders and in destination countries: a scoping review. BMC Public Health. 2022;22:227.

39. Bangladesh Planning Commission. SDG Snapshot: Bangladesh (Progress so far). https://sdg.gov.bd/ (2024).
40. Directorate General of Health Services. Health Bulletin 2020. https://dghs.portal.gov.bd/sites/default/files/files/dghs.portal.gov.bd/page/8983ee81_3668_4bc3_887e_c99645bbfce4/2022-09-20-12-31-58c5a0b12e3aad087eaa26c3ce0f1a7b.pdf (2022).
41. Keshaviah A et al. The Role of Wastewater Data in Pandemic Management. (2023). https://www.rockefellerfoundation.org/reports/the-role-of-wastewater-data-in-pandemic-management/.
42. Keshaviah A et al. Separating signal from noise in wastewater data: An algorithm to identify community-level COVID-19 surges in real time. Proc. Natl. Acad. Sci. U. S. A. 120, e2216021120 (2023).
43. Pakhtigian EL, Aziz S, Boyle KJ, Akanda AS, Hanifi SM. A. Early warning systems, mobile technology, and cholera aversion: evidence from rural Bangladesh. J Environ Econ Manag. 2024;125:102966.
44. Hagedorn BL, Gauld J, Feasey N, Hu H. Cost-effectiveness of using environmental surveillance to target the roll-out typhoid conjugate vaccine. Vaccine. 2020;38:1661–70.
45. UNICEF, Water, and the Global Climate Crisis.: 10 Things You Should Know. https://www.unicef.org/stories/water-and-climate-change-10-things-you-should-know (2023).
46. Chua PLC, Ng CFS, Tobias A, Seposo XT, Hashizume M. Associations between ambient temperature and enteric infections by pathogen: a systematic review and meta-analysis. Lancet Planet Health. 2022;6:e202–18.

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