Supplement: Modeling the Effect of Water, Sanitation, and Hygiene and Oral Cholera Vaccine Implementation in Haiti

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Supplementary Materials

METHODS

Summary. We developed a spreadsheet-based static model in Excel 2010 (Microsoft, Seattle, WA) to estimate the potential number of cholera cases averted through improvements in coverage for water, sanitation and hygiene (WASH) interventions (i.e., latrines, point-of-use chlorination, and piped water), the use of oral cholera vaccine (OCV), or a combination of both. It incorporates varying incidence data from Malawi, Mozambique and India applied to Haitian demographic data to generate expected annual cholera incidence in Haiti over a 20 year period; the underlying assumption of the model is that cholera is going to be endemic in Haiti for the next 20 years.

Demographics. Haitian demographic data were obtained from its last census in 2003 and were extrapolated accordingly to determine a best estimate for current population size as given by Institut Haitien de Statistique et d'Informatique (February 7, 2013) (Supplemental Table 1). The current estimate suggests that the urban and rural populations of Haiti are relatively equal in size. We made projections for cholera cases in Haiti over the next 20 years, assuming a constant growth rate.

We assumed that the current urban-rural ratio would not change for the next 20 years. We understand that this assumption may not hold in the future, but for the purpose of this study, we believe that this assumption is adequate. If the percentage of urban population in Haiti continues to increase, we could have underestimated the effect of interventions in urban areas and overestimated the effect of interventions in rural areas (assuming that the coverage percentages remain the same).

Expected annual incidence. As cholera has been absent in Haiti for more than 100 years before the 2010 outbreak, we do not have historical endemic cholera incidence data for Haiti. Therefore, we estimate the 20-year annual incidence of endemic cholera in Haiti, by using data from Malawi in our basic scenario and by using historical data from Mozambique and India and hypothetical data in our sensitivity analyses.

Basic scenario. We chose 1990–2010 annual cholera incidence data for Malawi for our basic scenario because Malawi faces similar socio-economic challenges as those faced by Haiti (e.g., poor infrastructure, relatively high infant mortality rate, a large population without piped water, rates of literacy < 80%, see https://www.cia.gov/library/publications/the-world-factbook/geos/mi.html). We used Malawian annual cholera incidence data as reported to the WHO (available at WHO Global Health Observatory at http://www.who.int/gho/epidemic_diseases/cholera/cases/en/index.html) and Malawian total population data (available at Food and Agricultural Organization data, FAO website: http://faostat3.fao.org/home/index.html#DOWNLOAD; Choose "Elements: Total Population – Both sexes (1000)"; access on Jan 29, 2013) to calculate the annual cholera incidence rate. We then apply this rate to the projected Haitian population data to estimate the expected annual cholera incidence in Haiti for 20 years.

Interventions modeled. We modeled WASH and OCV interventions and interventions that combined WASH and OCV. The effect of the interventions on the two subpopulations were modeled separately, labeled WASH/U, WASH/R, OCV/U, OCV/R, Combined/U and Combined/R. The scenarios were denoted as 1, 2, and 3 for the different rate of implementation, where 1 indicated the fastest. Therefore, we have the following scenarios: WASH/U 1, WASH/U 2, WASH/U 3, WASH/R 1, WASH/R 2, WASH/R 3, OCV/U 1, OCV/U 2, OCV/U 3, OCV/R 1, OCV/R 2, OCV/R 3, Combined/U 1, Combined/U 2, Combined/R 1, and Combined/R 2. The combination scenarios were modeled separately and were not a result of combining the results of the WASH and OCV scenarios.

For WASH interventions, we chose three interventions: latrines, point-of-use chlorination of drinking water, and community piped water (standpipes). Latrines and point-of-use chlorination are short-term interventions, and community piped water a long-term solution.

Intervention effectiveness. For each intervention, we included a non-linear relationship between coverage and effectiveness that takes into account indirect protective effects.

OCV. For OCV effectiveness data, while the direct effect data from the randomized control trial (RCT) of Shanchol™ in Kolkata, India, are evident,[1] the indirect effect data are not (The indirect protection was evident in the geographic information system approach but not the cluster design approach[2]). Given that the direct effect of Shanchol™ is similar to and slightly better than Dukarol®, we considered that it was reasonable to use the simulated results of the model by Longini et al.[3] that fit to the Dukarol® RCT at Matlab, Bangladesh. We fit the data to a best line in the form of: effectiveness at a coverage level = 1 – exp (–λ * coverage), which allowed us to model both the direct and indirect (herd immunity) effect of OCV (Figure 2, Supplemental Table 2).

WASH. For the effectiveness data, we obtained point estimates from Cochrane reviews.[4,5] We assumed that these point estimates applied to a coverage level of 100%. In order to be able to compare WASH interventions with OCV, we estimated the direct and indirect effect of WASH interventions, by fitting the OCV coverage-effectiveness curve equation

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Supplemental Table 1

Demographic parameters for the model

Description	Value	Reference or note
Population, Haiti		Direction des Statistiques Démographiques et Sociales, Institut Haïtien de Statistique et d'Informatique (obtained on Feb 7, 2013)
Urban	5,154,940	
Rural	5,258,271	
Total	10,413,211	
Population growth rate	0.89%	CIA fact book estimate 2012
Discount rate	3%	Assumption

to the WASH interventions' point estimates to obtain an estimate of λ and therefore, a coverage-effective curve for each WASH intervention: effectiveness at a coverage level = 1 − exp (−λ * coverage) (Figure 2, Supplemental Table 2). In our model, piped water confers the strongest protection, followed by point-of-use chlorination, and then latrines.

Intervention coverage over time. *WASH.* We assumed that in the first 5 years of implementation, resources would primarily be allocated towards point-of-use chlorination. Extension of piped water would only begin in year 6. Given that the evidence for aggregated effects of multiple WASH interventions is debatable, we assumed no additive effects for multiple WASH interventions applied simultaneously.[6,7] In our model, for example, if 10% of the population uses latrines and point-of-use chlorination, the protection conferred by both interventions will be the same as point-of-use chlorination only. Therefore, using a stepwise introduction of interventions over time, the intervention with the stronger protective effect supplanted the other.

We also input the annual coverage of the three WASH interventions being studied. For each year, x% of the population would be covered by piped water (and point-of-use chlorination and/or latrines, or none), y% of the population would be covered by point-of-use chlorination (and latrines or none, but not piped water), z% of population would be covered by latrines only, and (100-x-y-z)% of the population received no WASH interventions.

The intervention effects were then taken from the coverage-effectiveness curves. For the coverage attained by year 0, 5, and 20 for different scenarios (Tables 1–3). We assumed that 5 people would share 1 latrine and 50 people would share 1 standpipe. Supplemental Table 3 provides the corresponding figures for the estimated number of latrines built, number of people covered by point-by-use chlorination intervention, and number of standpipe constructed in the different scenarios as described in the main text.

Supplemental Table 2

Parameters for coverage-effectiveness curve equations for various interventions

	λ	Effect estimate (at 100% coverage)	Reference / Assumption
OCV	4.6975	-	Curve fitted to modeling output of Longini et al.[3]
Piped water	2.3019	90%	Assumption. Sensitivity analysis performed.
Point-of-use chlorination	1.0788	66%	CI, 32% – 83%[4]
Latrines	0.3425	29%	CI, 8% – 46%[5]

OCV = oral cholera vaccine; CI = Confidence interval.

OCV. An OCV study has been implemented in Haiti using the Shanchol™ vaccine.[8,9] The vaccine requires two doses to achieve its expected effect. In our model, we assume that people were effectively immunized by two doses. We did not examine partial vaccination effect (i.e., receiving only one dose).

Next we input the annual coverage of interventions for the model from year 0 to year 20. We modeled the effective coverage of OCV. Supplemental Table 4 provides the corresponding figures for the estimated number of number of doses of OCV needed in the different scenarios as described in the main text. We assumed that a booster dose is provided every three years to a previously vaccinated individual if he or she remains effectively covered.

Combined WASH and OCV. For the combined scenarios, we assumed that (a) people who would receive OCV would be those who would not be covered by any WASH interventions and vice versa; (b) the coverage of WASH and OCV would never exceed 50% respectively; (c) OCV coverage would increase at a constant rate from baseline to year 5 and then decrease at a constant rate from year 6 onwards; (d) latrines coverage would remain the same from baseline to year 5; (e) point-of-use chlorination will increase from baseline onwards; and (f) piped water will increase only from year 6 onwards at a constant rate.

We modeled an initial increase in OCV coverage, followed by a decrease after year 5 because we believed that OCV, which requires a booster every few years to maintain its effective coverage in the population, would not be a permanent solution to the cholera epidemic in Haiti.

Number of cases averted. We calculated for each year the cases averted by multiplying the protective effect of the intervention(s) at a given coverage in that year with the total expected number of cases in the same year. We calculated the cumulative number of cases averted by summing up the cases averted of each year with a discount rate of 3% per year. Discounting is applied to account for differential timing of costs and benefits.[10]

Given the static nature of the model, for each scenario, the number of cases averted for each year is the result of the direct and indirect effects of interventions applied in that year. However, this model does not take into account the effect of any interventions applied this year in the future.

Uncertainty and sensitivity analyses. To assess the robust nature of our model, we performed sensitivity/uncertainty analyses in three steps.

Varying baseline incidence rates. First, we applied different baselines (first, historical annual incidence data from Mozambique and India; second, hypothetical annual incidence data) to the Haitian demographic data for the expected number of cholera cases to illustrate how a change in the input of the annual incidence data will change our results.

(a) Historical scenarios (Supplemental Figure 1). As part of our sensitivity analyses, we used 1990–2010 historical cholera incidence data for Mozambique and 1961–1981 data India from, as reported to WHO, to represent a higher and a lower mean incidence respectively. (The data sources are the same as the Malawian data for the Basic scenario.).

(b) Hypothetical scenarios (Supplemental Figure 2). We also created three hypothetical scenarios as part of our

SUPPLEMENTAL TABLE 3
WASH scenarios*

	WASH/U 1	WASH/U 2	WASH/U 3	WASH/R 1	WASH/R 2	WASH/R 3	Combined/U 1	Combined/U 2	Combined/R 1	Combined/R 2
No. of latrines at baseline	103,099	103,099	103,099	105,165	105,165	105,165	103,099	103,099	105,165	105,165
New latrines built from Year 1 to 5	13,896	13,896	13,896	655,997	340,086	14,175	13,896	13,896	14,175	14,175
New latrines built from Year 6 to 20	0	5,617	72,448	1,375,322	2,823,002	193,421	0	0	0	0
People covered by point-of-use chlorination but not piped water at baseline	1,303,988	1,303,988	1,303,988	1,367,150	1,367,150	1,367,150	1,030,988	1,030,988	1,367,150	1,367,150
People covered by point-of-use chlorination but not piped water from year 1 to 5	14,879,093	11,684,030	8,488,967	9,301,403	7,671,849	7,671,849	6,891,436	6,891,436	7,671,849	7,671,849
People covered by point-of-use chlorination but not piped water from year 6 to 20	47,411,582	57,698,084	59,823,792	42,884,184	32,347,291	32,347,291	15,495,258	26,979,233	15,605,609	26,899,202
No. of standpipes at baseline	10,310	10,310	10,310	0	0	0	1,303,988	1,303,988	0	0
New standpipe built from year 1 to 5	1,390	1,390	1,390	0	0	0	1,390	1,390	0	0
New standpipe built from year 6 to 20	633,222	396,968	113,464	674,771	481,979	240,990	396,968	160,714	481,979	240,990

*Number of latrines, number of people covered by point-of-use chlorination and number of standpipes at the baseline coverage and the coverage for year 5 and 20. We assume that 5 people share one latrine and 50 people share one standpipe (without discounting).

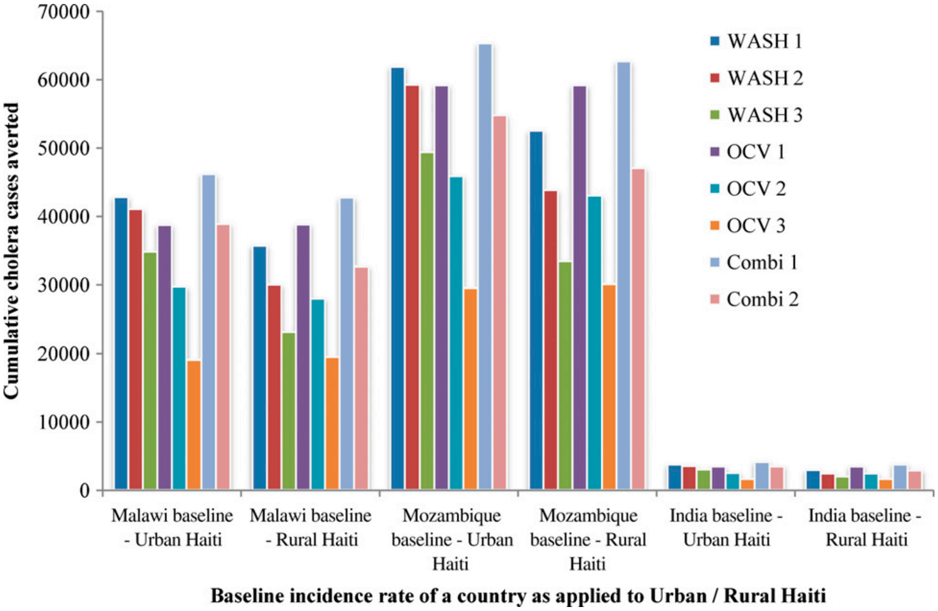
R = rural; U = urban; WASH = water, sanitation, and hygiene.

sensitivity analyses: stable incidence, growing incidence, and declining incidence. These helped us determine whether the increasing or declining annual incidence changes our results. These hypothetical scenarios were created by first picking a mean from the mean incidence of one of the four historical scenarios (mean) and then choosing a variation level (v). For the growing and declining scenarios, we choose a growing rate (rate$_1$) and a declining rate (rate$_2$), respectively. In our sensitivity analyses, we chose the mean of the Malawian incidence data, v = 20%, rate$_1$ = 10% and rate$_2$ = 10%. We use the RAND function in Excel to choose a random number

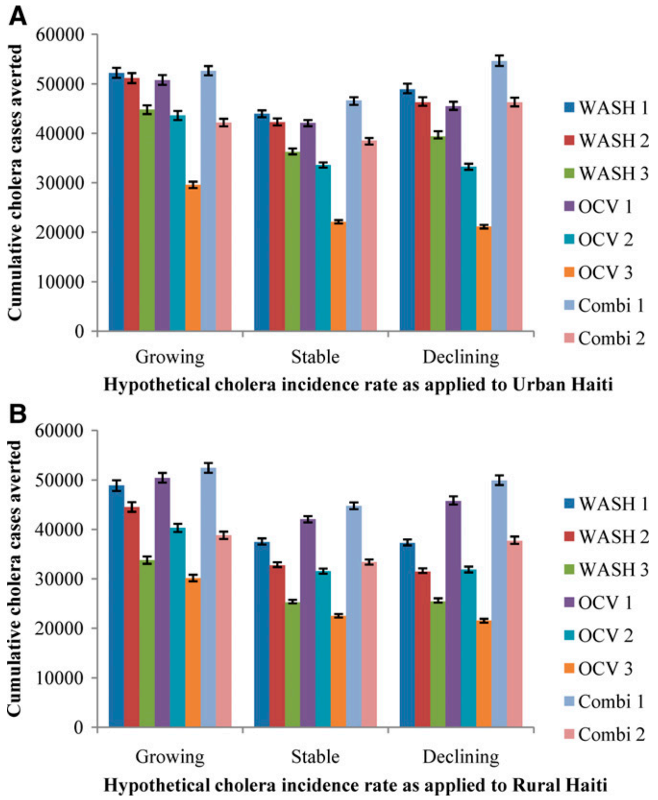
SUPPLEMENTAL TABLE 4
Number of doses of OCV needed in a particular year for different scenarios

Year	OCV/U – 1	OCV/U – 2	OCV/U – 3	OCV/R – 1	OCV/R – 2	OCV/R – 3	Combined/U 1	Combined/U 2	Combined/R 1	Combined/R 2
0	103,099	103,099	103,099	105,165	105,165	105,165	103,099	103,099	105,165	105,165
1	937,044	312,958	104,930	955,827	319,232	107,033	312,958	104,930	319,232	107,033
2	1,058,616	423,446	211,723	1,079,836	431,934	215,967	423,446	211,723	431,934	215,967
3	1,128,885	482,483	267,016	1,151,513	492,155	272,369	482,483	267,016	492,155	272,369
4	1,616,375	646,550	323,275	1,648,775	659,510	329,755	646,550	323,275	659,510	329,755
5	2,164,903	865,961	432,981	2,208,298	833,319	441,660	865,961	432,981	883,319	441,660
6	1,925,799	944,264	435,894	1,779,578	815,333	444,631	545,641	254,702	556,579	259,807
7	2,479,525	1,168,844	547,540	2,341,120	1,041,788	558,515	763,141	363,130	778,438	370,409
8	3,042,932	1,397,337	661,134	2,912,495	1,272,200	674,387	984,461	473,463	1,004,194	482,954
9	3,217,527	1,557,319	722,345	2,994,807	1,358,764	736,825	937,863	440,774	956,662	449,609
10	3,394,983	1,720,033	784,592	3,078,352	1,446,764	800,319	890,359	407,467	858,815	415,635
11	3,575,338	1,885,513	847,886	3,163,144	1,536,220	864,882	841,938	373,534	808,474	381,021
12	3,758,627	2,053,797	912,243	3,249,200	1,627,151	930,529	792,587	338,966	757,172	345,760
13	3,944,890	2,224,921	977,676	3,336,534	1,719,575	997,274	742,293	303,754	704,895	309,843
14	4,134,164	2,398,922	1,044,199	3,425,164	1,813,513	1,065,130	691,043	267,891	651,629	273,260
15	4,326,489	2,575,838	1,111,827	3,515,104	1,908,983	1,134,113	638,824	231,366	597,363	236,004
16	4,521,903	2,755,707	1,180,573	3,636,371	2,006,006	1,204,238	585,624	194,172	542,081	198,064
17	4,720,447	2,938,567	1,250,453	3,698,983	2,104,601	1,275,518	531,428	156,299	542,081	159,432
18	4,922,161	3,124,457	1,321,480	3,792,954	2,204,790	1,347,969	476,224	117,738	485,770	120,098
19	5,127,084	3,313,417	1,393,670	3,888,303	2,306,591	1,421,606	419,997	78,479	428,416	80,053
20	5,335,259	3,505,487	1,467,039	3,985,046	2,410,027	1,496,445	362,734	38,515	370,005	39,287

OCV = oral cholera vaccine; R = Rural; U = Urban.



Supplemental Figure 1. Cumulative cases of cholera averted by WASH interventions and/or OCV in Haiti in 20 years, assuming a baseline national incidence rate of Malawi (1990–2010), Mozambique (1990–2010), and India (1961–1981) as applied to urban and rural Haiti. WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine; Combi = combination of WASH and OCV.



Supplemental Figure 2. Cumulative cases of cholera averted by WASH interventions and/or OCV in Haiti in 20 years, assuming hypothetical baseline national incidence rates – growing, stable, or declining as applied to (A) urban and (B) rural Haiti. The mean = mean of national incidence rate in Malawi (1990–2010). Growing rate: 10%; Declining rate: 10%; Random variation by 20%. WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine; Combi = combination of WASH and OCV.

(rand) from a uniform distribution between 0 and 1 to generate stochasticity in the model. For the stable scenario, the incidence for each year = (rand*2*v+1–v)*mean. For the growing and declining scenarios, the incidence for each year is calculated using the equations in Supplemental Table 5.

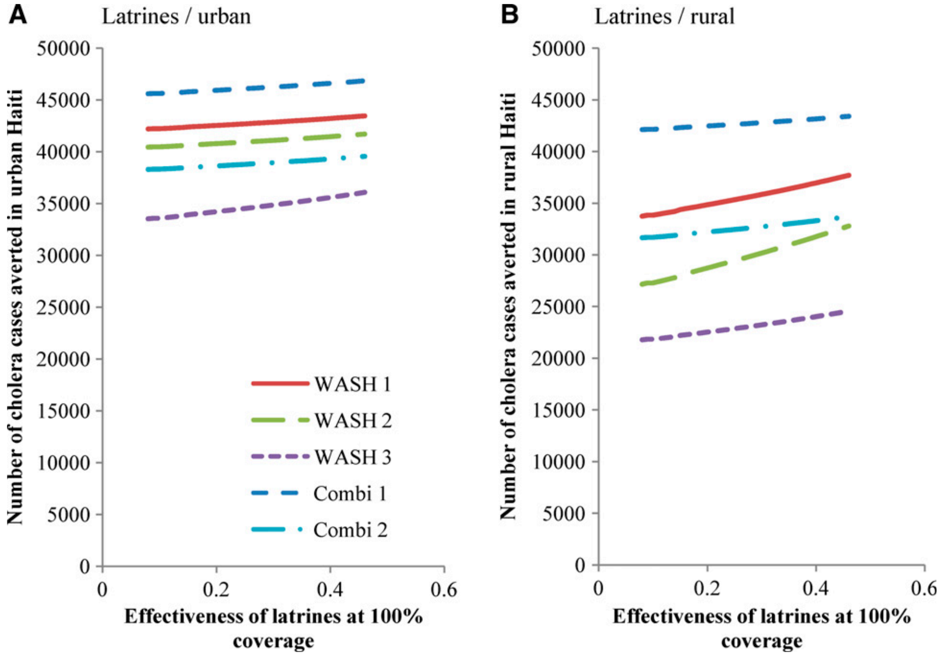
Uncertainty of protective effect of WASH. Second, we ran an uncertainty analysis for different estimates of the protective effectiveness data at 100% coverage against cholera of the three WASH interventions, namely latrines (Supplemental Figure 3), point-of-use chlorination (Supplemental Figure 4), and community piped water (Supplemental Figure 5). The coverage-effectiveness curves changed (change in λ) accordingly. The ranges are as follows: latrines: 8% (lower 95% confidence interval [CI]) and 46% (higher 95% CI) (Supplemental Figure 3); point-of-use chlorination: 32% (lower 95% CI), and 83% (higher 95% CI) (Supplemental

Supplemental Table 5

Equations for the baseline incidence for the hypothetical growing and declining incidence scenarios*

	Year	Baseline incidence
Growing incidence scenario	0 to 9	$= (rand*2*v+1-v)*mean/(1+rate_1)^n$
	10	$= (rand*2*v+1-v)*mean$
	11 to 20	$= (rand*2*v+1-v)*mean*(1+rate_1)^n$
Declining incidence scenario	0 to 9	$= (rand*2*v+1-v)*mean*(1+rate_2)^n$
	10	$= (rand*2*v+1-v)*mean$
	11 to 20	$= (rand*2*v+1-v)*mean/(1+rate_2)^n$

*The hypothetical annual incidence scenarios were created by first picking a mean from the mean incidence of one of the four historical scenarios (mean) and then choosing a variation level (v). For the growing and declining scenarios, we choose a growing rate ($rate_1$) and a declining rate ($rate_2$) respectively. We use the RAND function in Excel to choose a random number (rand) between 0 and 1 to generate stochasticity in the model. n refers to the absolute number of difference between year 10 and a particular year. For example, for year 8, n = 2.

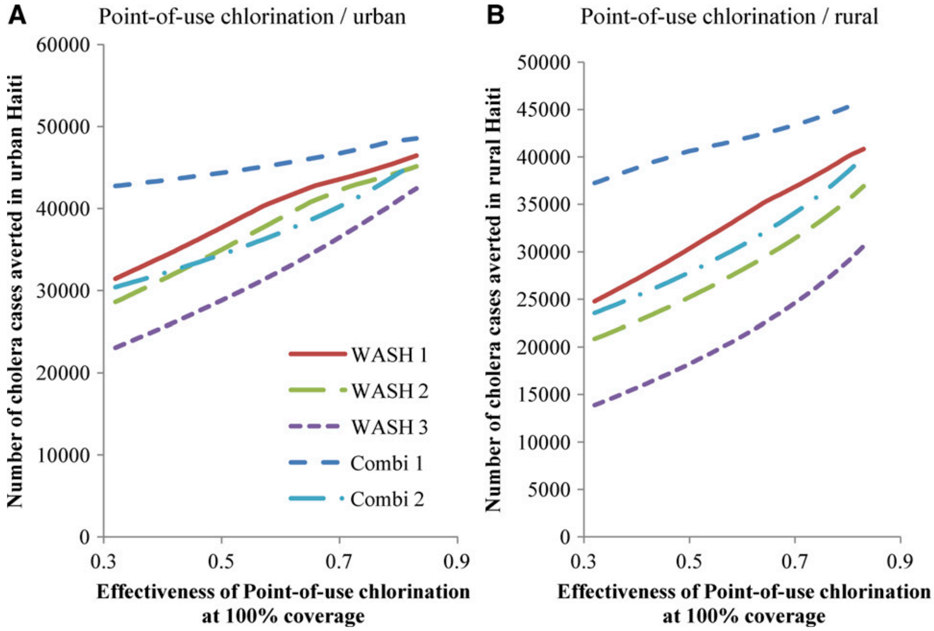


Supplemental Figure 3. The number of cholera cases averted by WASH scenarios 1, 2, and 3 and Combined WASH and OCV scenarios 1 and 2 in (A) urban and (B) rural Haiti as the protective effectiveness of latrines changes respectively. WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine; Combi = combination of WASH and OCV.

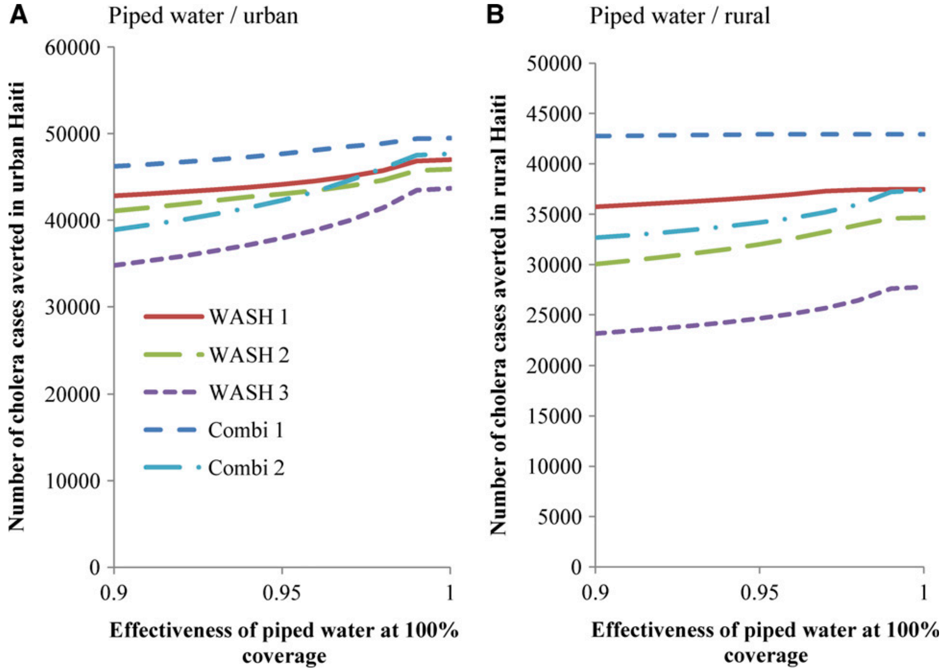
Figure 4); piped water 90% (the default value) and 100% (complete protection) (Supplemental Figure 5).

Varying coverage / implementation rate. We then proceeded to study the effect of the variation of the coverage/implementation rate. First, we performed sensitivity analysis for WASH interventions and OCV interventions for urban (Supplemental Figure 6) and rural (Supplemental Figure 7) Haiti and then for combined interventions for urban (Supplemental Figure 8) and rural (Supplemental Figure 9) Haiti.

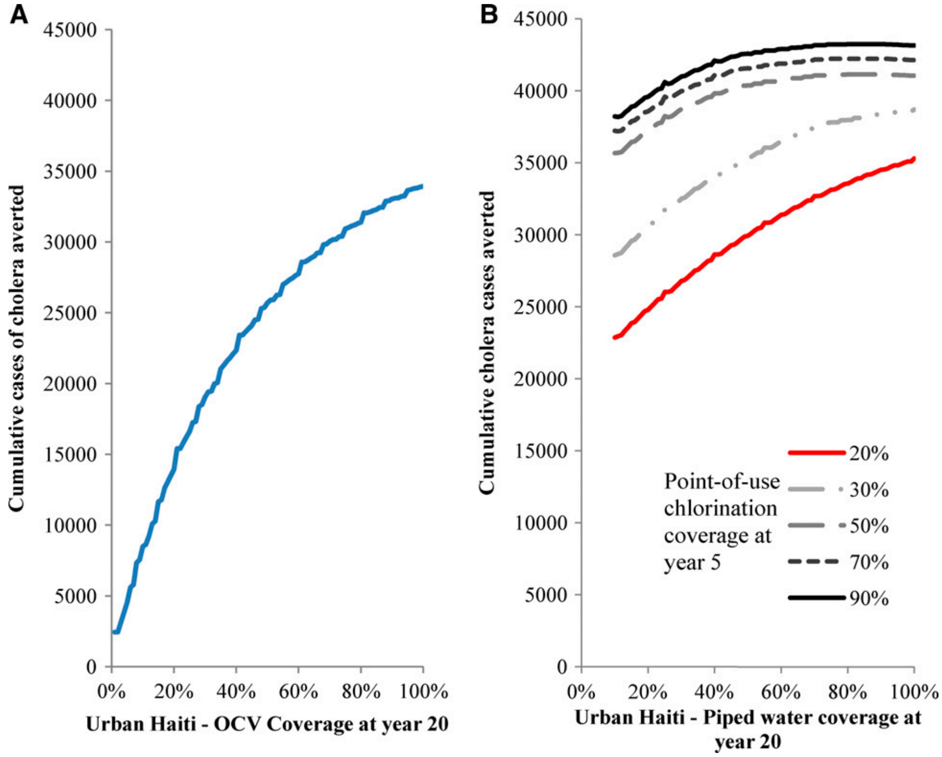
(a) *OCV uncertainty/sensitivity analyses*. As explained in the main text; see Supplemental Figures 6A and 7A. (Note: in the main scenarios, the rate of increase in the first 5 years can be different from that in the later 15 years.)



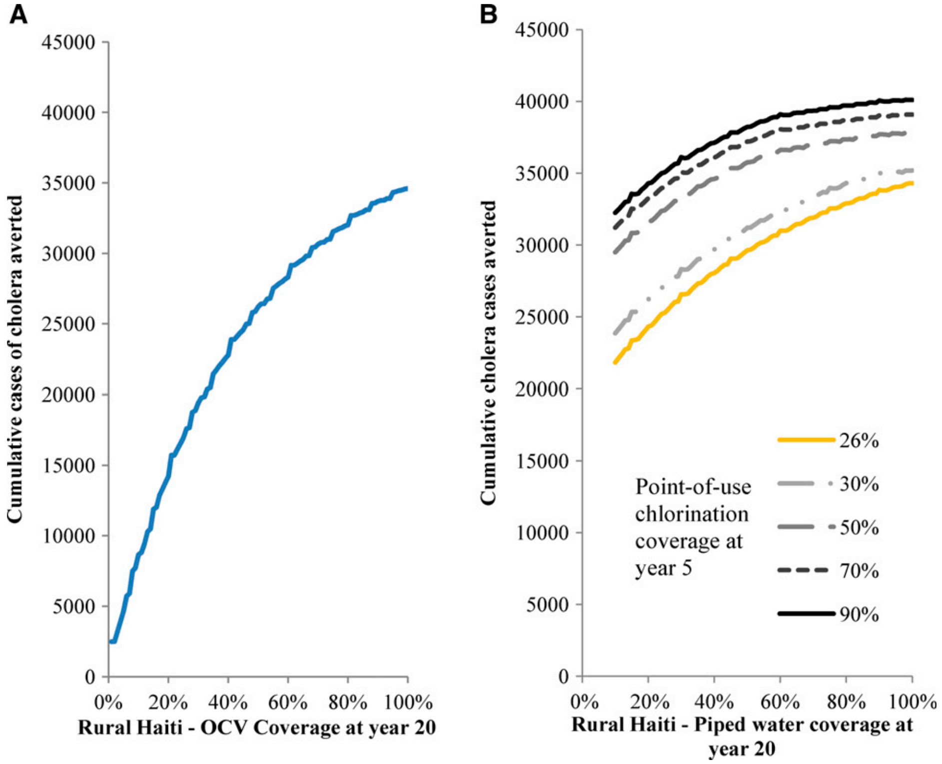
Supplemental Figure 4. The number of cholera cases averted by WASH scenarios 1, 2, and 3 and Combined WASH and OCV scenarios 1 and 2 in (A) urban and (B) rural Haiti as the protective effectiveness of point-of-use chlorination changes respectively. WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine; Combi = combination of WASH and OCV.



Supplemental Figure 5. The number of cholera cases averted by WASH scenarios 1, 2, and 3 and Combined WASH and OCV scenarios 1 and 2 in (A) urban and (B) rural Haiti as the protective effectiveness of piped water changes respectively. WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine; Combi = combination of WASH and OCV.



Supplemental Figure 6. Sensitivity analysis: Cumulative cases of cholera averted (20 years) in Urban Haiti. (A): OCV coverage at year 20, assuming that OCV coverage increases linearly for 20 years. (B): WASH interventions: Piped water coverage at year 20 (x-axis), assuming that starting in year 6, it begins to increase from its baseline of 10%. The different lines indicate different point-of-use chlorination coverage at year 5: Red line (20%; i.e., the baseline); light grey line-dot-dot (30%); broken grey line (50%); dotted dark grey line (70%); black line (90%). Latrine coverage remained the same (10%) for the first five years as in the baseline. In subsequent years, latrines will be taken over by point-of-use chlorination and piped water (i.e. people using latrines will be covered by another WASH interventions too). WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine.



Supplemental Figure 7. Sensitivity analysis: Cumulative cases of cholera averted (20 years) in Rural Haiti. (A) OCV coverage at year 20, assuming that OCV coverage increases linearly for 20 years. (B) WASH interventions: Piped water coverage at year 20 (x-axis), assuming that starting in year 6, it begins to increase from its baseline of 10%. The different lines indicate different point-of-use chlorination coverage at year 5: Yellow line (0.26; i.e. the baseline); light grey line-dot-dot (0.3); broken grey line (0.5); dotted dark grey line (0.7); black line (0.9). We assume that latrine coverage increased at a constant rate from 10% at the baseline to 30% at year 5. Latrine coverage continues to increase at a constant rate in subsequent years until it is taken over by point-of-use chlorination or piped water (i.e. people using latrines will be covered by another WASH interventions too). WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine.

(b) *WASH uncertainty/sensitivity analyses.* As explained in the main text; see Supplemental Figures 6B and 7B.

(c) *Combined WASH and OCV uncertainty/sensitivity analyses.* As explained in the main text; see Supplemental Figures 8 and 9. Note: Figure 5 in the main text presents the national estimates for the second scenario (Combined/U 2 + Combined/R 2).

RESULTS

In addition to the results we present in the main text, we have performed additional analyses. Their results are presented below.

We compare the results that take into account direct intervention effect only with those that take both direct and indirect results into account. Using scenarios WASH/U 1, WASH/R 1, OCV/U 1 and OCV/R 1 as examples, Supplemental Table 6 shows that if we do not account for indirect effect, the effect of both WASH interventions and OCV will be underestimated, as expected.

Uncertainty and sensitivity analyses. To test the robustness of our model, we performed the following sensitivity/uncertainty analyses.

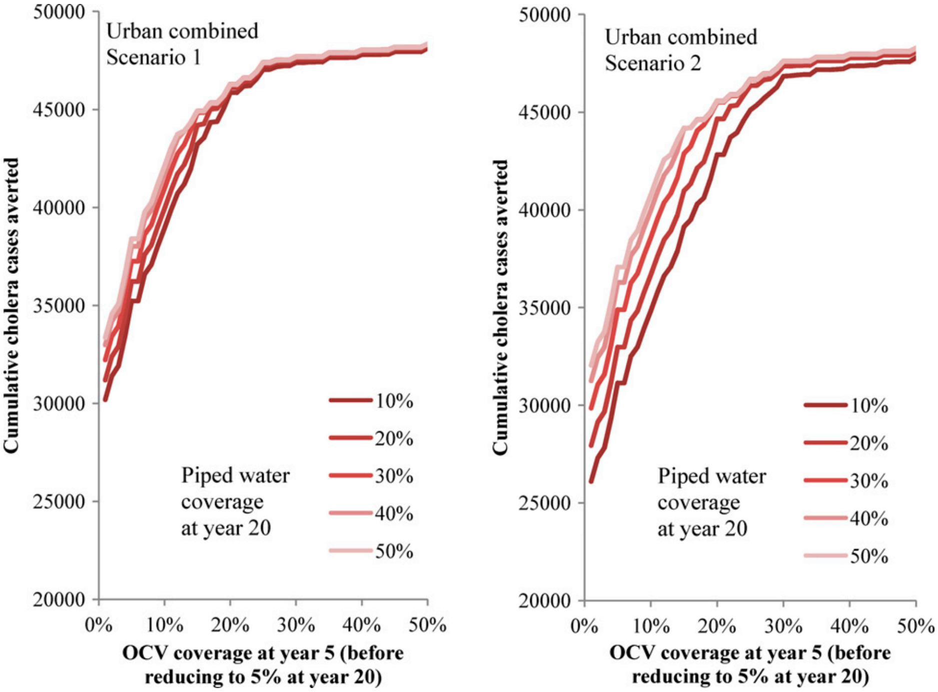
Uncertainty in the expected annual incidence.

(a) *Historical scenarios.* We compared the cumulative cases of cholera averted for a 20-year period with different historical baselines: Malawi (1990–2010), Mozambique (1990–2010), and India (1961–1981) as they were applied to the Haitian demographic data (Table 4 and Supplemental Figure 1). With a high baseline incidence rate (Mozambique scenario), the number of cases averted would be high. Similarly, the cases averted would be few, if the baseline was low (India scenario).

(b) *Hypothetical scenarios.* Sensitivity analysis was performed for three sets of hypothetical baseline cholera incidence curves over a 20-year period. The results shown in Supplemental Figure 2 indicate that the cumulative cholera cases averted would be similar whether the trend was growing, stable, or declining (assuming the same mean incidence over 20 years). In other words, our results were not sensitive to the direction of the 20-year secular trend of cholera incidence.

Given that the model was a static model and that the protection offered by the invention was calculated as a proportion of the expected cholera incidence, the relative magnitude of the number of cases averted across the scenarios would be the same, regardless of the baseline incidence.

Uncertainty of protective effect of WASH. We have also completed an uncertainty analysis of the coverage-effectiveness curves of the three WASH interventions modeled, namely latrines (Supplemental Figure 3), point-of-use chlorination (Supplemental Figure 4), and community piped water



Supplemental Figure 8. Cumulative cholera cases averted in 20 years (y-axis) in the combined intervention scenarios 1 and 2 in urban Haiti. The x-axis refers to OCV coverage at year 5 and the different lines (of varying darkness) refer to piped water coverage at year 20. WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine.

Assumptions: 1. WASH interventions and oral cholera vaccine (OCV) coverages never exceed 50% respectively and that people who receive WASH do not receive OCV or vice versa (i.e., OCV are allocated towards people who are not covered by WASH interventions); 2. Point-of-use chlorination remains at 20% (Urban) and will remain the same (Scenario 2) or increases from 20% increase to 30% at year 5 and will continue to increase (Scenario 1) until piped water takes over (provided assumption 1 met). 3. Latrines coverage remains 10% until it was taken over by point-of-use chlorination and/or piped water. 4. Piped water baseline = 10% in urban areas. Piped water coverage starts increasing at a constant rate from year 6 onwards. 5. OCV coverage peaks at year 5 and declines afterwards and reaches 5% at year 20.

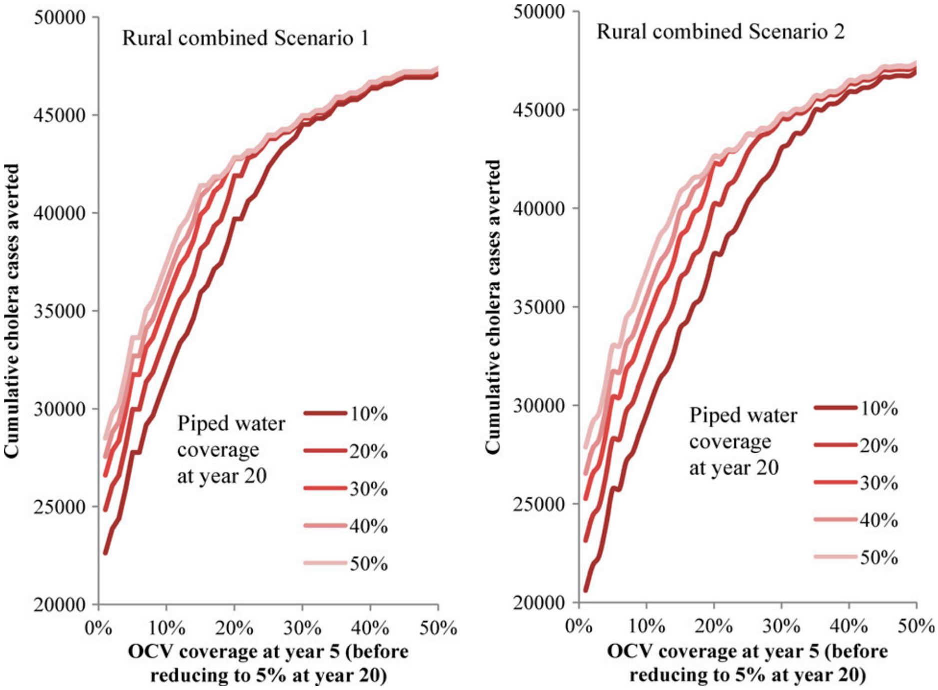
(Supplemental Figure 5) at 100% coverage against cholera. We found that the uncertainty around the magnitude of the protective effect does not alter our results in any significant way.

Uncertainty of rate of implementation and extent of coverage.

(a) *OCV*. Through the sensitivity analysis for OCV interventions (Supplemental Figures 6A and 7A), consistent with our main findings, we found that varying the rate of implementation of OCV campaign (as indicated by the final coverage attained in year 20) would change the number of cumulative cases of cholera averted by tens of thousands.

(b) *WASH*. For the sensitivity analysis for WASH interventions (Supplemental Figures 6B and 7B), we found that extending the coverage of point-of-use chlorination to a large segment of the population early (in the first 5 years) would avert a large number of cholera cases. The marginal returns of investment in piped water were not as high as we would expect. The explanation is that most cases would have been averted by point-of-use chlorination (assuming a high coverage has been achieved at year 5 and that its compliance can be maintained for years). Therefore, the additional benefit of piped water in terms of averted cholera cases may not be as pronounced as one would expect. However, piped water is still a valuable intervention, as compliance to point-of-use chlorination may be limited.[11–13]

(c) *Combined WASH and OCV*. We have also completed the sensitivity analysis for the scenarios of combined WASH and OCV interventions. Figure 5 in the main text presents the national estimates for the second combined scenario (Combined/U 2 + Combined/R 2). Supplemental Figures 8 and 9 present the data for urban and rural areas separately. Comparing Combined/U 1 and 2 scenarios in the sensitivity analysis (Supplemental Figure 8), we can identify the contribution of point-of-use chlorination, as it increase from a baseline of 20% to 30% at year 5 in scenario 1 while in scenario 2, it remains 20%. Similar observation can be made in the sensitivity analysis comparing Combined/R 1 and 2 scenarios (Supplemental Figure 9). Our sensitivity analyses results demonstrated diminishing returns on investment (marginal increase of the number of cholera cases averted) when both OCV coverage at year 5 and piped water coverage at year 20 were high. OCV coverage at 30% achieved similar outcomes with that at 50% (regardless of piped water coverage between 10% and 50% at year 20) (Figure 5 and Supplemental Figures 8 and 9). Additional sensitivity analyses were done for two specific sets of scenarios: We found that as (a) effective OCV coverage increases at a constant rate from 1%



Supplemental Figure 9. Cumulative cholera cases averted in 20 years (y-axis) in the combined intervention scenarios 1 and 2 in rural Haiti. The x-axis refers to OCV coverage at year 5 and the different lines (of varying darkness) refer to piped water coverage at year 20. WASH = water, sanitation, and hygiene; OCV = oral cholera vaccine.

Assumptions: 1. WASH interventions and oral cholera vaccine (OCV) coverages never exceed 50% respectively and that people who receive WASH do not receive OCV or vice versa (i.e., OCV are allocated towards people who are not covered by WASH interventions); 2. Point-of-use chlorination remains at 26% (Rural) and will remain the same (Scenario 2) or increases from 26% increase to 30% at year 5 and will continue to increase (Scenario 1) until piped water takes over (provided assumption 1 met). 3. Latrines coverage remains 10% until it was taken over by point-of-use chlorination and/or piped water. 4. Piped water baseline = 0% in rural areas. Piped water coverage starts increasing at a constant rate from year 6 onwards. 5. OCV coverage peaks at year 5 and declines afterwards and reaches 5% at year 20.

baseline at year 0, to 50% at year 5, and then decreases at a constant rate to 5% at year 20, cumulative cases of cholera averted over 20 years were 48337 (Combined/U 1), 48264 (Combined/U 2), 47375 (Combined/R 1), and 47374 (Combined/R 2) (Table 5) and (b) effective OCV coverage increases at a constant rate from 1% baseline at year 0, to 50% at year 5, and maintaining 50% coverage up to year 20, the cumulative cases of cholera averted over 20 years would be 48371 (Combined/U 1), 48298 (Combined/U 2), 47406 (Combined/R 1), and 47405 (Combined/R 2) respectively (Table 5). Comparing to main combined scenarios as described in Table 3 in the main text (where effective OCV coverage was 10% or 20%), rapid increase in the effective OCV coverage to 50% at year 5 would avert 2,124 to 9,276 more cases in the urban areas and 4,614 to 14,657 more cases in the rural areas. However, when we allowed for effective OCV coverage to reach 50% by year 5 and remain at that level to year 20 (i.e. no decline) (Table 5), we estimated very few additional cases averted: 31 to 34 more cases averted in the urban areas and 75 to 109 more cases averted in the rural areas.

Supplemental Table 6

The effect of indirect effect*

		Direct effect only		Direct and indirect effect		Difference	
Baseline incidence rate as applied to Haiti	U/R Haiti	WASH 1	OCV 1	WASH 1	OCV 1	WASH 1	OCV 1
Malawi (1990–2010)	U	31,423	13,050	42,828	38,793	11,405	25,743
	R	25,874	11,578	35,739	38,843	9,866	27,266
	Total	57,297	24,628	78,568	77,636	21,271	53,008
Mozambique (1990–2010)	U	47,661	20,542	61,879	59,223	14,218	38,681
	R	38,403	18,099	52,541	59,229	14,139	41,130
	Total	86,064	38,640	114,420	118,451	28,356	79,811
India (1961–1981)	U	2,730	1,091	3,711	3,421	982	2,330
	R	2,135	989.001	2,911	3,437	776	2,448
	Total	4,865	2,080	6,623	6,858	1,758	4,779

*Cumulative cases averted in Haiti in 20 years by WASH scenario 1 and OCV scenario 1.

Assumption: underreporting multiplier = 1; OCV = oral cholera vaccine; WASH = water, sanitation, and hygiene; R = Rural; U = Urban.

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