Cholera research scoping review: diagnostics, burden of disease, transmission dynamics and economic burden

London, UK, Sept 18-19, 2025. Harvard Global Health Institute

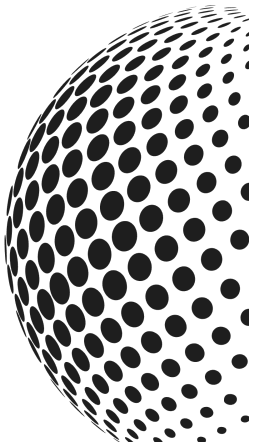
Suggested Citation

Ruitong (Amy) Wang, Wilfredo R Matias, Yodeline Guillaume, Azfar Hossain, Louise C Ivers. Cholera research scoping review: diagnostics, burden of disease, transmission dynamics and economic burden. Presented at a working meeting on cholera research priorities, London, UK, Sept 18-19, 2025. Harvard Global Health Institute.

Table of Contents

HARVARD
Global Health Institute

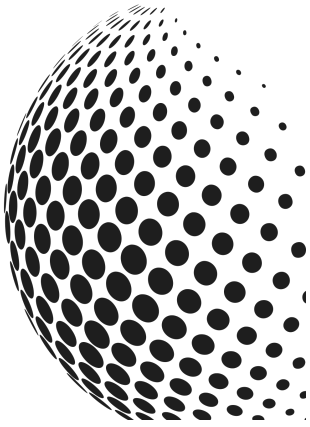
What are the best tools and approaches to diagnosis of cholera in routine and emergency settings?



Wilfredo R Matias, Ruitong (Amy) Wang, Yodeline Guillaume, Azfar Hossain, Louise C Ivers
September 18th -19th, 2025

HARVARD
Global Health Institute

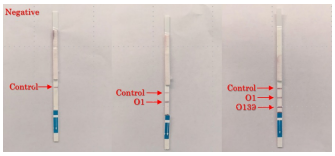
What is the current state of the evidence for cholera rapid diagnostic testing?



Today's diagnostic toolbox

Culture, biochemical and serologic ID	Molecular methods	Rapid diagnostic tests

• ~24 – 72h
• Identify serogroup and serotype
• Antibiotic susceptibility
• Toxin testing, molecular subtyping, archiving
	• ~Hours
	• Nucleic acid amplification (Thermostable, RT, Multiplex, LAMP)
		• <30 min or ~6-24h with enrichment
		• Immunochromatography
		• Probable case detection/surveillance
		• GTFCC benchmarks
		  • Sensitivity (≥90%)
		  • Specificity (≥85%)

		 Matias et al. 2017.

Background

Rapid detection ➡ **Fast outbreak response** ➡ **Accurate burden estimate** ➡ **Precise intervention targeting**

1. What is the diagnostic performance and cost-effectiveness of RDTs for cholera in routine and emergency settings?
   - Setting
   - Test brand
   - Sample processing type
   - Reference standard
   - Patient or other factors (age, symptom severity, etc.)

2. What RDTs are currently commercially available?
3. What ongoing research is evaluating RDTs?

Methods

Two-part narrative review:

1. Synthesize existing systematic reviews: 5 reviews (to 2021)
2. Primary studies published since 2021: 3 accuracy + 1 cost study (2021 – 2024)

1. Extracted sensitivity and specificity, stratified by setting, geography, brand, enrichment, reference standard, age, symptom severity and time since symptom onset. Synthesized cost literature.

2. Product scan of active RDTs (25 RDTs; 17 available).

3. NIH RePORTER review of active grants.

Results – Overall performance

- **Sensitivity is consistently high,** across studies
- **Specificity is more variable**, especially in field setting
- **Most median estimates (in 4 of 5 studies) exceed GTFCC benchmark**s for acceptable performance.

Study	N Studies	N Data Points	Sen	Spec
Dick et al. (2012)	18 (11 for RDTs)	24	95 (58-100)	93 (22-100)
Muzembo et al. (2022)	17	41	92 (58-100)	87 (49-100)
Muzembo et al. (2021)	20	48	87 (52-100)	93 (47-100)
Falconer et al. (2022)	23	46	94 (58-100)	90 (22-100)
Ndung'u et al. (2023)	14	24	91	80

Results – Setting

- **Lab-based testing outperforms field testing.**

	Field				Laboratory			Field & Laboratory		
Study	N Studies	N Data Points	Sen	Spec	N Data Points	Sen	Spec	N Data Points	Sen	Spec
Dick et al. (2012)	18 (11 for RDTs)	12	95 (58-100)	87 (60-100)	10	95 (83-100)	95 (22-100)	2	98 (95-100)	100
Falconer et al. (2022)	23	17	92 (67-100)	89 (73-100)	18	98 (81-100)	94 (22-100)	11	88 (58-100)	79 (43-100)

Photo Credits: Lorenz von Seidlen, Stop Cholera, 2010

Results – Test Brand

- **Crystal VC and SD Bioline** frequently met GTFCC performance benchmarks (Sen ≥90%, Spec ≥85%)
- **Cholkit** met Specificity but not Sensitivity benchmarks

Study	Crystal VC			SD Bioline			IP Dipstick			SMART			Cholkit			Medicos		
	N	Sens	Spec	N	Sens	Spec	N	Sens	Spec	N	Sens	Spec	N	Sens	Spec	N	Sens	Spec
Dick et al. (2012)	1	97	71-76		NA		10	95 (90-100)	93 (67-100)	6	96 (58-100)	97 (88-100)		NA		2	86 (84-88	80 (79-80)
Muzembo et al. (2022)	21	93 (66-100)	81 (49-100)	3	91 (81-96)	95 (91-100)	5	94 (93-97)	77 (67-97)	2	71 (58-83)	92 (88-95)	7	79 (64-100)	94 (81-100)	2	86 (84-88)	80 (79 - 80)
Muzembo et al. (2021)	26	89 (55-100)	85 (47-100)	6	81 (52-95)	96 (93-100)	5	96 (77-100)	92 (76-99)	3	79 (58-86)	92 (90-95)	7	79 (64-100)	94 (81-100)		NA	
Falconer et al. (2022)	17	92 (66-99)	85 (49-100)	3	91 (81-96)	95 (93-100)	9	94 (93-100)	92 (67-98)	6	96 (58-100)	100 (88-100)	3	79 (67-98)	94 (87-97)	2	86 (84-88)	80 (79-80)
Ndung'u et al. (2023)	NA	84	74	5	90	89	NA	98	96	NA	97	95		NA		NA	92	79

Results – Enrichment, Reference Standard

- **Enrichment improves specificity** but has little value on sensitivity.
- Using culture as the reference standard yielded sensitivity and specificity comparable to those using PCR.

Study	Unenriched Specimen			Enriched Specimen		
	N	Sen	Spec	N	Sens	Spec
Muzembo et al. (2022)	29	92 (58-100)	80 (49- 96)	12	88 (64-99)	97 (90-100)
Muzembo et al. (2021)	35	90 (52-100)	87 (47-100)	13	86 (64-100)	97 (90-100)
Falconer et al. (2022)	37	94 (58-100)	85 (22-100)	9	93 (67- 99)	97 (90-100)

Study	Culture			PCR			Culture & PCR		
	N	Sens	Spec	N	Sens	Spec	N	Sens	Spec
Dick et al. (2012)	21	95 (58-100)	93 (22-100)	1	97	71 - 76	2	95 (93-96)	95 (92-98)
Muzembo et al. (2022)	35	92 (58-100)	87 (49-100)	4	92 (86-97)	89 (75-100)	2	90 (88-92)	85 (83-89)
Muzembo et al. (2021)	30	92 (64-100)	90 (47-100)	4	90 (78-97)	89 (75-100)	14	80 (52-98)	94 (69-100)
Falconer et al. (2022)	37	94 (58-100)	90 (22-100)	4	92 (86-97)	89 (75-100)	4	91 (88-96)	92 (83-100)

Results – Cost of RDTs

1 Review: Falconer et al. (2022)

1 New study: George et al. (2024)

~$2 - $14 per test

Most studies did not include several operational costs (enrichment, shipping and customs, etc.)

Test Name	References	Cost
SMART	Kalluri et al. (2006)	$14 per device
Crystal VC	Elimian et al. (2022), Rashid et al. (2017), Ley et al. (2012), Bwire et al. (2017), George et al. (2014), Harris et al. (2009)	$2 per test
Medicos	Kalluri et al. (2006)	$4 per test
SD Bioline	Mwaba et al. (2018)	€2 per test

Results – New Studies

- Nigeria: Crystal VC RDT vs culture
- DRC: Crystal VC O1 vs. culture/PCR
  - Sensitivity lower in 0-5 y/o. No difference by case severity.
- Bangladesh: Cholkit
  - Bayesian modelling: RDT ≈ PCR, Sensitivity RDT > Culture

Study	Country	Time Periods	Sample Size	RDT	Gold Standard	Sensitivity (%, 95%CI)	Specificity (%, 95%CI)
Elimian et al. (2022)	Nigeria	Oct 2020–Oct 2021	1648	Crystal VC	Culture	95.6 (92.5, 97.7)	87.1 (77.0, 93.9)
George et al. (2024)	DRC	Mar 2020–Dec 2022	644	Crystal VC O1	Culture or PCR	90 (84 – 94)	94 (92, 96)
Perez-Saez et al. (2024)	Bangladesh	Jan 2021–Aug 2022	3744	Cholkit	Bayesian Latent Class Analysis	93.4 (91.3, 95.3)	97.3 (96.7, 97.8)

Results – Ongoing Projects – NIH Reporter

Search terms: “Cholera” AND (“test*” or “surveillance”).

Relevance to Cholera RDT	Project Title	Project Start Date	Project End Date	Contact PI / Project Leader	Organization Name
Yes. Describes evaluation of cholera RDTs	Epidemiology and Ecology of Cholera in Africa	04/01/2017	02/29/2028	SACK, DAVID A	JOHNS HOPKINS UNIVERSITY
Development of a rapid diagnostic test for multiple pathogens, including *V. cholerae*.	Rapid and Simple Paper Diagnostic Test to Detect Enteric Pathogens in the Developing World	09/01/2023	08/31/2025	KIM, CHANG HEE	GODX, INC.
Clinical prediction and biomarker-based tools to detect diarrhea.	Mentoring patient-oriented researchers in pediatric diarrhea	05/11/2023	04/30/2028	LEUNG, DANIEL TED	UNIVERSITY OF UTAH
Surveillance and intervention on emerging infectious diseases.	RFA-GH-24-033, Advancing Public Health Research in Bangladesh	09/30/2024	09/29/2029	BANU, SAYERA	INTERNATIONAL CTR/DIARRHOEAL DIS RES
Role of unobserved cholera infections in transmission and outbreak dynamics	The role of unobserved cholera: implications for prevention and control	08/01/2023	07/31/2025	WIENS, KIRSTEN E	TEMPLE UNIV OF THE COMMONWEALTH

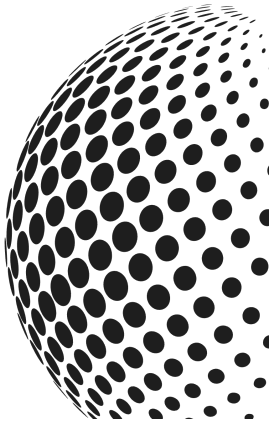
Results – Test availability

- Crystal VC, SDBioline on WHO/UNICEF list.
- Cholkit, SMART and Artron RDTs available and with evidence.
- Many other RDTs available but without evidence.

Product Name	Company/Institution	Country/Region
Appear available		
Crystal VC® Cholera RDT (Dipstick)	Arkray Healthcare Pvt. Ltd.	India
SD BIOLINE Cholera Ag O1/O139	Abbott	South Korea/Global
Cholkit (Cholera Rapid Test Dipstick)	Incepta Pharmaceuticals Ltd, icddr,b	Bangladesh
SMART™ II Cholera O1 RDT	New Horizons Diagnostics Corp.	USA
SMART™ II Cholera O139 RDT (Bengal)	New Horizons Diagnostics Corp.	USA
Artron Vibrio cholerae O1/O139 Combo RDT	Artron Laboratories Inc.	Canada
Cholera DFA Kit (O1)	New Horizons Diagnostics Corp.	USA
Bengal DFA Kit (O139)	New Horizons Diagnostics Corp.	USA
Rapid V. cholerae O1 Test	MP Biomedicals, LLC	USA/Europe
Rapid V. cholerae O139 Test	MP Biomedicals, LLC	USA/Europe
Vibrio cholerae O1/O139 Combo Rapid Test Cassette	Hangzhou AllTest Biotech Co., Ltd.	China
V. cholerae O1/O139 Antigen Rapid Test	Zhejiang Orient Gene Biotech Co., Ltd.	China
StrongStep® Vibrio cholerae O1/O139 Antigen Combo Rapid Test	Nanjing Liming Bio-products Co., Ltd.	China
Rapid V. Cholerae O1 Test (Strip/Card)	Xiamen Boson Biotech Co., Ltd.	China
Rapid V. Cholerae O139 Test (Strip/Card)	Xiamen Boson Biotech Co., Ltd.	China
RapidFor Cholera O1/O139 Rapid Test Kit	Vitrosens Biotechnology Inc.	Turkey
Cholera Ag O1 Rapid Test	Biogenix Inc Private Limited	India
Appear unavailable		
Vch-UPT-LF Assay (O1/O139)	Chinese CDC & Beijing Institute of Microbiology and Epidemiology	China
IP Cholera Dipstick	Institut Pasteur (IP)	France
Cholera Diagnostic Kit (mAb-based dot-blot ELISA)	Dept. of Medical Sciences (DMSc), Ministry of Public Health, Thailand	Thailand
SMART™ Cholera O1 RDT	New Horizons Diagnostics Corp.	USA
SMART™ Cholera O139 RDT (Bengal)	New Horizons Diagnostics Corp.	USA
Cholera Screen™ (COAT for O1)	New Horizons Diagnostics Corp.	USA
Bengal Screen™ (COAT for O139)	New Horizons Diagnostics Corp.	USA
Medicos™ Cholera Dip Stick	Advanced Diagnostics Inc.	USA

HARVARD
Global Health Institute

What role does inapparent infection play in cholera transmission?



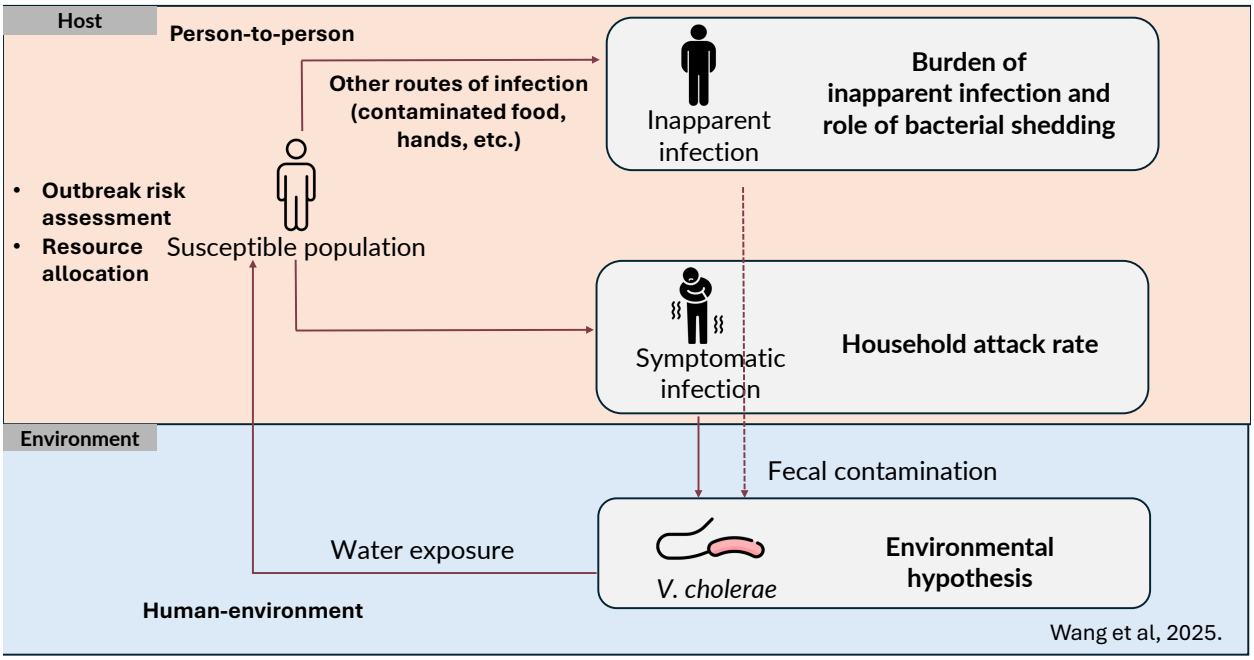
Wilfredo R. Matias, Ruitong (Amy) Wang, Yodeline Guillaume,
Azfar Hossain, Louise C. Ivers
September 18th -19th , 2025

A note on terminology

- **Asymptomatic cholera:** no symptoms, culture/PCR+.
- **Mild/subclinical cholera:** mild symptoms, no care sought.
- **Inapparent cholera:** asymptomatic + unrecorded symptomatic cases.
- **Other terms:** unobserved, hidden, etc.

HARVARD
Global Health Institute

Cholera Transmission Dynamic



Background

- **Cholera burden is underestimated** by case reporting alone
- **Inapparent infections are common** but poorly quantified
- **Clarifying their role in transmission is essential** for control

HARVARD Global Health Institute

Methods

- Narrative review
- Inclusion: human studies on burden of asymptomatic cholera, shedding among asymptomatic individuals, and asymptomatic transmission
- Outcome domains:
  - Prevalence/burden
  - Bacterial shedding
  - What is their contribution to transmission?
- Data sources: epidemiological and seroepidemiological surveys, household and field studies, modelling studies

HARVARD Global Health Institute

Table 2 Parameter values used in the Bogra and Calcutta simulations

Notation	Definition	Bogra	Calcutta	References
p	Proportion of infections being asymptomatic	0.76	0.98	King et al. (2008)
e_1	Cholera-related death rate (asymptomatic)	0 $year^{-1}$	0 $year^{-1}$	King et al. (2008), WHO Fact Sheet (2008)
e_2	Cholera-related death rate (symptomatic)	0.240 $year^{-1}$	4.662 $year^{-1}$	King et al. (2008)
e_3	Cholera-related death rate (symptomatic with treatment)	0.0240 $year^{-1}$	0.4662 $year^{-1}$	WHO Fact Sheet (2008)
γ_1	Recovery rate (asymptomatic)	0.15 day^{-1}	0.15 day^{-1}	Hendrix (1971)
γ_2	Recovery rate (symptomatic)	21.6 $year^{-1}$	11.3 $year^{-1}$	King et al. (2008)
γ_3	Recovery rate (symptomatic with treatment)	43.2 $year^{-1}$	22.6 $year^{-1}$	Pierce et al. (1968)[a]
η_1	Shedding rate (asymptomatic)	0.5 day^{-1}	0.5 day^{-1}	Levine et al. (1988) Kaper et al. (1995), Codeço (2001)[a]
η_2	Shedding rate (symptomatic)	50.0 day^{-1}	50.0 day^{-1}	Levine et al. (1988), Kaper et al. (1995)[a]
κ_H	Half saturation constant (hyperinf.)	10^6/700 cells/ml	10^6/700 cells/ml	Hartley et al. (2006)
κ_L	Half saturation constant (less-inf.)	10^6 cells/ml	10^6 cells/ml	Hartley et al. (2006)
β_H	Ingestion rate (hyperinf.)	0.15 $week^{-1}$	1.5 $week^{-1}$	Codeço (2001), Hartley et al. (2006)[b]
β_L	Ingestion rate (less-inf.)	1.5 $week^{-1}$	1.5 $week^{-1}$	Codeço (2001), Hartley et al. (2006)
ω	Immunity waning rate	0.4 $year^{-1}$	0.7 $year^{-1}$	Longini et al. (2007)[a] King et al. (2008)[a]
δ	Bacteria death rate	1/30 day^{-1}	1/30 day^{-1}	Hartley et al. (2006)
χ	Bacteria transition rate	5 day^{-1}	5 day^{-1}	Hartley et al. (2006)

[a]Parameter values used in simulations determined by suggested ranges in literature and results of sensitivity analysis

Burden of asymptomatic cholera – household studies

- 6 key household studies:
  - 1 historic, 5 modern
- Across studies: **~30-70% of infected contacts are asymptomatic** -> a major hidden reservoir of potential transmission.

Study	Setting	Contacts Infected	Asymptomatic (among infected)
Mosley 1968	East Pakistan (Bangladesh)	17%	~50%
Harris 2008	Dhaka	21%	~38%
Weil 2009	Dhaka	22%	~27%
Burrowes 2017	Dhaka	19%	~70–80%
George 2018	Rural Bangladesh	18%	~55%
George 2024	DRC	27%	~65–70%

HARVARD Global Health Institute

Burden of asymptomatic cholera – seroepidemiologic studies

- **Most infections are silent**
- **Infection:Case ratios** range from ~3:1 in outbreaks (Haiti, Micronesia) -> >3000:1 in hyperendemic settings (Bangladesh).
- **High attack rates** (10-50% of communities infected in a year)

- Sero-epidemiologic studies demonstrate a **large hidden burden** of past infection not captured by clinical surveillance.
- No studies to our knowledge in Africa.

Study	Setting / Population	Estimated Infection Rate	Infection-to-Case Ratio (I:C)
Hegde (2024)	Bangladesh, Sitakunda community	53.5% annually	3280:1
Kanungo (2024)	India, national (ages 9–45)	11.7%	
Finger (2024)	Haiti, Grande Saline epidemic	52.6% overall (35.5% age 2–4y, 53.1% ≥5y)	≥5y: ~3.2:1, 2–4y: ~1:1
Matias (2023)	Haiti, post-epidemic adults	9.5–12.4%	
Clutter (2023)	Haiti, pre-2022 outbreak	Very low (0% in <5y)	N/A
Azman (2020)	Bangladesh, national	17.3% annually	~20–40:1
Diep (2020)	Vietnam, post-elimination children	Near zero	
Jackson (2013)	Haiti, Grande Saline epidemic	39–64% (depending on cutoff)	~4:1
Ries (1992)	Peru, Piura epidemic	34% seropositive	
González-Bonilla (1994)	Mexico, epidemic	25–26%	
Suthienkul (1990)	Thailand, Krabi	65% IgG seropositive	
Harris (1986)	Micronesia, Truk epidemic	64% vibriocidal positive	~3:1
Gerichter (1973)	Jerusalem & Battir outbreak	Jerusalem 7.8%, Battir 57%	~100:1
Mosley (1969)	East Pakistan, children	~27% during season	~100:1

HARVARD
Global Health Institute

Bacterial shedding

- Typical shedding is brief: ~2 days on average.
- A minority shed longer (≈5% ≥4 days; some up to 12 days).
- Even mild/asymptomatic cases can shed, sometimes for prolonged periods.

Study	Setting (N)	Infected	Symptomatic	**Shedding duration**
Weil 2009 (CID)	Dhaka (944)	21%	73%	Mean ~2d; max 12d
Weil 2014 (AJTMH)	Dhaka (294)	24%	—	Mean 2d; 5% ≥4d
George 2025 (CID)	DRC (491)	27%	9%	Median 2d; range 1–7

HARVARD
Global Health Institute

Role in transmission

- To what extent do asymptomatic infections contribute to transmission?
- Can they sustain disease spread?

?

HARVARD
Global Health Institute

Bull. Org. mond. Santé
Bull. Wld Hlth Org. } 1965, 33, 645-649

Studies of Cholera El Tor in the Philippines *

3. Transmission of Infection among Household Contacts of Cholera Patients

J. F. TAMAYO,[1] W. H. MOSLEY,[2] M. G. ALVERO,[3] P. R. JOSEPH,[3] C. Z. GOMEZ,[4] T. MONTAGUE,[5] J. J. DIZON[6] & D. A. HENDERSON[7]

- 55 (18%) HH contacts infected; most asymptomatic
- New positives appeared *after* symptomatic index removed

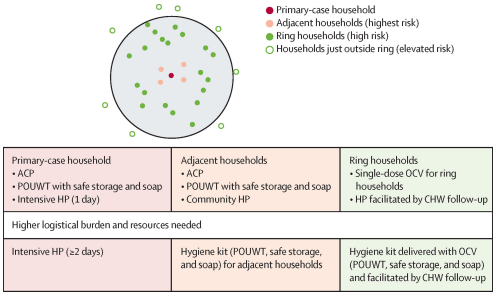
HARVARD
Global Health Institute

What is the attack rate among household contacts of cholera index patients?

Ruitong (Amy) Wang, Wilfredo R. Matias, Yodeline Guillaume, Azfar Hossain, Louise C. Ivers
September 18th – 19th, 2025

Background

- Individuals living with cholera patients face **higher risk of infection**
  - Shared exposure to contaminated food and water, direct fecal–oral transmission
- Case-area targeted interventions (CATIs) are initiated at the **household level**
- **Research gap**: No systematic synthesis of attack rates among household contacts of index patients
- **Objective:**
  - Estimate pooled household attack rates
  - Assess how household attack rates vary by study period, geographic region, intervention context, sex, and age group
  - Describe the proportion of symptomatic infections among secondary cases



Ratnayake R, Finger F, Azman AS, et al. Highly targeted spatiotemporal interventions against cholera epidemics, 2000-19: a scoping review. *Lancet Infect Dis*. 2021;21(3):e37-e48.

HARVARD
Global Health Institute

Methods

Meta-analysis of attack rate among household contacts of cholera index patients underway

- **Database:** PubMed, Web of Science, Embase, Cochrane library
- **Search terms:**
  - Cholera, *Vibrio cholerae*
  - household, contact, family
  - attack rate, incidence, transmission
- **Inclusion criteria:** Studies reporting cholera cases among enumerated household contacts of index cases
- **Exclusion criteria:**
  - Without sufficient data.
  - Reporting only community-level attack rates.
  - Without reporting the diagnostic method.

- **Overall AR** = (Total N of cases among household contacts during surveillance period)/(N of household contacts of index patients)
- Includes co-prevalent + secondary infections

HARVARD Global Health Institute

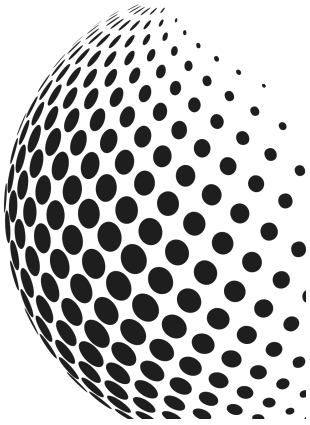
Remaining Questions

- What is the **timing and source** of infection within households?
  - Limited genomic sequencing evidence
  - Co-primary / secondary infection
  - Community / household infections
- What is the role of **asymptomatic** index cases?
  - The transmission potential of asymptomatic infections within households remains underexplored

HARVARD Global Health Institute

HARVARD
Global Health Institute

What is the environmental contribution to epidemic and endemic cholera? (i.e. the environmental reservoir hypothesis)



Azfar Hossain, Ruitong (Amy) Wang, Yodeline Guillaume, Wilfredo R. Matias, Louise C. Ivers
September 18th-19th, 2025

Environmental Reservoir Hypothesis

Does pandemic cholera form long-term environmental reservoirs in the absence of ongoing fecal shedding — and do these reservoirs lead to new outbreaks of disease?

HARVARD
Global Health Institute

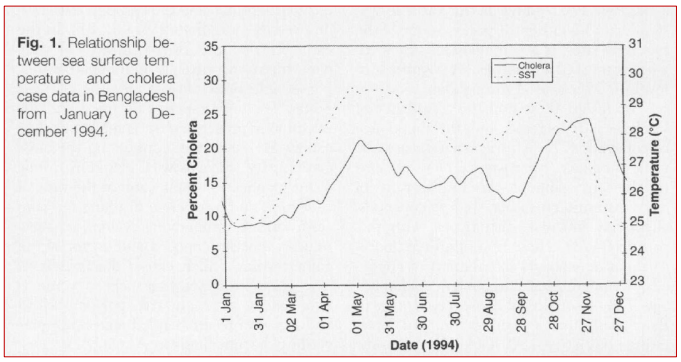
Methods

Narrative literature review

- Google Scholar, reference lists
- 16 studies/reviews (1985-2024)

HARVARD Global Health Institute

Evidence **supporting** environmental reservoirs: "the cholera paradigm"

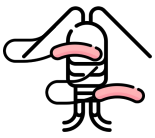


(Colwell, 1996)

HARVARD Global Health Institute

Survival phenotypes

- Viable-but-non-culturable state (Colwell, 1994)
- Persister state (Jubair, 2012)
- Biofilms (Sinha-Ray, 2017)



Copepod association
(Colwell, 1996)

Phage resistance
(Faruque, 2005)

Evidence **questioning** environmental reservoirs: genomic analyses

Pandemic *V. cholerae* ≠ Local *V. cholerae*

Other explanations for cholera persistence / reemergence?

- *Inapparent cholera*
- *Reintroductions (e.g., travel)*

HARVARD Global Health Institute

Domann et al, 2017. *Science*

established. Latin America and Africa bear different variants of cholera toxin with different transmission dynamics and ecological niches. The data are not consistent with the establishment of long-term reservoirs of pandemic cholera or with a relationship to climate events.

Dorman et al, 2020. *Nature Communications*

epidemic, the invariant epidemic clone co-existed alongside highly diverse members of the *Vibrio cholerae* species in Argentina, and we contrast the clonality of epidemic *V. cholerae* with the background diversity of local endemic bacteria. Our findings refine and add nuance

Chaguza et al, 2024. *Nature Communications*

genotype compared to historical Malawian *Vc* isolates. These data suggest that the devastating cyclones coupled with the recent importation of 7PET serogroup O1 strains, may explain the magnitude of the 2022–2023 cholera outbreak in Malawi.

Conclusion: evidence does not favor reservoir hypothesis, but **no current consensus**

This knowledge gap limits …

Epidemiologic understanding

Disease forecasting

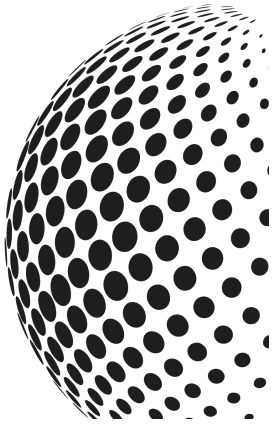
Resource allocation

HARVARD Global Health Institute

How can the reservoir hypothesis be evaluated?

HARVARD
Global Health Institute

What is the economic burden of cholera?



Ruitong (Amy) Wang, Wilfredo R. Matias, Azfar Hossain, Yodeline Guillaume, Louise C. Ivers
September 18th -19th, 2025

A note on terminology

Household Perspective

- **Direct medical costs:** out-of-pocket payment for medical services and outcomes (consultation, diagnostics, drugs and supplies, etc.)
- **Direct non-medical costs:** non-medical expenditures linked to care (transportation, food, and lodging, etc.)
- **Indirect costs:** productivity or income loss, etc.

Healthcare Provider Perspective

- **Variable costs:** costs that change with the number of patients treated (drugs and supplies)
- **Fixed costs:** costs that don't change with the number of patients treated (at least in the short term, infrastructure and logistics)

Societal perspective

- Broader economic impacts including tourism revenue losses, opportunity costs of diverted resources, etc.

HARVARD
Global Health Institute

Background

Vaccine 36 (2018) 4404–4424

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

The health economics of cholera: A systematic review

Amber Hsiao [a,*], Angela H. Hall [b], Vittal Mogasale [c], Wilm Quentin [a]

[a] Technische Universität Berlin, Department of Health Care Management, Berlin, Germany
[b] University of Canberra, Faculty of Education, Canberra, Australia
[c] International Vaccine Institute, Department of Policy & Economic Research, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 13 April 2017
Received in revised form 27 May 2018
Accepted 28 May 2018
Available online 12 June 2018

Keywords:
Cholera
Costs
Cost-effectiveness
Cost-benefit
Cost-utility
Health economics
Infectious diseases

ABSTRACT

Background: *Vibrio cholera* is a major contributor of diarrheal illness that causes significant morbidity and mortality globally. While there is literature on the health economics of diarrheal illnesses more generally, few studies have quantified the cost-of-illness and cost-effectiveness of cholera-specific prevention and control interventions. The present systematic review provides a comprehensive overview of the literature specific to cholera as it pertains to key health economic measures.

Methods: A systematic review was performed with no date restrictions up through February 2017 in PubMed, Econlit, Embase, Web of Science, and Cochrane Review to identify relevant health economics of cholera literature. After removing duplicates, a total of 1993 studies were screened and coded independently by two reviewers, resulting in 22 relevant studies. Data on population, methods, and results (cost-of-illness and cost-effectiveness of vaccination) were compared by country/region. All costs were adjusted to 2017 USD for comparability.

Results: Costs per cholera case were found to be rather low: <$100 per case in most settings, even when costs incurred by patients/families and lost productivity are considered. When wider socioeconomic costs are included, estimated costs are >$1000/case. There is adequate evidence to support the economic value of vaccination for the prevention and control of cholera when vaccination is targeted at high-incidence populations and/or areas with high case fatality rates due to cholera. When herd immunity is considered, vaccination also becomes a cost-effective option for the general population and is comparable in cost-effectiveness to other routine immunizations.

Conclusions: Cholera vaccination is a viable short-to-medium term option, especially as the upfront costs of building water, sanitation, and hygiene (WASH) infrastructure are considerably higher for countries that face a significant burden of cholera. While WASH may be the more cost-effective solution in the long-term when implemented properly, cholera vaccination can still be a feasible, cost-effective strategy.

© 2018 Elsevier Ltd. All rights reserved.

Hsiao A, Hall AH, Mogasale V, Quentin W. The health economics of cholera: A systematic review. Vaccine. 2018;36(30):4404-4424.

- **Economic consequences**
  - Households
  - Healthcare provider
  - Society
- **Evidence gap**
  - Last systematic review in 2018: broad overview but limited by scarce/heterogeneous data
  - Need more granular cost items or subgroup analyses (sex, age, inpatient vs. outpatient)
- **Objective**
  - Conduct an updated review of cholera economic burden
  - Provide cost estimates at a more granular level
  - Compare costs across regions and population subgroups

Method

Study inclusion

- **Cost-of-illness studies**
  - All studies in Hsiao et al. (2018)
  - Additional studies (post-2017, PubMed)
- **Cost-effectiveness studies**
  - From Hsiao et al. and PubMed, only if providing original sources of cost estimates.

Study exclusion

- No monetary values
- Cannot retrieve per-case estimates

Cost comparisons

- Conversion: 2025 USD
- Regional comparisons: Int$ (PPP-adjusted)
- Derive per case costs from total costs

HARVARD Global Health Institute

Study Characteristics

17 original studies between 1998–2024 (6 identified after 2017)

Data Sources

- Semi-structured interviews
- Treatment protocols, drug cost databases, and financial records

HARVARD Global Health Institute

Geographic Distribution

- Africa only: 10 studies (e.g., Malawi, Ghana, Tanzania, Zimbabwe)
- Asia only: 3 studies (Bangladesh, Thailand)
- Both Africa & Asia: 3 studies (Bangladesh, India, Indonesia, Mozambique)
- Americas: 1 study (Ecuador)

Study Setting

- Cholera treatment centers, hospitals, households, refugee camps
- High incidence, poor WASH conditions, dense population

Population

- Both inpatients & outpatients (majority)
- Only outpatients (1 study)
- Only inpatients (3 studies)

Perspective

- Household + provider: 8 studies
- Household only: 3 studies
- Provider only: 5 studies

Estimates of Costs Per Case

Total costs (8 studies)

Wide heterogeneity between estimates:

- Lowest: $20–$30 (2 studies, Asia)
- Highest: $700–$1,400 (1 study, Africa)
- Median: ~$100 per case

Low costs:

- Based on WHO treatment guidelines + productivity loss
- Did not capture direct household costs → underestimate

High costs:

- Included productivity loss from premature death (90% of total costs)

HARVARD Global Health Institute

Household (9 studies)

7 studies **< $100**
Median: ~$50

Direct costs (10 studies)

- Lowest: < $5
- Highest: > $100
- Median: ~$10

Medical / Non-medical

Most had **higher non-medical** costs

Indirect costs (11 studies)

- Lowest: $6.51
- Highest: >$100
- Median: $20–30

Patient / Caregiver

3 found higher patient costs
2 found higher caregiver costs

Provider (12 studies)

Variable costs only (6 studies)

- Lowest: $28 - 44
- **Highest: > $500**
- Median: ~$70

Outbreak in Zimbabwe, costs included treatment supplies, personnel, and diarrhoea kits.

Variable + Fixed costs (6 studies)

- Lowest: $14
- **Highest: > $200**
- Median: ~$90
- Fixed costs > variable costs

Outbreak in Mozambique refugee camps

Subgroup Analysis

By Income (one study)

Second-lowest income group > second-highest > highest > lowest > middle-income

By Disease Severity (two studies)

Costs increase with case severity

By Patient Sex (two studies)

Higher overall household costs among males than females

By Patient Status (five studies)

Inpatients generally > outpatients

By Patient Age (six studies)

Older patients generally > younger ones

HARVARD Global Health Institute

Regional Comparisons

Costs generally higher in Africa than in Asia, across total, household, and health sector estimates.

Study	Country	Cost from Health Sector (per case, Int$)	Total Cost from household (per case, Int$)	Cost per case (health sector + household sector, Int$)
Asia				
Wallace et al. (2024)	Thailand	$174.25	$71.80	$246.05
Lopez et al. (2013)	Bangladesh	$63.73	$84.17	
Sarker et al. (2013)	Bangladesh		$138.11	
Africa				
Figuereo et al. (2024)	Somalia	$227.73	$93.52	$321.25
Hsiao et al. (2022)	Malawi		Scenario 3: $68.93	
Ilboudo et al. (2017)	Malawi	$251.10	$275.92	$527.01
Naficy et al. (1998)	Malawi	Preventive treatment (300 – 900, 901 – 1500 cases): $592.41, $507.60 Reactive treatment (300 – 900, 901 – 1500 cases): $1013.31, $818.66		
Awalime et al. (2017)	Ghana		HIA: $1603.82; LIA: $1216.62	
Van Damme et al. (2004)	Guinea	Routine case management: $20.10; Improved case management: $53.86		
Schaetti et al. (2012)	Tanzania	$260.06	$185.78	$455.84
Cross-region				
Levin et al. (2012)				AFR $27.4 - 30.6; EMR $25.4; SEAR $23.1;

AFR: The African Region;
EMR: Eastern Mediterranean Region;
SEAR: South East Asian Region

Summary and Remaining Questions

Summary

- The majority of total costs estimates centered around **USD$50–100 per case**.
- Indirect costs and household non-medical expenses often outweighed direct and medical costs.
- Costs rise with disease severity, inpatient care, and longer hospital stays.
- Higher burden in Africa.

HARVARD
Global Health Institute

Remaining Questions

- How can we make more robust **comparisons** of costs across studies?
  - Differences in healthcare quality and system structures
  - Inconsistency in cost components
  - Few standardized multi-national costs estimation studies
- What would be a more appropriate **timeframe** for costing analyses?
  - Long-term costs
  - Fatal cases
  - Broader societal impacts and other intangible costs
- How might **intervention context** influence cost estimates?
  - Costs estimated without stratification by vaccination status or other interventions.
- How generalizable are cost estimates from endemic settings to **outbreak contexts**?
  - Limited outbreak-context data

HARVARD
Global Health Institute

What are the risk factors for mortality in cholera?

Yodeline Guillaume, Ruitong (Amy) Wang, Azfar Hossain,
Wilfredo R. Matias, Louise C. Ivers
September 18th -19th, 2025

Indicators of cholera-related mortality

- The GTFCC recommends two indicators:
  - **Case fatality ratio (CFR)**
  - **Number of community deaths**

Finger F, Heitzinger K, Berendes D, et al. Reporting of deaths during cholera outbreaks: case fatality ratio and community deaths. *Lancet Infect Dis*. 2024;24(6):e353. doi:10.1016/S1473-3099(24)00237-8.

Update since the GTFCC scoping review

- **Databases:** PubMed, Google Scholar, African Journals Online
- **Search terms and eligibility criteria:** Similar to the GTFCC review, but only reviewed articles written in English.
- **Number of relevant studies:** Identified 13 with descriptive information on fatal cases, but summarized findings of 8.*

Updated findings – Reported CFR

- **Sex-specific CFR**
  - In 4/6 studies, **males had the highest CFR**, ranging from 0.8% in Congo to 4.1 in Nigeria.
- **Age-specific CFR**
  - In 4/5 studies, **CFR increased with age** (e.g., > 40 years)
- **Disease-specific CFR**
  - 2.5% to 3.7% for cases with HIV (2 studies)

Study	Setting	Epidemic period	# of total cases	# of deaths	Overall CFR
Elimian et al. (2022)	Nigeria	2020-2021	93,598	3,298	3.5%
Bugeme et al.(2024)	Congo	2021-2023	2,209	24	1.1%
Demlie et al. (2024)	Ethiopia	2015-2023	99,945	1030	1%
Mboringong et al. (2025)	Cameroon	2018-2023	17,967	478	2.7%
Kiama et al. (2025)	Kenya**	2022-2023	196	38	
Chitatanga et al. (2025)	Malawi**	2022-2023	174	87	
Kamila et al. (2025)	Zambia	2023-2024	1,253	18	1.4%
Mbewe et al.(2025)	Zambia	2023-2024	5,020	51	1%

Updated findings – Reported Risk Factors

- **Older age and severe dehydration** are the most consistently reported risks (5/8 studies).
- Evidence on **sex** is mixed: 3/8 studies found male sex significant.
- Evidence on **comorbidities** remains scarce: 1/4 studies showed HIV and diabetes to be significant.
- Other risk factors included **outpatient treatment, inadequate IV fluid management, and rainy season**.
- Protective factors included **hospitalization and OCV**.

Updated findings – Global trends

Global trends in age-specific mortality rates of cholera (per 100,000 population), by sex, 1990–2019

Age (Years)	Males			Females		
	Age-Specific Rates		AAPC (95% CI)	Age-Specific Rates		AAPC (95% CI)
	1990	2019		1990	2019	
<5	7.3	8.4	+0.5 * (0.1 to 0.8)	7.2	8.4	+0.6 * (0.3 to 0.9)
5–19	0.1	0.2	+1.4 * (0.9 to 1.9)	0.2	0.3	+1.5 * (1.0 to 2.1)
20–54	0.4	0.4	−0.1 (−0.5 to 0.3)	0.4	0.6	−0.2 (−0.5 to 0.2)
55+	1.9	1.4	−1.4 * (−1.6 to −1.1)	1.5	1.1	−1.4 * (−1.7 to −1.1)

Ilic I, Ilic M. Global patterns of trends in cholera mortality. *Trop Med Infect Dis*. 2023;8(3):169. Published 2023 Mar 13. doi:10.3390/tropicalmed8030169

Research gaps and remaining questions

Risk Factor	Gap
Sex	• No consensus on observed differences and whether they are due to sex alone or sex and another characteristic.
Age	• Precise cut offs for defining age groups that confer risk and mechanisms underlying the patterns observed in some settings.
Comorbidities	• Risk conferred by comorbid conditions such HIV, hypertension, diabetes
Time-to-Accessing Care	• Magnitude of risk conferred per unit of time delay • Meaningful threshold to qualify “delayed” care
Socioeconomic status	• Do not have enough data to properly assess
Water source/treatment	
Access to care	

HARVARD
Global Health Institute

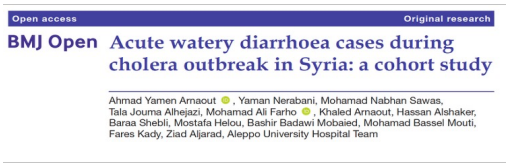
Morbidity: What is the evidence on cholera-related disability?

Yodeline Guillaume, Ruitong (Amy) Wang, Azfar Hossain,
Wilfredo R. Matias, Louise C. Ivers
September 18th -19th, 2025

Cholera-related disability

- **There is limited published evidence**

- A 2023 study in Syria found within one month of discharge:
  - 81% (858/1,059) of cases in good health
  - 14.6% in moderate health
  - 3.4% had poor health
  - 0.9% died


Open access Original research
BMJ Open Acute watery diarrhoea cases during cholera outbreak in Syria: a cohort study
Ahmad Yamen Arnaout, Yaman Nerabani, Mohamad Nabhan Sawas, Tala Jouma Alhejazi, Mohamad Ali Farho, Khaled Arnaout, Hassan Alshaker, Baraa Shebli, Mostafa Helou, Bashir Badawi Mobaied, Mohamad Bassel Mouti, Fares Kady, Ziad Aljarad, Aleppo University Hospital Team