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REVIEW

# Oral Cholera Vaccines as Transmission-Interrupting Tools for Cholera Control: A Narrative Review

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**Background:** Cholera remains a significant global health challenge, with an estimated 1.3 billion people at risk in endemic regions and recurrent outbreaks increasingly reported in fragile, conflict-affected, and humanitarian settings. Persistent transmission continues despite advances in case management and water, sanitation, and hygiene (WASH) interventions.

**Objective:** To synthesize current evidence on oral cholera vaccines (OCVs) as transmission-interrupting tools and to examine their implications for integrated cholera control strategies.

**Methods:** This narrative review synthesized published evidence on oral cholera vaccines (OCVs) and their role in interrupting cholera transmission. A literature search was conducted in PubMed, Scopus, Web of Science, Embase, Google Scholar, and relevant World Health Organization (WHO) and Global Task Force on Cholera Control (GTFCC) publications. Studies published between January 2000 and February 2026 were considered. Eligible sources included systematic reviews, randomized controlled trials, observational studies, outbreak investigations, mathematical modeling studies, and international policy documents addressing vaccine effectiveness, herd protection, transmission dynamics, operational deployment, and integration with Water, Sanitation and Hygiene (WASH) interventions. Evidence was narratively synthesized according to major thematic areas.

**Results:** Two-dose killed whole-cell OCVs provide 66–81% protection at six months post-vaccination. Empirical evidence and modeling studies demonstrate substantial herd protection when coverage exceeds 50–70%, with projected overall incidence reductions exceeding 75% in certain endemic contexts. Reactive campaigns implemented within the first week of outbreak detection can avert up to 70% of cases, although effectiveness declines rapidly with delayed deployment. Single-dose regimens provide moderate short-term protection but exhibit faster waning. Impact is context-dependent and influenced by baseline immunity, surveillance quality, and concurrent WASH interventions.

**Conclusion:** OCVs function most effectively as transmission-interrupting tools when deployed rapidly, targeted strategically, and integrated with WASH, surveillance, and community engagement. While not a substitute for structural prevention, vaccination represents a critical catalytic intervention within comprehensive cholera control and elimination frameworks.

**Keywords:** cholera, oral cholera vaccine, transmission interruption, herd immunity, reactive vaccination, water, sanitation and hygiene

## Background

Cholera remains one of the world's most persistent waterborne diseases and continues to pose a major threat to global public health, particularly in low- and middle-income countries affected by poverty, conflict, forced displacement, climate-related disasters, and inadequate access to safe water and sanitation.[1] The World Health Organization (WHO) estimates that approximately 1.3 billion people remain at risk of cholera globally, with recurrent outbreaks increasingly reported across sub-Saharan Africa, South Asia, and humanitarian settings.[2] Recent years have witnessed a resurgence of

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large and prolonged outbreaks, placing considerable pressure on already fragile health systems.[3] Despite substantial improvements in case management and investments in Water, Sanitation and Hygiene (WASH), cholera transmission continues to occur because structural improvements often require substantial financial resources and long implementation periods.[4] Consequently, rapid public health interventions capable of reducing transmission during outbreaks remain essential. Oral cholera vaccines (OCVs) have evolved from supplementary preventive tools into essential components of integrated cholera control strategies.[5] Currently, WHO-prequalified killed whole-cell oral cholera vaccines including Euvichol-Plus®, Euvichol-S®, Shanchol®, and Hillchol® are recommended for both preventive and reactive vaccination campaigns in endemic and epidemic settings. These vaccines are generally administered as two-dose regimens, although temporary single-dose strategies have been implemented during periods of global vaccine shortages to maximize population coverage.[6] Increasing evidence from observational studies, outbreak investigations, and mathematical modeling suggests that OCVs provide benefits extending beyond direct individual protection. When sufficiently high vaccination coverage is achieved, vaccination may generate indirect protection among unvaccinated individuals by reducing community-level transmission, lowering the effective reproductive number ($R_e$), and shortening outbreak duration.[7] This concept, commonly referred to as transmission interruption, has emerged as an important framework for evaluating vaccine impact at the population level. Recent global policy developments further justify reassessing the role of OCVs.[4] Between 2022 and 2025, unprecedented global vaccine shortages prompted WHO and the International Coordinating Group (ICG) to temporarily adopt single-dose emergency vaccination strategies. In 2026, improvements in vaccine production allowed the gradual resumption of preventive vaccination campaigns.[3] These evolving policies underscore the need to critically examine the evidence supporting OCV deployment under different epidemiological and operational contexts. Although numerous studies have evaluated vaccine effectiveness, herd protection, and outbreak response strategies, evidence remains dispersed across epidemiological investigations, modeling studies, and policy reports.[5] The present narrative review therefore synthesizes current evidence regarding oral cholera vaccines as transmission-interrupting tools and discusses their implications for integrated cholera prevention, outbreak response, and progress toward the Global Roadmap to End Cholera by 2030.

## Methods

This study was conducted as a narrative review to synthesize current evidence regarding the role of oral cholera vaccines (OCVs) as transmission-interrupting interventions within comprehensive cholera control strategies. A literature search was conducted in PubMed, Scopus, Web of Science, Embase, Google Scholar, and the websites of the World Health Organization (WHO), the Global Task Force on Cholera Control (GTFCC), and the Centers for Disease Control and Prevention (CDC). Searches covered publications from January 2000 to February 2026. The search strategy combined keywords including cholera, oral cholera vaccine, OCV, transmission interruption, herd immunity, herd protection, reactive vaccination, preventive vaccination, cholera outbreak, mathematical modeling, and water, sanitation and hygiene (WASH). Eligible publications included randomized controlled trials, observational studies, case-control studies, outbreak investigations, mathematical modeling analyses, systematic reviews, scoping reviews, WHO guidance documents, GTFCC reports, and policy papers addressing vaccine effectiveness, indirect protection, transmission dynamics, operational deployment, and integration with complementary cholera control interventions. Conference abstracts lacking sufficient methodological information, duplicate publications, studies unrelated to cholera vaccination, and articles without relevance to transmission dynamics were excluded. Grey literature from WHO and GTFCC was included because of its relevance to global cholera policy and implementation. The retrieved literature was reviewed narratively and organized into thematic areas, including vaccine characteristics, evidence for transmission interruption, operational deployment, integration with WASH interventions, policy implications, and research gaps.

## Defining Transmission Interruption in Cholera Control

Transmission interruption refers to the reduction or cessation of sustained community-level transmission of *Vibrio cholerae* following public health interventions. Within this review, transmission interruption is operationalized using several epidemiological indicators, including reduction of the effective reproductive number ($R_e$) toward or below one, decreased cumulative incidence, shortened outbreak duration, and measurable indirect protection among unvaccinated

individuals resulting from reduced pathogen circulation.[8] Unlike individual vaccine effectiveness, which measures protection among vaccinated persons, transmission interruption evaluates the broader population-level impact of vaccination on disease spread.[9] This distinction is fundamental because oral cholera vaccines contribute to both direct immunity and indirect community protection, particularly when high vaccination coverage is achieved.[10]

Several WHO-prequalified oral cholera vaccines are currently available for use in endemic and epidemic settings. Killed whole-cell vaccines, including Euvichol-Plus®, Euvichol-S®, Shanchol®, and Hillchol®, are administered orally in two doses separated by approximately two weeks and are recommended for individuals aged one year and older.[3] These vaccines provide substantial protection against cholera and constitute the principal products used through the global oral cholera vaccine stockpile.[8] In contrast, Dukoral®, which contains recombinant cholera toxin B subunit, is primarily indicated for travelers and is less commonly used in large-scale public health vaccination campaigns because of higher cost and administration requirements.[11] During periods of vaccine shortage, WHO temporarily recommended single-dose vaccination strategies to maximize population coverage while maintaining acceptable short-term protection.[3]

## Evidence Base: Empirical and Modeling Contributions

Field studies in endemic and outbreak settings consistently report two-dose effectiveness between 66% and 81% within six months. Protection extends up to three years in some contexts, though waning immunity is observed (7;8). Observational outbreak evaluations demonstrate substantial reductions in incidence following high-coverage campaigns. However, these studies may be influenced by concurrent behavioral change or WASH interventions, which complicates attribution of impact solely to vaccination.[12] Mathematical models predict that achieving 50% coverage in endemic settings could reduce overall incidence by more than 75%, with some projections approaching 90% under favorable assumptions. Modeling analyses also quantify the critical importance of timing: campaigns initiated within the first week of outbreak detection may avert up to 70% of cases, with effectiveness halving approximately every 2–3 weeks.[9,10] While informative for strategic planning, these projections rely on assumptions regarding reporting completeness, baseline immunity, and transmission heterogeneity. Therefore, modeling evidence complements but does not replace empirical validation.[11,12] The demonstration of herd protection represents a major advance in cholera vaccine research. Reduced incidence among unvaccinated individuals has been documented in settings achieving moderate-to-high coverage.[9,13] However, herd effects are not uniform. Their magnitude depends on: Population density; baseline immunity; WASH conditions; surveillance accuracy; outbreak detection timing. Overgeneralization should therefore be avoided. Coverage thresholds required for meaningful transmission reduction likely vary across epidemiological contexts.[11,12]

## Operational Use in Outbreak and Humanitarian Settings

Speed of deployment is a primary determinant of impact. Empirical and modeling evidence converge in demonstrating that delayed campaigns substantially reduce cases averted and cost-effectiveness.[4,13] This time sensitivity underscores the importance of pre-approved emergency financing mechanisms, stockpile accessibility, and robust surveillance systems capable of early detection.[14,15] Targeted preventive vaccination in historically high-risk areas may maintain population immunity above epidemic thresholds. Modeling suggests biennial vaccination in endemic hotspots could sustain low incidence, though operational feasibility depends on supply availability.[15,16] In fragile settings, infrastructure rehabilitation may be infeasible. OCVs provide an immediately deployable intervention capable of mitigating transmission under constrained conditions. However, logistical challenges including insecurity, population mobility, and cold chain disruptions limit optimal implementation.[2,15]

## Limitations and Equity Considerations

Protection declines over time, necessitating revaccination strategies. Long-term sustainability requires predictable manufacturing capacity and financing commitments.[17] Children under five exhibit lower and less durable immune responses. This presents both biological and equity challenges, as this group often bears high morbidity risk. Enhanced pediatric immunogenicity strategies remain a research priority.[18,19] Persistent vaccine shortages have forced adoption of single-dose policies during emergencies. While pragmatic, this approach may compromise durability of protection.[3] Allocation decisions raise ethical considerations: Prioritizing emergency response versus endemic

prevention; balancing equity with epidemiological efficiency; ensuring high-risk fragile settings are not systematically disadvantaged. Transparent prioritization frameworks are essential for equitable and effective distribution.[7,15]

## Integration Within Comprehensive Cholera Control

OCVs should not be viewed as substitutes for WASH interventions but as complementary accelerators of transmission reduction. Vaccination decreases susceptibility and environmental contamination, while WASH reduces exposure pathways.[18] Multicomponent strategies integrating vaccination, surveillance, case management, behavioral interventions, and infrastructure improvements produce more durable control than any single intervention alone.[20,21]

## Strengths and Limitations of This Review

This review synthesizes diverse evidence sources, including field studies, outbreak evaluations, and modeling analyses, to provide a comprehensive conceptual reframing of OCVs. By explicitly defining transmission interruption and distinguishing empirical from predictive evidence, it aims to enhance conceptual clarity.[22,23] However, several limitations must be acknowledged. Much of the evidence derives from observational designs rather than randomized studies measuring transmission endpoints. Herd protection estimates may be influenced by unmeasured confounders. Modeling projections depend on assumptions that may not generalize across settings. Additionally, long-term empirical data on sustained transmission interruption beyond immediate post-campaign periods remain limited.[23,24] Future research should prioritize standardized transmission metrics, longitudinal follow-up, and integration of environmental and epidemiological data.[25]

## Policy Implications

Reframing OCVs as transmission-interrupting tools shifts evaluation metrics toward: population-level incidence reduction; outbreak duration shortening; coverage thresholds linked to $R_e$ reduction; speed of deployment as a performance indicator. Alignment with global cholera elimination strategies requires embedding vaccination within national plans that integrate surveillance strengthening, WASH investment, and community engagement.[26,27]

## Recent Global Oral Cholera Vaccine Policy Changes

Global shortages of oral cholera vaccines between 2022 and 2025 substantially influenced international vaccination policy. To maximize vaccine availability during multiple concurrent outbreaks, WHO and the International Coordinating Group temporarily recommended a single-dose strategy for emergency response campaigns.[27] Although this approach increased immediate population coverage, concerns remained regarding the duration of protection, particularly among young children.[14] Expansion of manufacturing capacity in 2025 and 2026 enabled the progressive resumption of preventive two-dose vaccination campaigns.[15] These developments highlight the importance of flexible vaccination strategies that balance epidemiological effectiveness, vaccine supply, operational feasibility, and equity.

## Conclusion

Oral cholera vaccines provide more than individual protection; they can substantially reduce community-level transmission when deployed rapidly and strategically.[22] Available empirical and mathematical modeling evidence suggests that oral cholera vaccines can substantially reduce community transmission when deployed rapidly, strategically targeted, and integrated with complementary interventions.[28] However, the magnitude of indirect protection varies according to vaccination coverage, baseline population immunity, surveillance capacity, and local WASH conditions. Consequently, oral cholera vaccines should be regarded as an essential component of integrated cholera control rather than a standalone solution.[29] Nevertheless, vaccination alone cannot eliminate cholera. Sustainable progress requires multisectoral integration, equitable allocation, strengthened surveillance, and continued investment in WASH infrastructure. Recognizing OCVs as transmission-interrupting tools provides a pragmatic and epidemiologically grounded framework to optimize their impact within comprehensive cholera control and elimination efforts.

## Disclosure

The authors report no conflicts of interest in this work.

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