

Cost-Disruptive Tools for Enteric Disease Diagnosis and Surveillance

Enteric infections remain a major driver of morbidity and mortality in low- and middle-income countries (LMICs), especially among young children, and they continue to fuel outbreaks, delay detection, and contribute to inappropriate antibiotic use. The World Health Organization (WHO) estimates that diarrheal diseases cause hundreds of thousands of deaths annually among children under five years of age, with a large burden concentrated in sub-Saharan Africa and South Asia.¹ Cholera has also resurged globally, with 60 countries reporting more than 560,000 cases and over 6,000 deaths in 2024.² Typhoid fever remains a common cause of acute febrile illness in endemic settings, with persistent diagnostic limitations contributing to inappropriate antibiotic use and delayed public-health action.³ In addition to clinical management, accurate diagnostics play a critical role in surveillance and vaccine decision-making, as vaccines are available or in development for several high-burden enteric pathogens.

Syndromic management remains common because definitive testing is often inaccessible, slow, or unreliable at frontline facilities. For *Shigella*, large multi-site analyses using quantitative molecular diagnostics demonstrated that conventional stool culture substantially underestimates disease burden compared with molecular methods.⁴⁻⁶ Many *Shigella*-attributable episodes are non-dysenteric, meaning treatment algorithms restricted to bloody diarrhea miss a substantial proportion of bacterial infections.⁷ These findings support the need for accurate, near-patient *Shigella* diagnostics capable of detecting acute infection during the same clinical encounter and supporting differentiation of bacterial from viral diarrhea to guide antimicrobial stewardship. Although WHO has not published standalone TPPs for *Shigella* or bacterial-vs-viral diarrhea differentiation, performance expectations for high-quality enteric diagnostics consistently demonstrate that $\geq 90\%$ sensitivity and high specificity are feasible and appropriate thresholds to guide clinical decision-making and stewardship.

Typhoid fever presents a distinct diagnostic challenge. Blood culture, the conventional reference standard, requires laboratory infrastructure, may take several days, and has limited sensitivity in routine practice due in part to low circulating bacterial loads.³ As a result, widely used rapid serologic tests often fail to meet performance requirements. WHO has published a target product profile (TPP) for laboratory tests for acute typhoid fever surveillance, defining minimal and preferred performance characteristics for near-patient testing.⁸ The CARB-X 2025 diagnostics minimal entry criteria similarly emphasize detection of acute infection (excluding IgG- and IgM-only approaches), use of blood or less-invasive specimens, rapid turnaround time (≤ 60 minutes), and require $\geq 90\%$ sensitivity and $\geq 90\%$ specificity.⁹ These criteria define a clear performance-based pathway for cost-disruptive typhoid diagnostics.

Cholera surveillance and outbreak response depend on centralized laboratory confirmation, delaying public-health action. Current guidance from the Global Task Force on Cholera Control (GTFCC) recognizes that rapid diagnostic tests (RDTs) are useful for screening and early alerts but require additional testing for case confirmation.¹⁰ FIND and GTFCC TPPs specify high diagnostic sensitivity and specificity targets for cholera confirmation in decentralized settings.¹⁰⁻¹¹ A near-patient test that detects toxigenic *Vibrio cholerae* O1 or O139, or cholera toxin genes, and meets confirmatory performance thresholds could shorten time to outbreak confirmation.

Finally, pediatric diarrhea is etiologically heterogeneous, and improved attribution is essential for both surveillance and vaccine impact evaluation. Reanalyses of the GEMS and the MAL-ED cohort using quantitative molecular diagnostics showed that pathogen quantity thresholds substantially increase episode-level attribution compared with conventional culture.⁴⁻⁵ High-burden pathogens with existing or pipeline vaccines include rotavirus and *Shigella*, among others. Quantitative, flexible multi-target panels that can evolve with vaccine and surveillance needs are therefore central for scalable enteric diarrheal diagnostics.

Across these use cases, innovations must meet functional requirements for sensitivity, specificity, turnaround time, decentralization, and affordability in LMIC settings. Technologies of interest include novel assays, low-cost molecular architectures, host-pathogen signatures, or other emerging modalities capable of delivering credible diagnostic performance during the same patient encounter while maintaining a pathway to population-scale, cost-disruptive implementation.

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