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Cost-Effectiveness of a Target Point-of-Care Triage Test for Neonatal Sepsis in Low- and Middle-Income Countries

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Abstract

Neonatal sepsis is a leading cause of mortality in low- and middle-income countries (LMICs). The current diagnostic standard, blood culture, has long turnaround times and high infrastructure requirements, limiting its utility. Consequently, clinicians rely on non-specific clinical signs for initial management. To address this unmet need, the WHO published a 2025 Target Product Profile (TPP) for rapid point-of-care tests (POCTs). We developed a global expert-validated model to estimate the cost-effectiveness of a TPP-compliant POCT in LMICs.

A decision tree compared a TPP-compliant POCT integrated into standard of care (SOC) against SOC alone from a healthcare system perspective over a lifetime horizon. The model evaluated infants (0–59 days) with possible serious bacterial infection across facility-of-birth and community-presenting cohorts. Outcomes included incremental cost per disability-adjusted life-year (DALY) averted. Probabilistic and threshold sensitivity analyses assessed parameter uncertainty.

At a US$ 5·00 unit price, the POCT reduced costs by US$ 37 342 and averted 206 DALYs per 1 000 facility-of-birth patients compared to SOC. In community-presenting patients, it reduced costs by US$ 5 715 and averted 127 DALYs per 1 000. The POCT was dominant in 93·2% (facility) and 84·8% (community) of probabilistic iterations. Results remained robust across wide-ranging epidemiological and cost inputs.

These findings provide an evidence base supporting prioritised investment in developing a TPP-compliant POCT to improve neonatal sepsis management in LMICs.

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All data generated or analysed during this study, including the data dictionary, all extracted parameter values, and step-by-step calculation logic, are deposited in the Mendeley Data repository (DOI: 10.17632/j6kx34b9xm.1). The complete decision-analytic models, available in both R and Microsoft Excel formats, are shared to facilitate transparency and adaptation by other researchers and policymakers. All materials are currently under embargo and will be made fully available to the public without restriction upon publication at: https://doi.org/10.17632/j6kx34b9xm.1

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Evidence before this study

Neonatal sepsis (NS) is a leading cause of mortality in LMICs, but diagnosis remains reliant on blood cultures, which are slow and often inaccessible, or clinical judgment, which is limited in accuracy. A POCT could potentially fill these gaps by providing rapid, high-accuracy results, thereby reducing inappropriate antibiotic use, which causes antimicrobial resistance, and treatment delays, responsible for high case fatality rates (CFRs). To date, only one study has modelled the impact of a potential POCT introduction. The objective of that study was to support the development of the TPP, and it estimated that at a unit price of US$21 for hospitals and US$3 for community, the POCT could be cost-neutral through reductions in mortality of 19 to 76% and healthcare expenditure of 17 to 43%. The authors acknowledged several limitations in their analysis, including the high reliance of model parameters on the settings of India and Uganda, limiting the representativeness of the results, the assumption of zero blood culture contamination, perfect referral, and binary antibiotic treatment regimens. Another limitation was the consideration of short-term but not long-term antimicrobial resistance (AMR).

Added value of this study

In 2025, informed by the available evidence, the WHO established the TPP for a POCT for use in infants suspected of NS. Our study is the first to assess the potential cost-effectiveness of this WHO TPP-compliant POCT. To account for the differences in clinical management practices across LMIC settings, a de novo global decision model was developed in consultation with experts to represent the average situation across LMICs. Differences in parameter values were accounted for through prioritization of evidence derived from multi-country studies, expert-validation, and probabilistic sensitivity analysis. Additionally, the model considered blood culture contamination, potential deviations from prescribed referral pathways, and non-binary antibiotic treatment regimens. Another novelty of this model was the inclusion of short-term and long-term complications such as necrotising enterocolitis (NEC) and inflammatory bowel disease (IBD), respectively. These health effects were then translated into DALYs for the first time. An extra feature of the model is the convenient Excel user interface, accessible to all stakeholders.

Implications of all the available evidence

The 2025 WHO TPP is the first globally recognized document intended to guide the development of a POCT by defining the essential characteristics such test must possess to support early, accurate diagnosis of serious bacterial infections among infants. This study demonstrated that introducing a POCT with these characteristics into LMICs has the potential to improve health outcomes and reduce costs when compared to the current SOC, across diverse epidemiological and economic settings of LMICs. These results could support the decision of countries and donors to invest in the development of a TPP-compliant POCT. For settings where funding or policy requirements necessitate local evidence, a flexible decision model that can be populated with country-specific parameters to build a compelling, data-driven case for this POCT, is provided.

Introduction

Neonatal sepsis (NS) is a systemic bloodstream infection that occurs within the first 90 days of life. Globally, it estimated that there are between 1·3 to 3·9 million new cases of NS annually, causing 400 000 to 700 000 deaths, the majority of which occur in LMICs.[1] Whereas it is estimated that 84% of these deaths could be avoided through earlier diagnosis and appropriate treatment, diagnostic capabilities in resource-limited settings are currently constrained.[1,2]

The current diagnostic standard of care (SOC) relies on a combination of clinician judgment based on non-specific clinical signs and symptoms and blood culture (BC), the definitive method for confirming NS where available. However, BC takes up to 48 to 72 hours to yield results and cannot guide life-saving initial treatment decisions.[3] BC poses operational constrains as well. Venipuncture in unwell infants is often difficult or not possible, requiring high blood volumes, and expensive laboratory infrastructure.[4] These turnaround times and operational constrains are partially responsible for the lower BC uptake in LMICs when compared to higher income countries.[5,6] In LMICs, BC often yields false-negative results[4] Consequently, clinicians rely on non-specific clinical signs and symptoms to diagnose NS.[7,8] While this enables immediate decision-making, these signs have limited sensitivity and specificity, particularly in infants with ambiguous presentations.[7,8] This leads to preventable mortality from missed diagnoses, and inappropriate antibiotic use that drives AMR[7,9] and long-term complications.[10]

Currently, no POCT exists to accurately diagnose NS.[3,7] There is an urgent need for rapid triage diagnostics. Thus, the Indian Council for Medical Research[11] and the World Health Organization (WHO)[12] published a Target Product Profile (TPP) intended to guide the development of a POCT by defining the essential characteristics such test must possess to support early, accurate diagnosis of serious bacterial infections (SBI), including NS, in newborns and young infants. One study has assessed the potential cost-effectiveness of a POCT for NS using diverse accuracy scenarios.[13] The study found that across the different scenarios that were investigated, the POCT could decrease total healthcare costs by 17 to 43%, and deaths by 19% in hospitals and 76% in community settings.[13] This work was undertaken to inform the TPP and was used to define the performance characteristics specified within it. There is an opportunity to extend the available evidence by incorporating in the analysis the TPP details and factors such as missed cases, AMR, and long-term complications within an expert-validated framework, combined with a probabilistic sensitivity analysis (PSA) to provide a more comprehensive and representative picture of the cost-effectiveness of the prospective technology.

Our early health technology assessment (eHTA) bridges existing evidence gaps by modeling POCT parameters against benchmarks defined in the 2025 WHO TPP. The model structure was developed in consultation with experts to account for the diversity in clinical management and resource availability across LMICs. This approach was combined with a PSA to explore setting-specific variability, to arrive at a robust POCT cost-effectiveness estimate in the existing heterogenous

LMIC landscape. The objective was to quantify the value proposition of a TPP-compliant POCT across facility-of-birth and community-presenting infant populations.

Methods

Study design and data sources

A decision tree model was developed to estimate the cost-effectiveness of POCT in addition to SOC in a theoretical cohort of 1 000 infants (Figure 1). The current SOC for the management of suspected NS in LMICs comprises clinician judgement (CJ) which relies on the WHO possible serious bacterial infection (PSBI) risk classification system.[8] A suspected case was defined as an infant aged zero to 59 days presenting with any of the WHO-defined pSBI clinical signs.[8] Cases were categorized into two cohorts. Cohort (c_1) is restricted to infants managed in the facility of birth. Cohort 2 (c_2) is restricted to infants managed in the community. The study was conducted from a healthcare system perspective with a lifetime time horizon. A willingness-to-pay (WTP) of US$1 500 per DALY averted was used in the base-case analysis, representing the median of published LMIC estimates, rounded to avoid false precision.[14] Future costs and health outcomes were discounted at a 3·0% annual rate, following the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and WHO guidelines.[15,16]

Model development used an iterative expert elicitation process, and the parameterisation followed the ISPOR Good Research Practices.[15] The iterative process began with a non-exhaustive literature review, review of clinical guidelines, and unstructured interviews with experts; this was subsequently targeted via targeted literature searches. Then, the preliminary model was reviewed by experts through semi-structured questionnaires and manuscript comments to validate structural logic and parameter values. In the next iteration, the model was updated based on stakeholder feedback, and an additional targeted literature search was performed. Where evidence was lacking, parameters were populated through expert consultation. The comments from the experts are listed in the Supplementary appendix. This study follows the CHEERS 2022 reporting guidelines.[17] The model and all the analysis were implemented in R (version 4·3·1). For validation purposes and to promote stakeholder use, the model was also built in Microsoft Excel 365. All data and code are available under the data availability statement.

Model structure

Both cohorts were stratified into low (L), moderate (M), and high (H) risk groups upon presentation (Supplementary appendix). In the SOC arm, management decisions were based on CJ alone or in combination with BC. In the intervention arm, L-risk and M-risk groups were managed based on the POCT result, which overrides the initial clinical assessment, alone or in combination with BC. To maintain clinical safety and reflect clinical realities, H-risk infants in both arms followed a

safety-override logic where treatment was initiated and maintained regardless of diagnostic results. For infants in c_2, the initiation of empiric antibiotics and hospital referral success were contingent upon the diagnostic strategy as only the proportion of patients believed to have NS based on CJ or with a positive POCT result were eligible for antibiotic treatment and/or referral. The probability of successful referral was defined based on adherence rates observed in the literature. Infants in c_2 judged not to have sepsis (true negatives [TN] and false negatives [FN]) were assigned a referral probability of 0·0 to capture community-level outcomes. Conversely, for infants in c_1, a structural value of 1·0 was assigned to ensure all infants proceeded to the shared inpatient sub-tree where secondary diagnostic revision based on BC results remains possible. Given that the impact of POCT implementation on referral is difficult to predict, the model structure does not allow for a different referral probability between the two arms. Only patients entering the inpatient decision tree branches are eligible to receive a BC test, and thus for their diagnosis and treatment to be revised. If patients belong to the H risk group, there is no revision to ensure safety. For patients undergoing BC testing, the length of stay (LOS) includes a two-day observation period, reflecting the time required for BC results to become available. During this period patients are treated with antibiotics if initially suspected of NS. On day three a decision is made whether to continue, discontinue, or start antibiotic treatment. If results stay negative, one additional day is added to the LOS to represent the transition to discharge. When results change to negative, three days are added to the LOS for safety reasons. Whenever they stay positive, patients continue their inpatient stay and antibiotic treatment for eight more days to complete the ten-day regimen. If patients' results change to positive, they follow the ten-day antibiotic regimen until completion in the inpatient setting. Further detail on the model structure is provided in Supplementary appendix.

Epidemiology

The risk distribution and prevalence data specific to each cohort were derived from academic literature. For risk strata distribution, two studies in the setting of India were identified (Table 1).[18,19] Where multiple studies were identified, the midpoint of reported estimates was used. Cohort-specific prevalence of true NS among infants with pSBI was informed by multi-country data from South Asia and Africa.[20,21] Prevalence estimates were adjusted for imperfect BC performance using the Rogan-Gladen formula. As prevalence data by specific risk group were unavailable, an expert elicitation process derived multipliers to distribute corrected cohort-level prevalence: 1·0× for the M-risk group (baseline), 0·5× for L-risk, and 2·0× for H-risk.

Diagnostic accuracy

The sensitivity and specificity of CJ represented the accuracy of classifying NS versus no NS based on clinical symptoms. Expert consensus suggested that while literature values focused on community settings, they are representative of the facility-of-birth environment.[22] Consequently, c_2 sensitivity for L-risk and M-risk groups was adjusted 5% lower than c_1 values to reflect the clinical

assessment environment. For H-risk infants, sensitivity was set to 1·0 across cohorts to reflect high clinician risk aversion. POCT accuracy was parameterised directly from the 2025 TPP for NS diagnostics.[12] Whereas WHO recommends 100% referral, observed successful referral rates were used to reflect real-world adherence.[19] BC sensitivity and specificity were retrieved from published literature.[23] These values were also used in the Rogan-Gladen adjustment to ensure internal consistency. Barriers such as low infant blood volume and laboratory downtime, were reflected via an effective BC uptake parameter of 6·0%, a value in the lower end reported by the literature of 5·0 to 15·0%.[6] All sensitivities and specificities directly translated into antibiotic treatment vs. no antibiotic treatment and continuation of inpatient stay or discharge.

Costs

Healthcare resource use and unit prices were derived from the literature. To accurately reflect the economic realities of diverse LMIC settings while maintaining relevance for international donors, costs were adjusted using a mixed approach that stratified inputs into tradable and nontradable resources.[24] The TPP-compliant POCT was classified as a tradable good and valued at a uniform international price of US$ 5·00. Nontradable local resources, such as hospital bed-days and antibiotics, were estimated by extracting historical cost data from representative LMICs. These local costs were first back-converted to their original local currencies (where necessary), inflated to the 2024 base year using country-specific Gross Domestic Product (GDP) deflators from the World Bank, and subsequently converted to 2024 US Dollars (US$) using official market exchange rates. The estimated cost per NS inpatient day ranged from US$ 10[25] to US$ 198[26–28] depending on the setting (community hospital vs. secondary/tertiary neonatal intensive care). The daily costs for inpatient antibiotics ranged from US$ 0·86 to US$ 1·54.[29] Blood culture (BC) costs ranged from US$ 4·78 to US$ 12·22.[25,27,28,30] The cost of the POCT was set as per the WHO TPP.[12] The total costs for an outpatient antibiotic course ranged between US$ 1·55 and US$ 11·68.[31] Outpatient visit costs, excluding antibiotics, were derived from studies in Africa and India, ranging from US$ 1·46 to US$ 10·51 per case.[32,33] The average of each range was taken to represent the representative cost within the LMIC setting. The costs for base-case analysis are presented in Table 1. Details regarding the resources considered in the cost estimation and the specific conversion calculations are available in the files under the data availability statement.

The total cost per inpatient episode was calculated as the sum of the product of LOS, which included 11·2 additional bed-days added when HAI occurred,[34] and the cost per NS inpatient day excluding antibiotics, and the product of antibiotic duration and the cost per day of inpatient antibiotic treatment. The total cost per outpatient episode was calculated as the sum of the outpatient visit cost excluding antibiotics and the cost of outpatient antibiotic course. The costs for long-term complications and AMR were excluded due to high uncertainty in per-episode attribution and the risk of double-counting resources captured as part of HAI.

Disability-adjusted life-years

In the absence of publicly available utility values, disability-adjusted life-years (DALYs) were used as the primary health outcome of the analysis, calculated as the sum of the years of life lost (YLL) and the years lived with disability (YLD) attributed to distinct components to isolate the incremental impact of changes in antibiotic duration and LOS. Morbidity was operationalized as the sum of YLDs due to the inflammatory bowel disease (IBD) complication and AMR. There was no evidence on the relationship between antibiotic use and any other complication. For IBD, a disability weight derived from the literature was extended over ten years and applied to the incidence of IBD in patients exposed to antibiotic treatment early in life, which was estimated by applying a corresponding odds ratio (OR) to GBD cumulative incidence rates.[35]

Mortality included necrotising enterocolitis (NEC), AMR, HAI and the case fatality rates (CFRs) of patients suspected of NS or patients without PSBI symptoms for patients with true NS or non-NS status as proxies, respectively. The estimates were derived from the literature. The NS CFR was adjusted based on expert feedback to reflect differences across risk categories (Table 1). These CFRs were applied to true NS patients receiving a full antibiotic course. To estimate the CFR for untreated NS patients, the NS CFR for treated patients was divided by the antibiotic treatment effect, expressed as relative risk (RR).[36] YLL was calculated using the WHO frontier life table without age-weighting.[37] For NEC, a mortality rate derived from the literature was applied to the incidence of NEC in patients exposed to antibiotic treatment early in life, which was estimated by applying a corresponding OR to the incidence rate of NEC.[38] For HAI, whenever a HAI occurred, an attributable CFR was applied.[34]

The AMR morbidity and mortality was calculated as an expected DALY benefit per prescription avoided, adjusted by a correlation coefficient (0·462) reflecting the association between consumption and resistance.[39–46] An expert-recommended 60% discount was applied to the community-level (c_2) AMR benefit to reflect lower resistance selection pressure (Table 1).

Sensitivity analysis

The sensitivity of results to parameter uncertainty was explored by means of a PSA which employed a Monte Carlo simulation with 10 000 iterations. The values of all parameters were varied simultaneously in each iteration through sampling from the selected probability distributions (Table 1). To determine the key drivers for the ICER, a one-way sensitivity analysis (OWSA), where each parameter value was varied separately, was performed. The base case parameter values were derived from literature that was limited to one or a few LMIC settings. To account for a potentially wider range of clinical, operational and epidemiological heterogeneity across LMIC settings, the lower and upper bounds for the sensitivity analyses were calculated as the mean parameter values ±25% (Table 1).

A performance frontier analysis was conducted to identify acceptable WTP-POCT price-accuracy combinations. Clinical harm was defined as a combination of POCT sensitivity-specificity that

resulted in non-zero DALY loss upon POCT introduction into the SOC. WTP thresholds representing the 25th, 50th, 75th, and 95th percentiles of published LMIC estimates (US$250, US$1 500, US$4 000, and US$8 000 per DALY averted, respectively) were used to capture setting variability.[14] POCT test prices were bound between the aspirational TPP target (US$ 5·00) and an upper exploratory threshold of US$ 15·00. Scenario boundaries were purposefully selected to evaluate a 100% price premium (US$ 10·00, closely approximating the mean blood culture cost of US$ 9·09) and a 200% premium (US$ 15·00). This upper bound accounts for the added clinical value of rapid turnaround times compared to traditional laboratory diagnostics, and allows us to determine the maximum price threshold that remains meaningful for the healthcare system.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit the paper for publication.

Results

Base-case analysis

Integrating POCT into the current SOC resulted in 48 fewer missed NS cases per 1 000 infants in c_1, and 26 per 1 000 in c_2 (Table 2). It also resulted in a 58·6% and 51·4% reduction in unnecessary treatment, respectively (Table 2).

Table 3 summarises the estimated costs and health outcomes under the SOC and SOC + POCT. In the base-case analysis, the SOC + POCT strategy was dominant across both cohorts, resulting in both lower costs and DALYs. In the facility-of-birth (c_1) and community (c_2) cohorts, POCT usage in 1 000 infants was estimated to reduce costs by US$37 342 and US$5 715, and avert 206·0 DALYs and 127·0 DALYs, respectively.

In c_1, the introduction of POCT into the current inpatient SOC resulted in patients receiving appropriate treatment early and reducing unnecessary treatment in the model, reducing the number of NS and HAI deaths, by six deaths and one death per 1000 infants respectively. The POCT acquisition cost (US$5 000 per 1 000 infants) was negligible compared with the US$37 342 saved by avoiding 985 unnecessary inpatient bed-days.

In c_2, the introduction of POCT into the current community SOC was estimated to reduce false positives by 51·4% (from 461 to 224 per 1 000) and false negatives by 70·3% (from 37 to 11 per 1 000). This diagnostic improvement resulted in an estimated four total deaths being avoided per 1 000 infants (Table 3). In patients who were not referred, the introduction of POCT led to a cost increase; however, this increase was offset by the reductions in hospital expenditures for referred infants, resulting in US$5 715 being saved per 1 000 infants. Overall, the mechanism behind the reduction in

costs, LOS, deaths, and DALYs across all dimensions was the improvement in antibiotic prescription, inpatient management, and referral practices, which resulted from earlier access to more accurate diagnosis.

Sensitivity analyses

The PSA confirmed the robustness of base-case results. Adopting POCT as part of SOC was found to be the dominant strategy in 93·2% and 84·8% of c_1 and c_2 iterations, respectively, demonstrating cost-effectiveness across a wide range of values (Supplementary appendix). The maximum VBP was estimated at US$ 351·30 for c_1 and US$ 200·61 for c_2. For c_1, OWSA identified CJ sensitivity for moderate-risk infants as the main driver, followed by POCT sensitivity and POCT specificity (Supplementary appendix). For c_2, the key drivers were POCT sensitivity, CJ sensitivity for moderate-risk patients, and the CFR for untreated moderate-risk NS (Supplementary appendix).

In the performance frontier analysis, when the specificity of POCT was held constant at the same value as CJ, the minimum sensitivity required to avoid clinical harm and remain cost-effective was 72% for c_1 and 66% for c_2, at the price of US$ 5.00 and WTP of US$ 1 500. Similarly, when sensitivity of POCT was fixed at that of CJ, the minimum specificity required was 52% for c_1 and 58% for c_2. At a sensitivity of 95%, the POCT remained cost-effective even if specificity dropped to 0% (c_1) or 0% (c_2). At a sensitivity and specificity of 90%, the VBP was around US$ 396.17 for c_1 and US$ 218.49 for c_2, due to the cost-savings from avoided or shortened inpatient admissions for patients without NS.

Discussion

This study fills the gaps in the current evidence by providing the first comprehensive, LMIC-level and expert-validated assessment of a WHO TPP-compliant POCT. We found that the implementation of this POCT is the dominant strategy in both facility-of-birth and community-presenting PSBI infants when compared to the SOC alone. The improvements in health outcomes came from better identification and timely treatment of infants with NS who are missed under the current SOC. This reduction in FN diagnoses directly translates in lower neonatal mortality, particularly in community settings where diagnostic gaps are most pronounced.

Beyond mortality reduction, the diagnostic provides a gatekeeping effect that is clinically and economically relevant. In the facility-based model, the reduction in FP diagnoses led to a net saving of 985 inpatient bed-days per 1 000 infants. This decongestion of neonatal wards is an important secondary benefit, as it prevented 5·71 cases of HAI per 1 000 infants. By reducing unnecessary facility-based exposure, the POCT addresses a major driver of iatrogenic morbidity in resource-limited settings. Furthermore, the inclusion of externalities such as AMR and antibiotic-related complications, including NEC and IBD, suggests that the benefits of rapid diagnostics extend beyond the acute episode to long-term health and stewardship goals.

The identification of a performance frontier defining clinical safety is a central insight of this analysis. We established a minimum sensitivity floor of 72% for c_1 and 66% for c_2, considering equal performance of the POCT to the CJ in terms of specificity; below these cutoffs, the diagnostic enters a zone of net clinical harm where the DALY burden resulting from missed NS cases outweighs the benefits of reduced hospital exposure. These frontiers provide a benchmark for future TPPs, indicating that a diagnostic failing to meet these sensitivity floors may not be economically or ethically viable. However, provided these safety floors are maintained, the POCT remains cost-effective at unit prices well above US$5·00. This is driven by the cost asymmetry between a rapid diagnostic and the US$420 cost of a 10-day inpatient neonatal admission.

Our findings build upon the foundational work by Chevalier et al. (2025), which first highlighted the significant mortality reductions achievable through rapid neonatal diagnostics.[10] While that study reported potential mortality reductions of up to 76%, our analysis suggests a more moderate relative impact of approximately 8·2% in the community cohort. This difference reflects our inclusion of additional parameters, such as clinician adherence and referral success, as well as a more granular accounting for the health burden of HAI and antibiotic-related complications. By incorporating these dimensions, our study provides a complementary perspective that reinforces the high value of TPP-compliant diagnostics while adopting a conservative approach to clinical impact across diverse epidemiological landscapes.

Importantly, this analysis was designed as a global early-HTA model rather than a setting-specific economic evaluation. This structure enables jurisdictions, particularly LMICs, to adapt and parametrize the framework with country-level epidemiology, care-seeking patterns, local treatment pathways, unit costs, and health system constraints. This enables locally contextualized value evidence to inform reimbursement, procurement, and donor investment decisions.

Additionally, this study extends beyond direct treatment effects to include system efficiency, antimicrobial stewardship, and downstream morbidity avoidance. By capturing these broader externalities within a unified decision model, this work provides a quantifiable and decision-relevant justification for diagnostics funding that is typically absent from conventional prioritization approaches.

The 2025 WHO TPP was published to promote the development of a rapid and accessible test that could reduce the discrepancies in health outcomes and reduce the economic burden between LMICs. The findings of this study illustrate the mechanisms through which improvements in health outcomes and costs reductions can operate, resulting in prompt treatment of NS cases and reduction in the risk of HAI, AMR and complications as well as resource use in patients without NS. Which, consequently, frees resources for other patients.

This study has several limitations. There is limited LMIC-specific evidence for some parameters, particularly the AMR DALY burden, the incidence of long-term complications, and stratifications by

early and late onset sepsis. We adopted cautious assumptions to avoid overstating benefits. Whereby direct costs associated with AMR externalities were excluded, which results in an underestimation of total economic gains. Additionally, we did not select the societal perspective as the definition varies widely across LMICs. Including societal costs such as those attributed to caregiver time lost could build a more favourable case toward the implementation of the POCT. However, real-world impact will depend on local implementation, health system capacity, and clinician adherence to diagnostic guidance. Despite these constraints, the PSA confirmed the robustness of the POCT's dominance in most simulations.

Conclusion

A rapid triage point-of-care diagnostic for NS has the potential to deliver robust health and economic gains in LMICs. These findings provide an evidence-based benchmark to align diagnostic innovation with the clinical realities of neonatal care. Our results should inform investment from global health donors and manufacturers to accelerate the transition of these diagnostics from the TPP stage into development, prioritizing neonatal point-of-care triage as a component of global newborn care strategies.

References

1. World Health Organization. Global report on the epidemiology and burden of sepsis: Current evidence, identifying gaps and future directions. [Internet]. Geneva; 2020. Report No. Available from: https://iris.who.int/server/api/core/bitstreams/d4ce3613-bf94-4205-85c8-14f3fc0609db/content

2. Dramowski A, Bolton L, Fitzgerald F, Bekker A. Neonatal Sepsis in Low- and Middle-income Countries – Where Are We Now? Pediatr Infect Dis J. 2025 Apr 1;44(6):e207. doi:10.1097/INF.0000000000004815 PubMed PMID: 40168607.

3. Iroh Tam PY, Bendel CM. Diagnostics for neonatal sepsis: Current approaches and future directions. Pediatr Res. 2017 Oct;82(4):574–83. doi:10.1038/pr.2017.134

4. Stanley JL, Hettle D, Poffley R, Bolton L, Gres E, Coelho I, et al. Investigating neonatal sepsis: Anti-Infectives, diagnostics and Guidelines used in Health sysTems across sub-Saharan Africa – The INSIGHTS study. BMJ Paediatr Open. 2026 Jan 23;10(1). doi:10.1136/bmjpo-2025-004132 PubMed PMID: 10.1136/bmjpo-2025-004132.

5. Orfanos I. Prevalence of serious bacterial infections and management of febrile infants ≤60 days in Swedish Pediatric Emergency Departments.

6. Blood culture versus antibiotic use for neonatal inpatients in 61 hospitals implementing with the NEST360 Alliance in Kenya, Malawi, Nigeria, and Tanzania: A cross-sectional study | BMC Pediatrics | Full Text [Internet]. [cited 2025 Nov 19]. Available from: https://bmcpediatr.biomedcentral.com/articles/10.1186/s12887-023-04343-0

7. Gleeson B, Ferreyra C, Palamountain K, Jacob ST, Spotswood N, Kissoon N, et al. A call to bridge the diagnostic gap: Diagnostic solutions for neonatal sepsis in low- and middle-income countries. BMJ Glob Health. 2024 Sep 10;9(9):e015862. doi:10.1136/bmjgh-2024-015862 PubMed PMID: 39260829; PubMed Central PMCID: PMC11404204.

8. World Health Organization. Guideline Managing possible serious bacterial infection in young infants when referral is not feasible [Internet]. Switzerland; 2015. Report No. Available from: https://iris.who.int/server/api/core/bitstreams/8c8ff2e2-5d07-4f85-ac69-48abf3c797e2/content

9. Rallis D, Giapros V, Serbis A, Kosmeri C, Baltogianni M. Fighting Antimicrobial Resistance in Neonatal Intensive Care Units: Rational Use of Antibiotics in Neonatal Sepsis. Antibiotics. 2023 Mar;12(3):508. doi:10.3390/antibiotics12030508

10. Ong WJ, Seng JJB, Yap B, He G, Moochhala NA, Ng CL, et al. Impact of neonatal sepsis on neurocognitive outcomes: A systematic review and meta-analysis. BMC Pediatr. 2024 Aug 7;24(1):505. doi:10.1186/s12887-024-04977-8

11. Sharma M, Jain M, Veeraraghavan B, Rodrigues C, Bansal N, Nambi PS, et al. Target product profiles for diagnosis of sepsis: Proposing a new approach for diagnostic innovation. Indian J Med Res. 2023 May;157(5):395–402. doi:10.4103/ijmr.ijmr_1936_22 PubMed PMID: 37322632; PubMed Central PMCID: PMC10443725.

12. WHO releases new target product profile for diagnostic tests to detect serious bacterial infections in young infants [Internet]. [cited 2025 Dec 29]. Available from: https://www.who.int/news/item/06-08-2025-who-releases-new-tpp-for-diagnostic-tests-to-detect-serious-bacterial-infections-in-young-infants

13. Chevalier JM, Hansen MA, Grantz KH, Gleeson B, Blumel B, Chuchu V, et al. Potential health and cost impacts of a point-of-care test for neonatal sepsis and possible serious bacterial infections in infants: A modeling analysis in two settings [Internet]. medRxiv; 2025 [cited 2025 Sep 7]. p. 2024.12.03.24318382. Available from: https://www.medrxiv.org/content/10.1101/2024.12.03.24318382v2. doi:10.1101/2024.12.03.24318382

14. Ochalek J, Lomas J, Claxton K. Estimating health opportunity costs in low-income and middle-income countries: A novel approach and evidence from cross-country data. BMJ Glob Health. 2018;3(6):e000964. doi:10.1136/bmjgh-2018-000964 PubMed PMID: 30483412; PubMed Central PMCID: PMC6231096.

15. Caro JJ, Briggs AH, Siebert U, Kuntz KM. Modeling Good Research Practices—Overview: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-1. Value Health. 2012 Sep 1; 15(6):796–803. doi:10.1016/j.jval.2012.06.012

16. Bertram MY, Lauer JA, Stenberg K, Edejer TTT. Methods for the Economic Evaluation of Health Care Interventions for Priority Setting in the Health System: An Update From WHO Choice. Int J Health Policy Manag. 2021 Nov 1;10(Special Issue on WHO-CHOICE Update):673–7. doi:10.34172/ijhpm.2020.244

17. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health. 2022 Jan 1;25(1):10–31. doi:10.1016/j.jval.2021.10.008

18. Roy S, Patil R, Apte A, Thibe K, Dhongade A, Pawar B, et al. Feasibility of implementation of simplified management of young infants with possible serious bacterial infection when referral is not feasible in tribal areas of Pune district, Maharashtra, India. PLOS ONE. 2020 Aug 24; 15(8):e0236355. doi:10.1371/journal.pone.0236355

19. Puri D, Nisar YB, Tshefu A, Longombe AL, Esamai F, Marete I, et al. Prevalence of clinical signs of possible serious bacterial infection and mortality associated with them from population-based surveillance of young infants from birth to 2 months of age. PLoS ONE. 2021 Feb 24;16(2): e0247457. doi:10.1371/journal.pone.0247457 PubMed PMID: 33626090; PubMed Central PMCID: PMC7904202.

20. Milton R, Gillespie D, Dyer C, Taiyari K, Carvalho MJ, Thomson K, et al. Neonatal sepsis and mortality in low-income and middle-income countries from a facility-based birth cohort: An international multisite prospective observational study. Lancet Glob Health. 2022 Apr 12; 10(5):e661–72. doi:10.1016/S2214-109X(22)00043-2 PubMed PMID: 35427523; PubMed Central PMCID: PMC9023753.

21. Saha SK, Schrag SJ, Arifeen SE, Mullany LC, Islam MS, Shang N, et al. Causes and incidence of community-acquired serious infections among young children in south Asia (ANISA): An observational cohort study. The Lancet. 2018 Jul 14;392(10142):145–59. doi:10.1016/S0140-6736(18)31127-9 PubMed PMID: 30025808.

22. Fung A, Shafiq Y, Driker S, Rees CA, Mediratta RP, Rosenberg R, et al. Diagnostic Accuracy of Clinical Sign Algorithms to Identify Sepsis in Young Infants Aged 0 to 59 Days: A Systematic Review and Meta-analysis. Pediatrics. 2024 Aug 1;154(Supplement 1):e2024066588D. doi:10.1542/peds.2024-066588D

23. Yadav AK, Wilson CG, Prasad PL, Menon PK. Polymerase chain reaction in rapid diagnosis of neonatal sepsis. Indian Pediatr. 2005 Jul;42(7):681–5. PubMed PMID: 16085969.

24. Turner HC, Lauer JA, Tran BX, Teerawattananon Y, Jit M. Adjusting for Inflation and Currency Changes Within Health Economic Studies. Value Health. 2019 Sep 1;22(9):1026–32. doi:10.1016/j.jval.2019.03.021

25. Garg P, Krishak R, Shukla DK. NICU in a community level hospital. Indian J Pediatr. 2005 Jan 1; 72(1):27–30. doi:10.1007/BF02760575

26. Narang A, Kiran PSS, Kumar P. Cost of neonatal intensive care in a tertiary care center. Indian Pediatr. 2005 Oct;42(10):989–97. PubMed PMID: 16269829.

27. Ibrahim NA, Bakry MM, Ishak S, Tahir NAM, Shah NM. Exploring the potential impact of empiric antibiotic de-escalation for suspected early onset neonatal sepsis. J Infect Dev Ctries. 2025 Jun 30;19(06):896–903. doi:10.3855/jidc.20654

28. Karambelkar G, Malwade S, Karambelkar R. Cost-analysis of healthcare in a private-sector neonatal intensive care unit in India. Indian Pediatr. 2016 Sep 1;53(9):793–5. doi:10.1007/s13312-016-0933-x

29. Thomson KM, Dyer C, Liu F, Sands K, Portal E, Carvalho MJ, et al. Effects of antibiotic resistance, drug target attainment, bacterial pathogenicity and virulence, and antibiotic access and affordability on outcomes in neonatal sepsis: An international microbiology and drug evaluation prospective substudy (BARNARDS). Lancet Infect Dis. 2021 Dec;21(12):1677–88. doi:10.1016/S1473-3099(21)00050-5 PubMed PMID: 34384533; PubMed Central PMCID: PMC8612937.

30. Aerts C, Leahy S, Mucasse H, Lala S, Bramugy J, Tann CJ, et al. Quantifying the Acute Care Costs of Neonatal Bacterial Sepsis and Meningitis in Mozambique and South Africa. Clin Infect Dis Off Publ Infect Dis Soc Am. 2021 Nov 2;74(Suppl 1):S64–9. doi:10.1093/cid/ciab815 PubMed PMID: 34725702; PubMed Central PMCID: PMC8776306.

31. Garg CC, Tshefu A, Longombe AL, Kila JSN, Esamai F, Gisore P, et al. Costs and cost-effectiveness of management of possible serious bacterial infections in young infants in outpatient settings when referral to a hospital was not possible: Results from randomized trials in Africa. PLOS ONE. 2021 Mar 15;16(3):e0247977. doi:10.1371/journal.pone.0247977

32. Chauhan AS, Prinja S, Srinivasan R, Bahuguna P, Downey L, Garg CC, et al. Cost of delivering primary healthcare services through public sector in India. Indian J Med Res. 2022 Sep; 156(3):372–80. doi:10.4103/ijmr.IJMR_67_19. PubMed PMID: 36588362; PubMed Central PMCID: PMC10101352.

33. Getzzg. Cost of treating sick young infants (0–59 days) with Possible Serious Bacterial Infection in resource-constrained outpatient primary care facilities: An insight from implementation research in two districts of Haryana and Uttar Pradesh (India). JOGH [Internet]. 2023 Aug 18 [cited 2026 Feb 8]. Available from: https://jogh.org/2023/jogh-13-04062/

34. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. The Lancet. 2005 Mar 26;365(9465):1175–88. doi:10.1016/S0140-6736(05)71881-X

35. Institute for Health Metrics and Evaluation. Institute for Health Metrics and Evaluation [Internet]. 2025 [cited 2025 Dec 29]. GBD Results. Available from: https://vizhub.healthdata.org/gbd-results/

36. Zaidi AKM, Ganatra HA, Syed S, Cousens S, Lee ACC, Black R, et al. Effect of case management on neonatal mortality due to sepsis and pneumonia. BMC Public Health. 2011 Apr 13;11 Suppl 3(Suppl 3): S13. doi:10.1186/1471-2458-11-S3-S13 PubMed PMID: 21501430; PubMed Central PMCID: PMC3231886.

37. World Health Organization. WHO methods and data sources for global burden of disease estimates 2000–2019 [Internet]. Geneva. Report No. Available from: https://www.who.int/docs/default-source/gho-documents/global-health-estimates/ghe2019_daly-methods.pdf

38. Jones IH, Hall NJ. Contemporary Outcomes for Infants with Necrotizing Enterocolitis-A Systematic Review. J Pediatr. 2020 May;220:86–92.e3. doi:10.1016/j.jpeds.2019.11.011 PubMed PMID: 31982088.

39. Goossens H, Ferech M, Stichele RV, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: A cross-national database study. The Lancet. 2005 Feb 12;365(9459): 579–87. doi:10.1016/S0140-6736(05)17907-0 PubMed PMID: 15708101.

40. Martínez EP, van Rosmalen J, Bustillos R, Natsch S, Mouton JW, Verbon A, et al. Trends, seasonality and the association between outpatient antibiotic use and antimicrobial resistance among urinary bacteria in the Netherlands. J Antimicrob Chemother. 2020 Aug 1;75(8):2314–25. doi:10.1093/jac/dkaa165

41. Meyer E, Gastmeier P, Deja M, Schwab F. Antibiotic consumption and resistance: Data from Europe and Germany. Int J Med Microbiol. 2013 Aug 1;Special Issue Antibiotic Resistance303(6): 388–95. doi:10.1016/j.ijmm.2013.04.004

42. Wushouer H, Zhang ZX, Wang JH, Ji P, Zhu QF, Aishan R, et al. Trends and relationship between antimicrobial resistance and antibiotic use in Xinjiang Uyghur Autonomous Region, China: Based on a 3 year surveillance data, 2014–2016. J Infect Public Health. 2018 May 1;11(3):339–46. doi:10.1016/j.jiph.2017.09.021

43. Kagami K, Ishiguro N, Iwasaki S, Usami T, Fukumoto T, Hayasaka K, et al. Correlation between antibiotic use and antibiotic resistance: A multicenter study using the Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE) system in Hokkaido, Japan. Am J Infect Control. 2023 Feb 1;51(2):163–71. doi:10.1016/j.ajic.2022.05.025

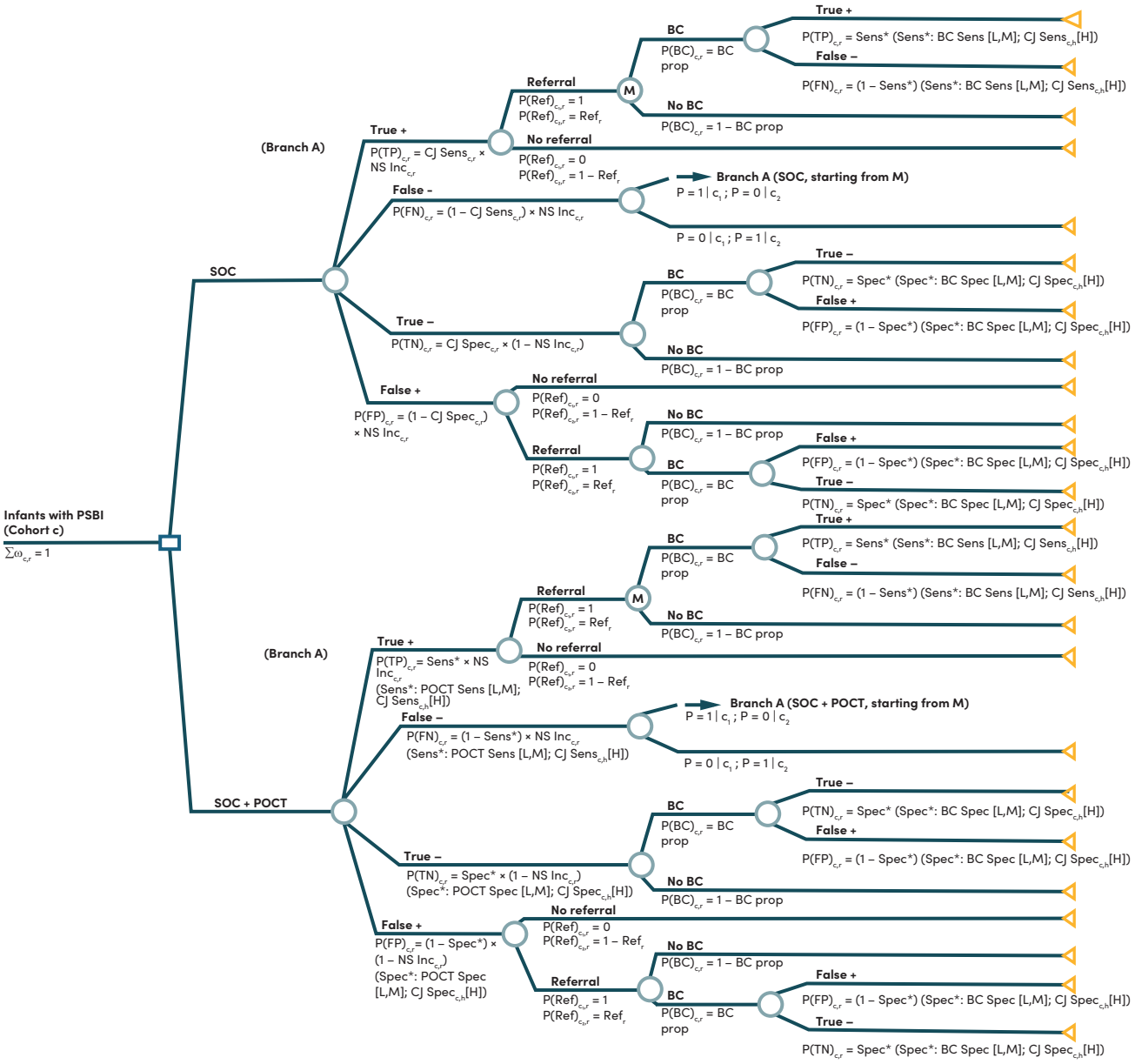
44. van de Sande-Bruinsma N, Grundmann H, Verloo D, Tiemersma E, Monen J, Goossens H, et al. Antimicrobial Drug Use and Resistance in Europe. Emerg Infect Dis. 2008 Nov;14(11):1722–30. doi:10.3201/eid1411.070467 PubMed PMID: 18976555; PubMed Central PMCID: PMC2630720.

45. Willemsen I, Bogaers-Hofman D, Winters M, Kluytmans J. Correlation between antibiotic use and resistance in a hospital: Temporary and ward-specific observations. Infection. 2009 Oct 1; 37(5):432–7. doi:10.1007/s15010-009-8325-y

46. European Centre for Disease Prevention and Control (ECDC), Authority (EFSA) EFS, Agency (EMA) EM. ECDC/EFSA/EMA second joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals. EFSA J. 2017;15(7):e04872. doi:10.2903/j.efsa.2017.4872

Figures and Tables

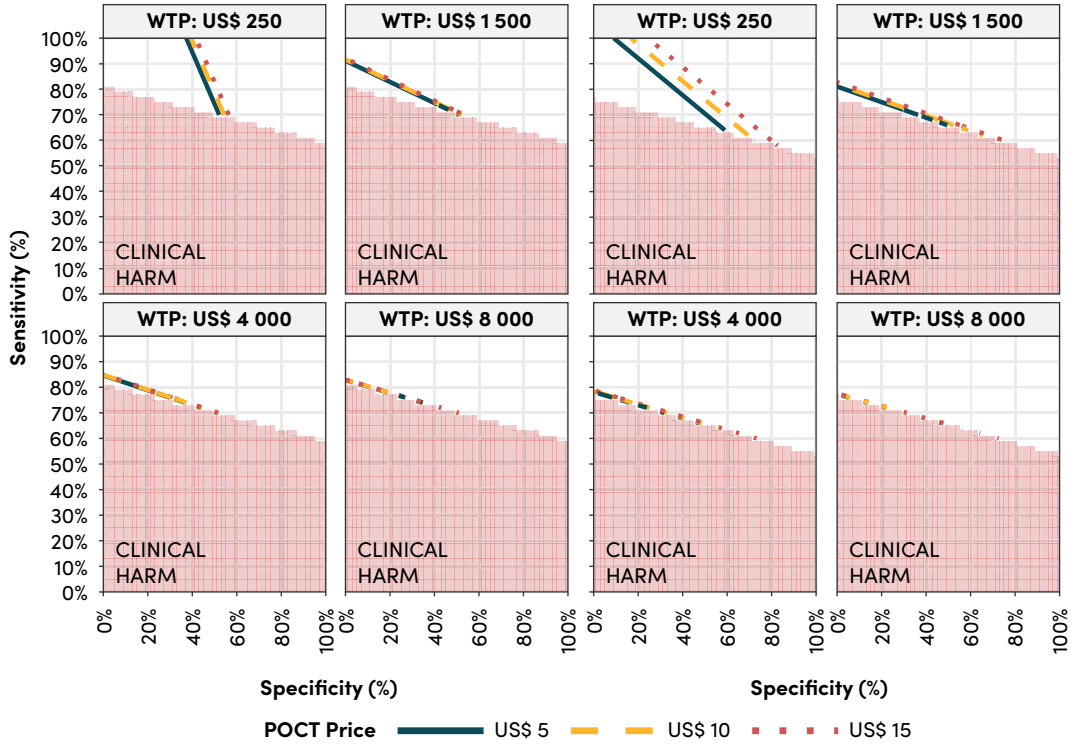
FIGURE 1. Clinical pathways of an infant with possible serious bacterial infection (PSBI) engaging with the healthcare system



Notes: Illustrates the clinical pathways of an infant with possible serious bacterial infection (PSBI) engaging with the healthcare system. The figure focuses on diagnosis and referral. Antibiotic treatment was omitted because sensitivity and specificity directly translate into treatment decisions. Before entering the model, infants are distributed into three risk groups (L, M, and H) based on presenting symptoms. In c1, the referral pathway is bypassed. The outcome is determined by antibiotic duration and length of stay (LOS), which depend on diagnostic results (SOC ± BC, POCT ± BC). High-risk infants are defaulted to treatment for safety reasons.

Abbreviations: SOC, standard of care; SOC + POCT, standard of care plus point-of-care test; c1, facility-of-birth cohort; c2, community cohort; c, cohort index; r, risk stratum; L, low risk; M, moderate risk; H, high risk; PSBI, possible serious bacterial infection; NS, neonatal sepsis; NS Inc, neonatal sepsis incidence; CJ, clinician judgment; POCT, point-of-care test; BC, blood culture; BC prop, proportion receiving blood culture; Ref, referral; P(·), probability of event; Sens, sensitivity; Spec, specificity; Sens*, effective sensitivity used in the model; Spec*, effective specificity used in the model; TP, true positive; FP, false positive; TN, true negative; FN, false negative; ω, branch weight (with $\Sigma\omega(c,r) = 1$).

FIGURE 2. Minimum accuracy requirements for cost-effective POCT use across cohorts and willingness-to-pay thresholds



Notes: Divided into panel (A) facility-of-birth cohort (c_1) and panel (B) community cohort (c_2). Panels are stratified into four boxes representing different willingness-to-pay (WTP) thresholds, defined as the maximum amount LMIC societies are WTP per DALY averted. Straight and dashed lines indicate minimum POCT accuracy requirements for the unit prices shown in the legend. The red shaded area denotes the net clinical harm zone, where adoption of POCT results in DALY loss. POCT is cost-effective for combinations of sensitivity (y-axis) and specificity (x-axis) that fall within the regions defined by these lines and outside the clinical harm zone.

TABLE 1. Input variables of the deterministic and probabilistic cost-effectiveness analysis

	Notation	Inborn (c_1)	Community (c_2)	Dist.
Cohort Distribution	$\omega_{c,r}$			
Prevalence of low risk PSBI (r=L)	$\omega_{c,L}$	0·67[EO]	0·55[1,2]	β
Prevalence of moderate risk PSBI (r=M)	$\omega_{c,M}$	0·22[EO]	0·35[1,2]	β
Prevalence of high risk PSBI (r=H)	$\omega_{c,H}$	0·11[EO]	0·10[1,2]	β
Epidemiology	NS $Inc_{c,r}$			
Incidence of NS (low risk)	NS $Inc_{c,L}$	0·23[3,4,EO]	0·08[5,EO]	β
Incidence of NS (moderate risk)	NS $Inc_{c,M}$	0·47[3,4,EO]	0·17[5,EO]	β
Incidence of NS (high risk)	NS $Inc_{c,H}$	0·93[3,4,EO]	0·34[5,EO]	β

(Continued)

TABLE 1. (Continued)

	Notation	Inborn (c_1)	Community (c_2)	Dist.
Diagnostic Accuracy				
POCT Sensitivity	POCT Sens	0·90[6]	0·90[6]	β
POCT Specificity	POCT Spec	0·80[6]	0·80[6]	β
CJ Sensitivity (r∈{L,M})	CJ $Sens_{c,r}$	0·70[EO,7]	0·65[EO,7]	β
CJ Specificity (r∈{L,M})	CJ $Spec_{c,r}$	0·50[EO,7]	0·50[EO,7]	β
CJ Sensitivity (r=H)	CJ $Sens_{c,H}$	1·00[EO,7]	1·00[EO,7]	Fixed
CJ Specificity (r=H)	CJ $Spec_{c,H}$	0·00[EO,7]	0·00[EO,7]	Fixed
Secondary Testing (BC)				
Fraction receiving BC	BC prop	0·06[8]	0·06[8]	β
BC Sensitivity	BC Sens	0·69[9]	0·69[9]	β
BC Specificity	BC Spec	1·00[9]	1·00[9]	β
Referral Pathway (c_2 only)				
Low risk referral (r=L)	Ref_L	NA	0[1,10]	Fixed
Moderate risk referral (r=M)	Ref_M	NA	0·30[1,10]	β
High risk referral (r=H)	Ref_H	NA	0·60[1,10]	β
Clinical Outcomes				
CFR treated NS (L/M/H)	—	0·04/0·09/0·20[11,EO]	0·04/0·09/0·20[2,EO]	β
CFR untreated NS (L/M/H)	—	0·11/0·26/0·57[2,EO,12]	0·11/0·26/0·57[2,EO,12]	β
CFR for non NS	—	0·02[5]	0·02[5]	β
RR mortality (treated/untreated)	—	0·35[12]	0·35[12]	ln
HAI risk target (per inpatient stay)	—	0·06[13]	0·06[13]	β
HAI risk (per inpatient day)	—	0·0058[13,14]	0·0058[13,14]	β
CFR for HAI (inpatient case)	—	0·12[13]	0·12[13]	β
Costs (US$)				
Cost of POCT device/reagents	—	5·00[6]	5·00[6]	γ
Hospital bed per day	—	41·55[15–18]	41·55[15–18]	γ
BC test	—	9·09[16–19]	9·09[16–19]	γ
Outpatient visit	—	NA	5·81[20,21]	γ
Antibiotics per case (outpatient)	—	NA	6·30[30]	γ
Antibiotics per day (inpatient)	—	1·07[23]	1·07[23]	γ
DALYs				
DALYs per death	—	31·10[24]	31·10[24]	γ
DALYs for AMR	—	0·13[25–32]	0·07[25–32,EO]	γ
DALYs for NS NEC Complication (inpatient)	—	0·01[33–35]	0·01[33–35]	γ
DALYs for NS IBD Complication (inpatient)	—	0·00006[36–39]	0·00006[36–39]	γ

Abbreviations: c_1, inborn cohort; c_2, community cohort; c, cohort index; r, risk stratum; L, low risk; M, moderate risk; H, high risk; PSBI, possible serious bacterial infection; NS, neonatal sepsis; CJ, clinician judgment; POCT, point-of-care test; BC, blood culture; Sens, sensitivity; Spec, specificity; BC prop, proportion receiving blood culture; RefL/RefM/RefH, probability of successful referral for low-/moderate-/high-risk infants (c_2); CFR, case fatality rate; RR, relative risk; HAI, healthcare-associated infection; NEC, necrotizing enterocolitis; IBD, inflammatory bowel disease; AMR, antimicrobial resistance; DALY, disability-adjusted life year; US$, United States dollars; Dist., probability distribution; β, Beta distribution; γ, Gamma distribution; ln, log-normal distribution; EO, expert opinion; Comp., complications; NA, not applicable.

TABLE 2. Distribution of final status for 1 000 infants with PSBI

	Inborn Cohort (c_1)			Community Cohort (c_2)		
	SOC (n)	SOC and POCT (n)	Increment (n)	SOC (n)	SOC and POCT (n)	Increment (n)
TP	285	333	48	102	128	26
FN	78	30	–48	37	11	–26
TN	334	512	178	400	637	237
FP	304	126	–178	461	224	–237

Abbreviations: PSBI, possible serious bacterial infection; c_1, inborn cohort; c_2, community cohort; SOC, standard of care; POCT, point-of-care test; TP, true positives; FN, false negatives; TN, true negatives; FP, false positives; n, number of cases.

TABLE 3. Cost-effectiveness analysis of management of 1 000 infant with PSBI

	Inborn Cohort (c_1)			Community Cohort (c_2)		
	SOC	SOC and POCT	Increment	SOC	SOC and POCT	Increment
Deaths						
Total Deaths	61	55	–6	49	45	–4
NS Deaths	45	39	–6	33	30	–3
HAI Deaths	5	4	–1	1	1	0
DALYs						
Total DALYs	1 964	1 758	–206	1 109	982	–127
NS DALYs	1 396	1 228	–168	577	474	–103
AMR DALYs	77	60	–17	48	31	–17
HAI DALYs	148	129	–19	23	19	–4
Comp. DALYs	7	6	–2	7	4	–3
Resource use						
Total LOS (Days)	7 613	6 628	–985	1 208	984	–223
Costs (US$)						
Total cost (US$)	323 245	285 904	–37 342	60 102	54 387	–5 715

Notes: Components may not sum to totals due to rounding. PSBI, possible serious bacterial infection; c_1, inborn cohort; c_2, community cohort; SOC, standard of care; POCT, point-of-care test; NS, neonatal sepsis; HAI, healthcare-associated infection; AMR, antimicrobial resistance; DALY, disability-adjusted life year; Comp., complications; LOS, length of stay; US$, United States dollars.