Evaluating the Clinical, Economic, and Societal Value of Rapid Diagnostic Testing in Emerging Markets: A Systematic Literature Review Assessing Infectious Diseases

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Key Research Takeaways

The quick turnaround times of rapid diagnostic tests (RDTs) reduce the time to diagnosis and treatment, and subsequently improve patient clinical outcomes

RDTs can lead to potential cost savings and more efficient healthcare resource utilization by reducing time and burden on patients and healthcare workers

RDTs are accurate, portable, easy to use, and have minimal training and storage requirements which allow for implementation in decentralized settings

Introduction & Objective

Introduction

- **Rapid diagnostic tests (RDTs)** are designed to enable access to diagnostic testing at the **point of care** for **faster screening and improved outcomes:**
  - accurate and timely diagnosis
  - where the patient is located across decentralized settings
  - broadening patient access in difficult-to-reach and improving pathways to diagnosis.[1]
- Health systems in Asia, Africa, and Latin America with high burden of infectious diseases and need for quick diagnostic testing in a variety of clinical situations.[2]
- Current literature on the impact of point-of-care devices on infectious disease burden tends to focus on specific indications and sub-populations. There is a lack of a comprehensive summary focusing on decentralized health settings.
- Therefore, it is important to identify the existing evidence on the **value of rapid diagnostics on infectious disease burden in those LMIC***.

* LMIC: Low and Middle Income Countries

Objective

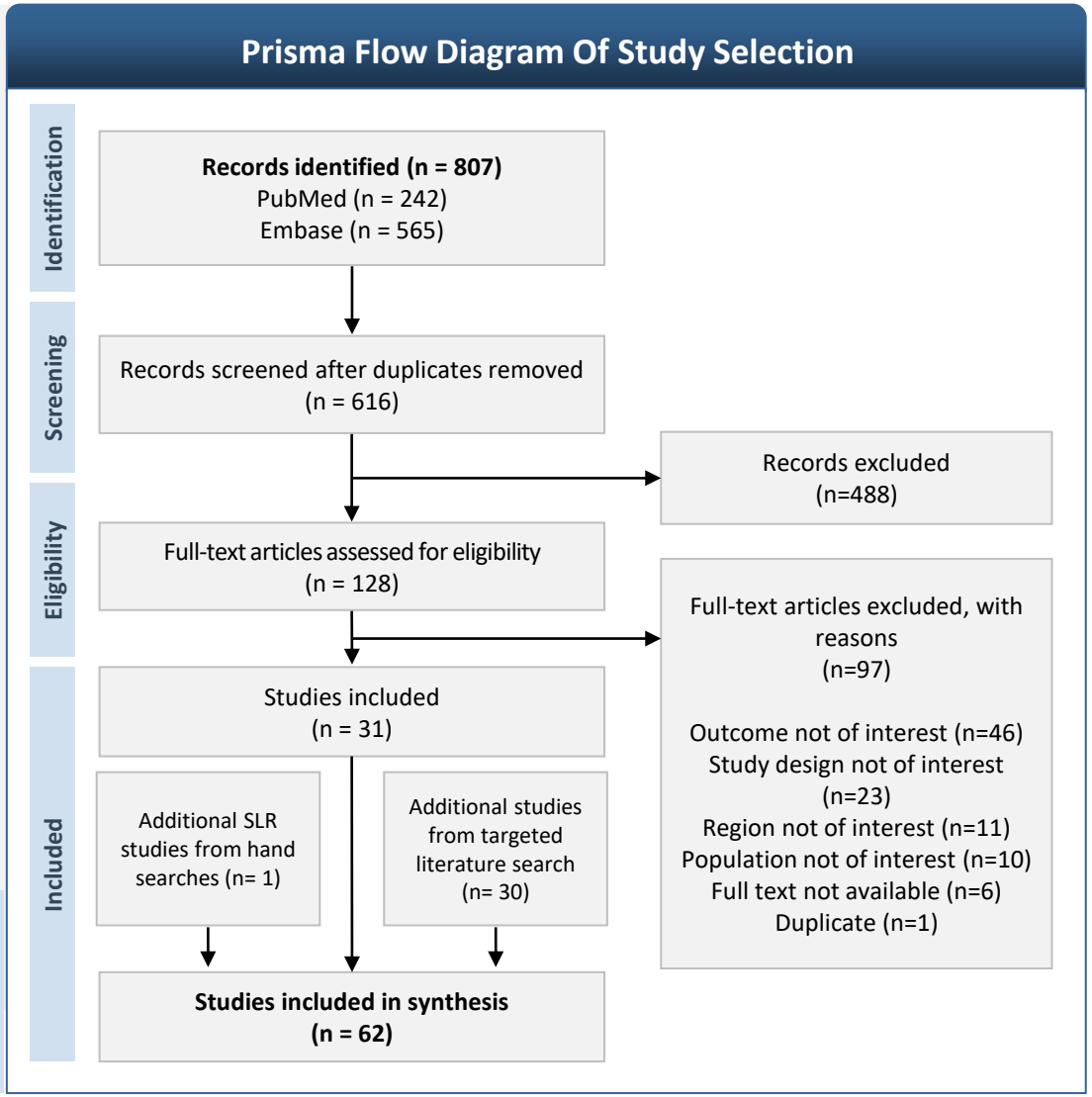
- This study aimed to synthesize published literature on the clinical, societal, and economic value of RDTs for infectious diseases across Asia, Africa, and Latin America.

1. Vashist SK. Point-of-Care Diagnostics: Recent Advances and Trends. Biosensors (Basel). 2017;7(4):62. Published 2017 Dec 18. doi:10.3390/bios7040062
2. Michaud CM. Global Burden of Infectious Diseases. Encyclopedia of Microbiology. 2009;444-454. doi:10.1016/B978-012373944-5.00185-1

Methods

- This systematic literature review (SLR) was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[3]
- PubMed and Embase were used to identify publications dated 2017 to 2021 and limited to English-language and human studies.
- This SLR was supplemented by a targeted literature search (TLR) and hand searches to evaluate guidelines and recommendations for RDTs from non-governmental organizations or other bodies (e.g., WHO).
- Study eligibility criteria included testing for 10 infectious diseases, clinical, economic, and societal impact outcomes, and study designs including randomized trials, observational studies, and economic models (use the QR code for full study eligibility criteria).

Please access the QR code for detailed data tables and full reference list



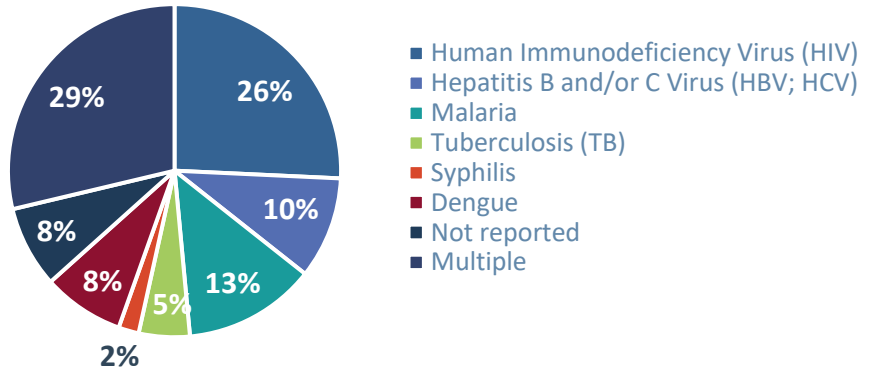
3. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4:1

Results

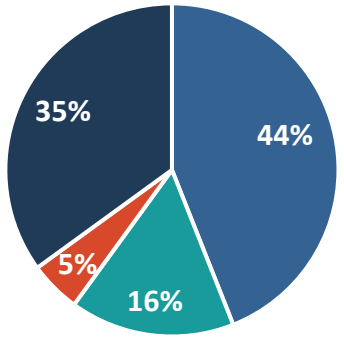
- Source Type:
  - Of the 62 papers included, 68% were academic papers
  - 32% were non-peer reviewed papers
- Diseases covered:
  - HIV is the most research disease (26% of articles), followed by malaria (13%) and hepatitis B and/C virus (10%).
  - 29% of articles covered multiple diseases and 8% were not disease-focused.
- Geographical coverage:
  - Almost half of the studies originated from Africa (44% of articles), followed by Asia Pacific (16%).
  - 35% of articles were global or covered multiple regions.

Overall Study Characteristics

Diseases Covered

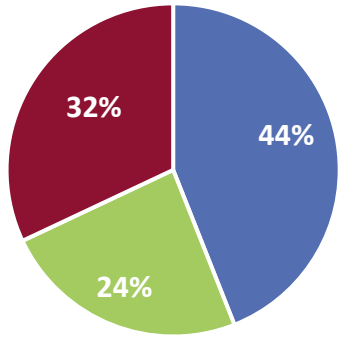


Geographical Coverage



Africa
Asia Pacific
South America
Global/Multiple Regions

Outcome Types



Clinical Impact
Economic Impact
Societal Impact

Percentages may not add up to 100% due to overlap across studies.

Results

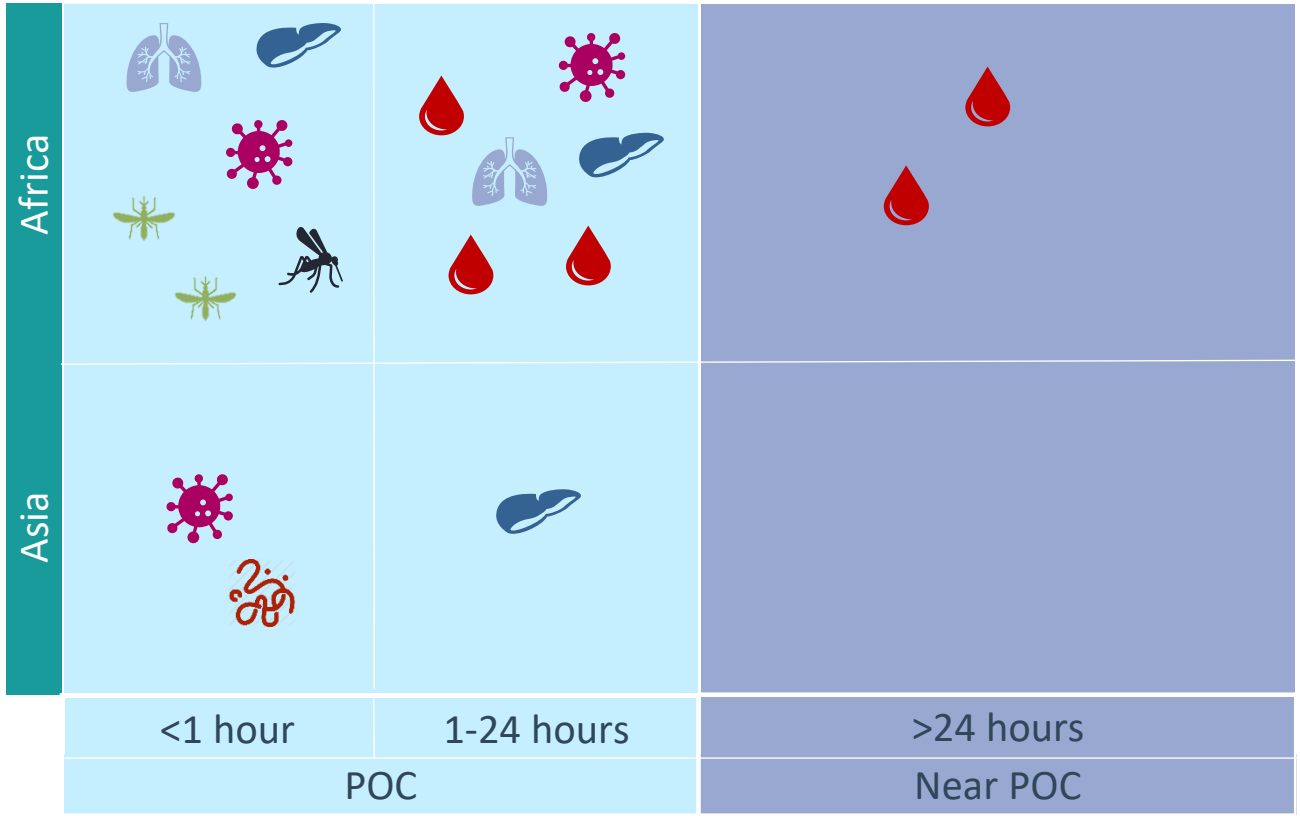
RDTs Reduce Turnaround Time → **Faster Time to Diagnosis & Increased Diagnosis Rate** → **Reduced Time to Appropriate Treatment** → **Improved Patient Clinical Outcomes** → **Economic Cost Offsets**

RDTs allow for more immediate diagnosis and treatment initiation for patients, which can lead to improved clinical outcomes and subsequent cost offsets

Results: **RDTs Reduce Turnaround Time for Results**

RDTs Reduce Turnaround Time → Faster Time to Diagnosis & Increased Diagnosis Rate → Reduced Time to Appropriate Treatment → Improved Patient Clinical Outcomes → Economic Cost Offsets

RDT Turnaround Times Across Studies (n=17)[4-6,9,11,15,17,18,20,23,25,26,29,31,34,36,40]



Disease Areas

- HIV
- Hepatitis B/C Virus
- Malaria
- Tuberculosis (TB)
- Syphilis
- Dengue
- Multiple

Near POC refers to a portable device easily carried around by healthcare workers for individual, immediate diagnostic testing. Some studies reported "same-day" results and were categorized under 1-24 hours.

Please see Appendix for full reference list

Results: **Rapid Turnaround Time Facilitates a Faster Diagnosis**

RDTs Reduce Turnaround Time | **Faster Time to Diagnosis & Increased Diagnosis Rate** | Reduced Time to Appropriate Treatment | Improved Patient Clinical Outcomes | Economic Cost Offsets

In total, 13 articles reported reduced time to diagnosis. Rapid turnaround time of RDTs positively impacts clinical management, including triage and diagnosis.[4-6,9,15,17,18,20,26,29,34,36,40]

Boeke et al, 2021[5]

Measure	N	Median (IQR)
Time to return results to the clinic (Near-POC)	3,446 Patients	**1 Day** (0-1)
Time to return results to the clinic (Centralized)	9,734 Patients	**35 Days** (20-48)

Time from sample collection to return of results to the clinic according to test location (near-POC or centralized lab)[5]

> *Febrile patients were liberally screened using the kit even if dengue fever was not high on the list of differential diagnoses. Doctors described that patients with symptoms not typically associated with dengue fever sometimes had positive blood test results.*
>
> **– Commentary on increased diagnosis rates from dengue RDT testing[26]**

Healthcare workers can perform more tests in a single day, and potentially screen a larger number of patients (e.g., patients who might not be initially presenting for the disease), increasing the overall diagnosis rate

Please see Appendix for full reference list

Results: **Faster Diagnosis Results in More Rapid Treatment**

RDTs Reduce Turnaround Time → Faster Time to Diagnosis & Increased Diagnosis Rate → **Reduced Time to Appropriate Treatment** → Improved Patient Clinical Outcomes → Economic Cost Offsets

Significant Reduction in Time to Appropriate Treatment

Source	Disease	Countries	Outcome Description	Outcomes/Data
Chibwesha et al, 2021[6]	HIV	Zambia	Median days to antiretroviral (ART) treatment (IQR)	RDT: **0 days** (0-1.5) Core Lab: **36 days** (28-47)
Lessels et al, 2017[11]	TB	South Africa	Percentage of patients starting TB treatment within 60 days	RDT: **71.6%** Core Lab: **6.5%**
Sacks et al, 2020[20]	HIV	Zimbabwe	Time from sample collection to ART initiation	RDT: **1.7 days** Core Lab: **67.8 days** (mean difference = 56 days)
Shiha et al, 2020[23]	HCV	Egypt	Hours from RDT to treatment initiation	**3 hours**
Draper et al, 2021[7]	HCV	Myanmar	Median days after first visit to HCV treatment initiation (IQR)	**3 days** (2-5)

Median difference of over a month

Median difference of ~2 months

> A qualitative study assessing South African healthcare workers' perspectives on rapid CD4 tests described the consensus that RDTs are ideal for use in resource-limited settings because they can lead to **immediate treatment decisions**[22]
>
> *CD4 count results could be relayed to the patient immediately and decisions about follow-up treatment be made there and then. Undoubtedly, participants saw this as the greatest strength of the test.*
>
> **– Commentary**[22]

In total, 14 articles report on time to treatment. **Patients can begin treatment quickly after obtaining results, usually on the same day or within two to three days**[6,7,9,11,12,15,17,20,22,23,29,34,35,42]

Please see Appendix for full reference list

Results: **Patients Have Improved Clinical Outcomes**

RDTs Reduce Turnaround Time → Faster Time to Diagnosis & Increased Diagnosis Rate → Reduced Time to Appropriate Treatment → **Improved Patient Clinical Outcomes** → Economic Cost Offsets

Two studies **demonstrated improved patient clinical outcomes**, including reduced incidence of cirrhosis and liver-related deaths[6,34]

Source, Disease, Country	Outcome Description	Outcomes/Data
Chibwesha et al, 2021[6] HIV, Zambia	Relative risk (RR) of being alive and in-care; RDT vs. Core Lab	1.2 (95% CI: 0.85-1.7)
Markby et al, 2021[34] HCV, India	Reduction in 30-year cumulative incidence of decompensated cirrhosis	110 per 100,000
	Reduction in 30-year cumulative incidence of hepatocellular carcinoma	60 per 100,000
	Reduction in 30-year cumulative incidence of liver related deaths	110 per 100,000

20% more likely to be alive and in-care

Substantial reduction in incidence of serious complications and death

Please see Appendix for full reference list

Results: **Economic Value of RDTs**

RDTs Reduce Turnaround Time → Faster Time to Diagnosis & Increased Diagnosis Rate → Reduced Time to Appropriate Treatment → Improved Patient Clinical Outcomes → **Economic Cost Offsets**

Efficient tests reduce time and burden on patients and healthcare workers, ultimately improving use of healthcare resources and potential cost savings[8,22,24,34,37]

Sohn et al, 2019[24]

Costs savings of decentralized testing vs. centralized testing over 10 years for tuberculosis	Median
Per 20 million people	**$338,000**
Per disability-adjusted life year averted	**$3,161**

Decentralization of infectious disease testing is likely to be **cost-saving or cost-effective** in most settings, optimizing the resources available in resource-limited settings[24]

Fast turnaround time of RDTs resulted in **~75% reduction in unnecessary antimalarial prescriptions**, saving costs for patients and clinics[37]

Delivery of RDTs and all hepatitis C services at a single site resulted in **more quality-adjusted life years and lower costs** than other strategies[34]

RDTs may reduce the need to conduct additional verification testing, leading to **potential cost savings[8]**

Please see Appendix for full reference list

Results: **Societal Value of RDTs**

Healthcare Worker Perspective

- **Improved ease to obtain results:** >80% of patients obtained a valid test result[16,27] with high (>90%) usability index scores for self-tests across multiple diseases[14]
- **Increased patient comprehension:** >90% of patients correctly interpreted results[14]
- **Enhanced workflow efficiency:** Results can be relayed to patients immediately and treatment decisions can be made right away, improving continuity of care[22]

Patient Perspective

- **Increased accessibility to testing and self-testing:** Preference for HIV self-testing over other technologies was higher among those never tested than prior testers[28]
- **Reduced travel time:** RDTs can reduce time spent traveling[4,12] and reduce loss to follow-up up to 64% thanks to same-day results[42]
- **Improved perception of privacy:** Over a third of patients were concerned about disclosing intimate personal information to a provider[28]
- **Reduced risk of stigma:** 21-31% of patients fear gender identity/sexual orientation-related stigma related to HIV testing[28]

Results: **Effective Rapid Diagnostic Device Attributes Identified in TLR/SLR Sources**

Attributes Identified	Citation
Easy to use	4,14,16,19,22,27,31,45-47,49,51-54,56
Accuracy (Sensitivity & Specificity)	46,47,49,51,52,54,57,59
Turnaround time (Speed)	14,22,46,49,53,54,57
No power supply/electricity requirement	15,17,22,27,28,54
Affordability	24,54
Portability	24,28,45,46
Storage (shelf-life and temperature)	46,47,49,52,54,56
High quality control standards	45,46,47,51

Please see Appendix for full reference list

Conclusions

- Several studies across multiple infectious diseases and various emerging markets have demonstrated that the **rapid turnaround time** of RDTs leads to **faster diagnosis and time to appropriate treatment** compared to central lab testing
- Existing literature has demonstrated **improved patient clinical outcomes**, including **survival benefits**.
- The improved turnaround time and accessibility of RDTs in decentralized settings allow for **improved use of healthcare resources and potential cost savings or cost-effectiveness**
- In addition to clinical and economic improvements, RDTs can ensure **patient privacy and reduced fear of stigma** with home and **self-testing**
- RDTs are easy to use and preferred by providers due to **workflow efficiencies, reduced training required, and improved patient understanding of results.**
- **Further published work is needed** to translate existing evidence into longitudinal, population-level studies to determine the **economic impact of RDT implementation** and the potential to reduce infectious disease progression

Please access the QR code for detailed data tables and full reference list

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Study Eligibility Criteria

Parameter	Inclusion Criteria	Exclusion Criteria
Population	Patients that are tested for tuberculosis, influenza, RSV, hepatitis B or C virus, HIV/AIDS, malaria, syphilis, COVID-19 or dengue fever	Any indication not listed in inclusion criteria
Intervention/Comparator	N/A	N/A
Outcomes	• Clinical Impact (e.g., improved screening, improved diagnosis, improved monitoring, improved time to initiation of therapy, improved patient outcomes, mortality, morbidity) • Economic Impact (e.g., healthcare resource utilization, cost of management, cost of screening, diagnosis and monitoring, economic modelling, economic analysis, cost savings) • Societal Impact (convenience, access for rural populations, patient quality of life, limiting disease expansion)	• Any impact not noted in inclusion criteria • Reports accuracy outcomes only (sensitivity, specificity, accuracy, etc.)
Study Design	• Randomized controlled trials or non-randomized clinical trials evaluating treatments • Observational studies – prospective, retrospective, longitudinal, or cross-sectional • Economic models or analyses- budget impact or cost-effectiveness models, healthcare cost and resource utilization studies	• Editorials • Commentaries • Guidelines* • Genetic studies • Case reports/series* • Animal models • Narrative reviews • Other published SLRs* • Protocols
Geographical Limits	• Asia Pacific • Africa • Latin America • Other emerging markets including but not limited to Middle East, Eastern Europe, Australia	All regions not listed in inclusion criteria
Database Limits	• Human studies • Abstracts available • English Language only	N/A
Temporal Limits	Original research published from 2017 onward	• Original research prior to 2017 • Records with no abstracts

Time to Results/Diagnosis

Source	Disease Area	Countries	Study Design	Sample Size	Outcome Description	Endpoints/Outcomes/Data
Wang et al, 2018	HIV / Syphilis	China	Prospective	1,828	Percentage of patients with results within 30 min - RDT Percentage of patients with same day results	55% 98%
Bianchi et al, 2020	HIV	Africa	Prospective	175	Turnaround time of POCT	Within 2 hours
Tan et al, 2017	Dengue	Singapore	Focus Groups	21	Turnaround time of POCT	20 minutes
Gupta et al, 2020	HCV	India	Feasibility	38,853	Turnaround time for confirmatory testing	Median: 1 day (IQR: 0-2 days)
Sacks et al, 2020	HIV	Kenya and Zimbabwe	RCT	9,539 infants	Proportion of EID results returned to caregiver by 12 weeks of age Percentage lab-based EID vs. RDT EID	76.0% vs. 99.3% Likelihood ratio = 1.29 (IQR: 1.27 – 1.3)
Boeke et al, 2021	HIV	Cameroon, Democratic Republic of Congo, Kenya, Malawi, Senegal, Tanzania and Zimbabwe	Retrospective	6,795 tests near-POC 17,614 centralized lab	Median time from sample collection to return of results to patient Near POC vs. Centralized Lab	6 vs. 68 days Effect size: −32.2% (95% CI: −41.0% to −23.4%)
Chibwesha et al, 2021	HIV	Zambia	RCT	4,000 infants	Proportion of patients receiving same-day RDT results	99.99%
Markby et al, 2021	HCV	India	Prospective	37,425	Time between viral load testing to return of results to patients Hospital Arm vs. Clinic Arm vs. Camp Arm	Hospital Arm: 0 Days (IQR: 0-1) Clinic Arm: 1 day (IQR: 1-2) Camp Arm: 11 days (IQR: 2-13)
Palmer et al, 2020	Malaria	Ghana	Cross-sectional	9 focus group discussions, 11 interviews	Time to results commentary	Malaria POCT: Between 2 and 45 minutes Anemia POCT: 5 and 15 minutes
Marks et al, 2018	Syphilis	Solomon Islands	Cross-sectional	20	Time to results commentary	15 minutes [for POCT] is a short time compared to other tests where the antenatal mothers might have to walk 3,4,5 hours to reach a facility
Mwaura et al, 2021	TB	Uganda, Kenya, and South Africa	Cross-sectional	15	Time to results commentary	25 minutes
McMorrow et al, 2011	Malaria	Africa	Secondary Research	NR	Time to results commentary	15-20 minutes
Mtapuri-Zinyowera et al, 2010	HIV	Zimbabwe	Cross-sectional	165	Time to results commentary	By producing same-day results, POC CD4 facilitates immediate decision-making, patient management and referral and may help improve patient care and retention

CI – confidence interval; EID – early infant diagnosis; HCV – hepatitis C virus; HIV - human immunodeficiency virus; IQR - interquartile range; NR – not reported; POC – point-of-care; POCT – point-of-care test; RDT – rapid diagnostic test; RCT – randomized control trial; TB - tuberculosis

Time to Treatment

Source	Disease Area	Countries	Study Design	Sample Size	Outcome Description	Endpoints/Outcomes/Data
Lessells et al, 2017	TB	South Africa	RCT	1,297	Percentage of patients starting TB treatment within 60 days due to RDT vs. core lab vs. clinical or radiological grounds Proportions of culture-positive participants initiated on appropriate TB treatment within 30 days of enrollment with RDT vs. core lab	RDT: 71.6% Core Lab: 6.5% Clinical / Radiological Grounds: 20.9% RDT: 79.5% Core Lab: 76.5% (Odds ratio=1.13)
Chibwesha et al, 2021	HIV	Zambia	RCT	4,000 infants	Time to antiretroviral treatment initiation (Days) at POC vs Core lab	0 vs. 36 days
Gupta et al, 2020	HCV	India	Feasibility	38,853	Turnaround time from confirmed test to treatment initiation (Days)	Median: 8.5 days (IQR: 4-20 days)
Sacks et al, 2020	HIV	Kenya and Zimbabwe	RCT	9,359 infants	Time from sample collection to ART initiation with RDT vs. core lab Proportion of HIV-infected infants initiated on ART within 60 days with RDT vs. core lab	Kenya: RDT: 4.1 days, Core Lab: 26.2 days (mean difference=17.01) Zimbabwe: RDT: 1.7 days, Core Lab: 67.8 days (mean difference=56.00) Kenya: RDT: 100%, Core Lab: 91.7% (likelihood ratio=1.09) p=0.095 Zimbabwe: RDT: 79.6%, Core Lab: 43.1% (likelihood ratio=1.81) p<0.001
Shiha et al, 2020	HBV, HCV	Egypt	Feasibility	3,663	Time from RDT to treatment initiation for HCV	3 hours
Draper et al, 2021	HCV	Myanmar	Feasibility	633	Time after first visit to HCV treatment initiation for those not requiring a specialist review vs. those requiring a specialist review	No Specialist Median: 3 days (IQR: 2-5 days) Specialist Median: 20 days (IQR: 15-36 days) P < 0.001
Markby et al, 2021	HCV	India	Prospective	37,425	Time between HCV serological test and treatment initiation for hospital vs. clinic vs. camp arms Time between results returned to participants and initiation of treatment for hospital vs. clinic vs. camp arms	Hospital Arm Median: 14 days Clinic Arm Median: 17.5 days Camp Arm Median: 31 days Hospital Arm Median: 8 days Clinic Arm Median: 8 days Camp Arm Median: 16 days
Kitojo et al, 2021	Malaria	Tanzania	Cross-sectional	143	Time to treatment commentary	The existing integration of point-of-care tests has allowed HCWs to provide the results and treatment quickly, saving clients' time as services are provided under one roof.
Mwaura et al, 2021	TB	Uganda, Kenya, and South Africa	Cross-sectional	15	Time to treatment commentary	Treatment can be initiated sooner than with existing technologies, reducing loss to follow-up and improving care
Macharia et al, 2020	HIV	Kenya	Cross-sectional	74	Time to treatment commentary	POC testing at the community level can further expand EID coverage by reaching infants born at home who do not utilize hospital-based care and fail to be linked to much needed HIV testing and treatment in a prompt manner
Scorgie et al, 2019	HIV	South Africa	Cross-sectional	8	Time to treatment commentary	CD4 count results could be relayed to the patient immediately and decisions about follow-up treatment be made there and then
Marks et al, 2018	Syphilis	Solomon Islands	Cross-sectional	20	Time to treatment commentary	There is potential value of reducing travel time to access tests and the ability to offer same day treatment and testing to patients
Manabe et al, 2012	HIV	RSA, Kenya, Uganda, Thailand, Senegal	Prospective	206	Percentage of patients lost to follow up between enrolment and antiretroviral therapy initiation Centralized lab vs. POCT	64% to 33% Adjusted OR: 0.27 95% CI: 0.21–0.26
Drain et al, 2014	Multiple	Resource-limited settings	Secondary Research	NR	Time to antiretroviral therapy initiation commentary	POC testing is used to accelerate treatment initiation in order to reduce mortality

CI – confidence interval; EID – early infant diagnosis; HBV – hepatitis B virus; HCV – hepatitis C virus; HIV - human immunodeficiency virus; IQR - interquartile range; NR – not reported; OR – odds ratio; POC – point-of-care; POCT – point-of-care test; RDT – rapid diagnostic test; RCT – randomized control trial; TB - tuberculosis

Effective Rapid Diagnostic Device Attributes Identified in TLR/SLR Sources

Value Aspect	Recommendation	Source(s)
Accuracy (sensitivity and specificity)	• Low rates of false negative and false positive results • The ideal scenario is to approach those of laboratory-based assays wherever possible • Sensitivity: 95% for smear-positive, culture-positive patients; 60-80% for smear negative, culture positive patients • Specificity: 95% compared to culture	WHO / FIND / CDC (2018) WHO / FIND (2013) WHO - Global Malaria Program (2011) WHO / TDR (2004) Land K. (2019) The Academy of Medical Sciences / IAP (2016) Batz H.G. (2011) UNICEF / UNDP / World Bank / WHO (2004)
Turnaround time (speed)	• Results can be read directly, within 30m of the time, without calibration or calculations	WHO / TDR (2004) Land K. (2019) The Academy of Medical Sciences / IAP (2016) USAID (2013) Batz H.G. (2011) Majam (2019) Scorgie (2019) UNICEF / UNDP / World Bank / WHO (2004)
Portability	• Fits in a backpack	Vasconcelos (2021) Sohn (2019) Batz H.G. (2011) WHO (1999)
No power supply requirement	• Can be operated in small portable devices that use solar or battery power • Equipment-free	Bianchi (2020) Marks (2021) Mwaura (2021) Scorgie (2019) Tonen-Wolyec (2021) Vasconcelos (2021) UNICEF / UNDP / World Bank / WHO (2004)
Affordability	• Accessible to end-users • Affordable by those at risk of infection	Land K. (2019) Sohn (2019) UNICEF / UNDP / World Bank / WHO (2004)
Usability (training requirement and ease of use)	• Simple to perform, uses non-invasive specimens • After initial addition of specimen and reagents, the test kit should require only minimal operator intervention or procedural steps during the analysis, the test kit must use direct, unprocessed specimens • One day maximum of training required; can be used by any healthcare worker • Tests should be easy to perform in 2–3 steps and require minimal user training with no prior knowledge	WHO / FIND / CDC (2018) WHO / FIND (2013) WHO - Global Malaria Program (2011) WHO / TDR (2004) Land K. (2019) USAID (2013) Batz H.G. (2011) UNICEF / UNDP / World Bank / WHO (2010) WHO (1999) Prah (2019) Bianchi (2020) Majam (2021) Morrison (2021) Scorgie (2019) Tonen-Wolyec (2021) Young (2019) UNICEF / UNDP / World Bank / WHO (2004)
Storage (shelf-life and temperature)	• Can operate at different temperatures (very high and very low), depending on conditions of intended use • Shelf life of 24 months, including reagents; stable at >30 degrees and in high humidity situation • Ability of the test to withstand the supply chain (temperature, humidity, time delays, mechanical stresses) without requiring additional transport and storage conditions (e.g., refrigeration)	WHO / FIND / CDC (2018) WHO - Global Malaria Program (2011) WHO / TDR (2004) USAID (2013) Batz H.G. (2011) UNICEF / UNDP / World Bank / WHO (2010) UNICEF / UNDP / World Bank / WHO (2004)
Quality	• Quality control of blood safety, instruction quality, number of steps, time to results, blood transfer device, format and kit completeness; • Manufacturer must be certified by ISO 13485:2003	WHO / FIND (2013) WHO - Global Malaria Program (2011) Batz H.G. (2011)