Point-of-care testing as a solution for timely early infant diagnosis

Ravikiran Bhairavabhotla[1]

[1]Centers for Disease Control and Prevention

01 Rationale

Despite remarkable progress in prevention of mother-to-child transmission of HIV (PMTCT), 160,000 children were newly infected with HIV in 2016.[1] Less than half of HIV exposed infants (HEI) received early infant diagnosis (EID) within 6 weeks of life, a major challenge for early antiretroviral therapy (ART) for HIV-positive infants.[2] Although introduction of dried blood spot (DBS) has increased EID access, conventional laboratory networks, have relatively long (22-60 days) turnaround time (TAT), resulting in low proportions of results returned, and missed opportunities for ART initiation.[3] The WHO conditionally recommends introduction of point-of-care (POC)/ near-POC nucleic acid testing (NAT) for EID. Recent encouraging evidence for POC/ near-POC EID warrants consideration of rapid adoption and strategic scale-up of this solution complementing the existing laboratory network.[2, 4-6]

02 Barriers and facilitators of implementation

Barriers

- Low coverage of EID testing by 2 months
- Poor access to sites/facilities with EID services
- Failure to implement systematic screening for infant exposure status
- Poor EID testing uptake in high-yield entry points, like pediatric inpatient wards
- Long TAT for EID result returned to caregivers
- Poor linkages of HEI and HIV-infected infants to ART services
- Lack of national quality assurance for conventional and decentralized EID services

Facilitators

- Updated national policies based on WHO recommendations mean POC tests may be used at birth and in children up to 18 months of age
- Simplified and integrated pediatric HIV-related services: EID should be provided in the community/facility, and where possible integrated into broader child health care services
- Strengthened tiered national laboratory networks for standardized testing, supervision, training, mentorship, quality assurance, supply chain, maintenance and results documentation
- Strategic introduction of POC EID complementary to conventional laboratory within national systems. Two CE marked POC EID prequalified by the WHO for EID — Alere™q HIV 1/2 Detect and Xpert® HIV-1 Qual — have the potential for same day diagnosis and treatment initiation

- Engagement of relevant national stakeholders in technical working groups (TWG) and ensuring comprehensive tools, guidance and monitoring are deployed to leverage technological and programmatic innovations

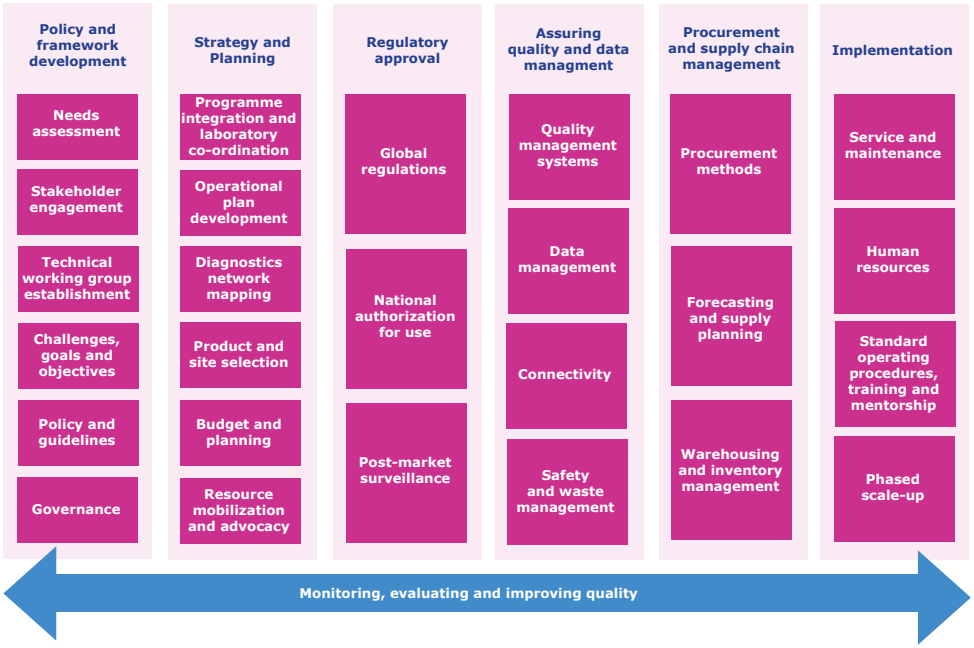
03 Policy and legal considerations

National policies, guidelines and testing algorithms should be updated to include POC testing for EID. National regulatory agencies are encouraged to prioritize registrations and approvals to support and adopt POC EID. Existing evidence is sufficient to warrant adoption of POC testing, which should not be delayed.

04 Steps for scale-up

In April 2018, global health partners (ASLM, CDC, CHAI, EGPAF, UNICEF, Unitaid and WHO) launched Key Considerations for Introducing New HIV Point-of-Care Diagnostic Technologies in National Health Systems (KCD).[7] As displayed in Figure 1, this document describes key steps for countries to consider for the strategic and sustainable introduction of POC diagnostics within their national health systems.

Figure 1: Framework of key considerations for introducing HIV POC diagnostic technologies in national health systems



To improve EID in national programs, countries should:

1. Establish and regularly engage key stakeholders in TWG to plan, develop and strengthen programs through tiered national laboratory networks and strategic placement of POC EID.
2. Orchestrate procurement and supply chain of consumables nationally, based on unmet need and demand for EID. Enable all-inclusive pricing/reagent rental or other models with transparent, strong and reliable service level agreements.
3. Map laboratory instruments and POC devices for placement and optimization of testing networks. Considerations for placement of POC devices include, but not limited to, the following:
   - o Programs/sites with a high volume of potentially HIV-infected infants, for example tuberculosis (TB) clinics, pediatric inpatient wards and malnutrition clinics
   - o Geographic areas with high HIV prevalence among pregnant/breastfeeding women
   - o Sites with low PMTCT coverage

- Sites in remote locations where challenges exist with sample transportation
- Sites with long (>3 weeks) TAT of existing laboratory systems

4. Train and certify laboratory technologists and POC testers in competencies for performing required tests. POC sites need supportive supervision and may require additional resources, including equipment, reagents, services and maintenance.
5. Engage in continuous quality improvement (CQI) for laboratories and POC testing sites, through stepwise laboratory quality improvement processes towards accreditation (SLIPTA), stepwise process for improving quality of POC tests (SPI-POCT), checklists and scorecards (viral load and infant virologic testing) to allow identification of gaps and monitor improvements.
6. Harmonize CQI with specimen referral and results return systems to ensure quality assured testing.
7. Ensure POC testing data is captured nationally in laboratory information systems (LIS).
8. Enable site level support. POC EID testing may have higher error rates than laboratory-based testing, although most errors can be resolved with repeat testing. Put in place routine preventative equipment maintenance (PEM) and curative maintenance either through contracts or reagent rental agreements to avoid disruption of services.
9. Implement suitable biosafety and waste management practices in accordance with national policy to minimize exposure to biohazardous materials.
10. Strengthen linkage to care to ensure early treatment initiation of HIV positive infants diagnosed.
11. Implement management and oversight from national to site/facility level for key performance indicators across products, programs and impact of solution.

05 Case example of successful implementation

Kenya has developed two national documents to support implementation of POC testing:

- A roadmap to implement POC testing in HIV care and treatment programs.[8]
- Utilization of multi-disease testing platforms for optimizing early infant diagnosis in Kenya[9]

In Mozambique, a cluster randomised trial demonstrated that POC EID enabled rapid diagnosis and treatment initiation, improved retention, significantly reduced TAT and reduced loss to follow-up.[4]

In Zimbabwe, a study with GeneXpert platform confirmed the feasibility of integrated for multi-disease testing (EID, TB and viral load) and improved access to testing for priority populations.[6]

In Malawi, POC EID resulted in significantly improved TAT and ART initiation rates.[9] A multi-country evaluation of routine use of POC EID revealed significantly improved results return and ART initiation as compared to conventional EID.[10]

06 Tools to support implementation

HIV Point-of-Care Diagnostics Toolkit - An extension of the KCD, this toolkit contains various practical tools and guidance to support countries. http://childrenandaids.org/poc-toolkit-page

U.S. President's Emergency Plan for AIDS Relief (PEPFAR) 2018 Country Operational Plan Guidance - Succinctly outlines the considerations for introduction of POC/near-POC in testing strategies for achieving high testing coverage and early initiation of ART for HEI. https://www.pepfar.gov/documents/organization/276459.pdf

07 Monitoring

Amend existing registers, monitoring and evaluation tools and systems to integrate and capture POC/near-POC testing activities. Ensure good device internet connectivity for reporting results as well as monitoring the POC NAT fleet. Robust and prospective post-market surveillance for performance of POC/near POC devices is encouraged.

08 Conclusion

For over a decade, conventional laboratory-based technologies have been the backbone of EID, and many countries are missing the opportunity to use their laboratory network effectively. Ending pediatiric AIDS will require complementing existing laboratory network with new technological and programmatic strategies to overcome persistent barriers. We now have evidence and tools to support the strategic introduction of POC EID as part of a tiered national laboratory network. POC EID can simplify and significantly improve timely identification, early treatment initiation, reduce loss-to-follow-up and enhance retention. Program managers are encouraged to derive a national framework and guidance for POC EID at the respective TWGs based on the resources with steps summarized.

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Disclaimer: The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the funding agencies.

This brief has been supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control and Prevention.

For more information:

Child Survival WORKING GROUP

daniella@teampata.org or nputta@unicef.org

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