ACCELERATING ACCESS TO POINT-OF-CARE VIRAL LOAD TESTING FOR PREGNANT AND BREASTFEEDING WOMEN LIVING WITH HIV

Increased access to ART and treatment monitoring for pregnant and breastfeeding women living with HIV is a priority for promoting health during the pregnancy and post-partum periods, and to minimize the risk of vertical transmission of HIV to their infants. Evidence shows that maternal viral load (VL) is closely associated with the risk of vertical transmission,[1,2,3,4] and the World Health Organization (WHO) therefore recommends urgently initiating HIV-positive women on antiretroviral therapy (ART) in order to reduce maternal VL.[5] The impact of the successful scale up of prevention of mother-to-child transmission (PMTCT) programs to increase access to treatment for pregnant women living with HIV has been significant, resulting in more than 1.6 million new child infections averted since 2010.[6]

Although access to VL testing has increased in many countries to allow for better monitoring of all patients on ART,[7] laboratory-based conventional VL systems often face long result turnaround times,[8,9,10] and low result return rates, making it difficult to take timely clinical action when elevated VL is detected.[11,12] Timely VL monitoring is particularly important for pregnant and breastfeeding women, as there is a limited window of time to identify women who have elevated VL (>1,000 copies/ml) and implement fast-acting interventions to promote re-suppression and prevent transmission. Interventions such as initiating enhanced adherence counseling, switching to an optimal ART regimen that rapidly reduces maternal VL, or providing enhanced infant prophylaxis can all reduce the risk of transmission in the context of elevated maternal VL.[13,14]

IMPACT
OF PMTCT SCALE-UP

DECREASE
IN ANNUAL NEW INFANT INFECTIONS FROM
450,000
IN 2000 TO
160,000 IN 2018

INCREASE
IN PMTCT ENROLLMENT FROM
44%
IN 2010 TO
82%
IN 2018

1.6 MILLION +
NEW CHILD INFECTIONS
AVERTED

Source: UNAIDS, July 2019

VL policies are not designed for pregnant and breastfeeding women

In many countries, the current algorithm for VL monitoring for all people living with HIV (PLHIV) on ART is to test at 6 months and 12 months post ART initiation, then annually thereafter, consistent with WHO recommendations.[15] For pregnant and breastfeeding women, this timeline may be inadequate as it may not align with the window of transmission risk during pregnancy and breastfeeding.[16] A simulation study projected that 69 percent of pregnant women will not receive a VL test if current WHO guidelines for VL monitoring are followed, with the first VL only performed after 6 months on ART.[17] Furthermore, current failure management protocols recommend three months of adherence counseling, followed by a second VL test to ascertain whether an elevated VL measurement is due to adherence challenges or drug resistance, prior to making a regimen switch decision. With result return times averaging 30 days,[18] women who are tested may not receive their VL result before delivery, and these protocols – which take at least 3-months to confirm treatment failure – may be inadequate to manage pregnant and breastfeeding women and maximize rates of viral suppression. The misalignment between the testing algorithm and duration of the infant exposure period, combined with weaknesses within VL testing systems that delay result availability, have resulted in low VL coverage for pregnant and breastfeeding women (below 50% in some countries) and low viral suppression rates at delivery and postpartum (which vary, but have been reported as low as 30%).[19,20,21,22]

In recognition that the WHO guidelines for VL monitoring do not reflect the unique needs of pregnant and breastfeeding women, some countries have adopted national guidelines with differentiated recommendations for providing VL during the pre- and post-partum exposure periods, including recommending earlier and/or more frequent VL monitoring [see Box 1]. VL monitoring guidelines tailored to pregnant and breastfeeding women include testing at the first antenatal care (ANC) visit regardless of when the last VL test was conducted, VL testing at three- or six-month intervals throughout pregnancy and breastfeeding (compared to annually), or a shorter time window between the first elevated VL result and follow up VL test (one month compared to three months). These modifications to the testing algorithm increase the likelihood that a woman with viremia during the infant exposure period will be identified promptly, and that action can be taken to reduce the risk of transmission.

Box 1. Country Highlights: Differentiated national guidelines for VL monitoring for pregnant and breastfeeding women

	Pregnant and breastfeeding women already on ART	Pregnant and breastfeeding women newly initiating ART	In the event of elevated VL
Kenya[27]	Obtain VL at first ANC visit irrespective of when prior VL was done, then every 6 months until cessation of breastfeeding	Obtain VL 3 months after treatment initiation, and then every 6 months until cessation of breastfeeding	• If VL > 1000: repeat VL after 3-months of intensified adherence support • If repeat VL >1000: Switch regimen • If repeat VL <1000 but detectable: consult regional or national TWG • If undetectable: Continue routine monitoring
South Africa[28]	Obtain VL at first ANC visit irrespective of when prior VL was done, then at months 3, 6,12,18, and 24 throughout pregnancy and breastfeeding.	Obtain VL 3 months after treatment initiation, and then every 6 months throughout pregnancy and breastfeeding.	• If VL < 400: 6 monthly VL and routine adherence support • If VL 400 – 1000: assess adherence, consider another VL within 6 months, repeat VL at 6 months • If VL > 1000: adherence counseling and follow up VL 1 month later • If follow up VL, under or greater than 1 log decrease, maintain current regimen • If VL result unchanged or less than 1 log drop, switch to 2L • If 2L switch, provide intensive adherence counseling to ensure rapid VL suppression
Zimbabwe[29,30]	Obtain VL at first ANC visit and review result within 2 weeks, then every 6 months throughout pregnancy and breastfeeding	Initiate on ART on the same day as first ANC visit and obtain VL 3 months after starting ART, repeat VL every 6 months throughout pregnancy and breastfeeding period.	• If VL > 1000: commence adherence counseling and repeat follow up VL after 1 month • If repeat VL > 1000: cpm prepare to switch regimen

Point-of-care viral load testing can address systemic challenges and support PMTCT efforts

Point-of-care (POC) VL, which allows testing to be conducted at or near the point of patient care, has the potential to increase access to VL testing, reduce result return time and increase result return rates for pregnant and breastfeeding women. In combination with improved testing algorithm recommendations tailored for pregnant and breastfeeding women, the use of POC VL testing could facilitate faster clinical action and time to viral re-suppression. For example, POC VL could allow same day result return and same-day start of adherence counseling, same-day return of results to confirm treatment failure, and same-day switching to an optimal treatment regimen. Currently, there are three POC VL platforms available for use: Cepheid GeneXpert, Abbott mPima and DRW Samba II.

Emerging data demonstrate the feasibility and impact of POC VL for improved patient management. POC VL was shown to improve rates of viral suppression and retention in care for PLHIV newly initiating ART in a high-volume clinic in South Africa by 13.9 percent and decreased the median time that VL results were communicated to the patient from 28 days to same day.[23] Similarly, pilots in Zimbabwe found that POC VL increased the proportion of results received by clients compared to referral-based VL, with 96 percent of clients with elevated VL receiving their result using POC VL compared to 48 percent of clients using centralized VL testing,[24] and decreased the median time to result receipt back to clients from 26 days to next day.[25] Although none of these studies were specific to pregnant and breastfeeding women, the outcomes of using POC VL are expected to be similar for this population, and in combination with timely counseling or regimen switch, is likely to reduce the risk of vertical transmission. In recognition of this potential impact, the PEPFAR 2019 Country Operational Plan Guidance endorsed the use of POC VL for pregnant and breastfeeding women [see Box 2]. Given the positive results experienced with POC VL in these early studies, consideration is being given to expand use of POC VL for other populations at high risk of viremia, such as pediatric and adolescent patients, and those with a history of elevated VL.

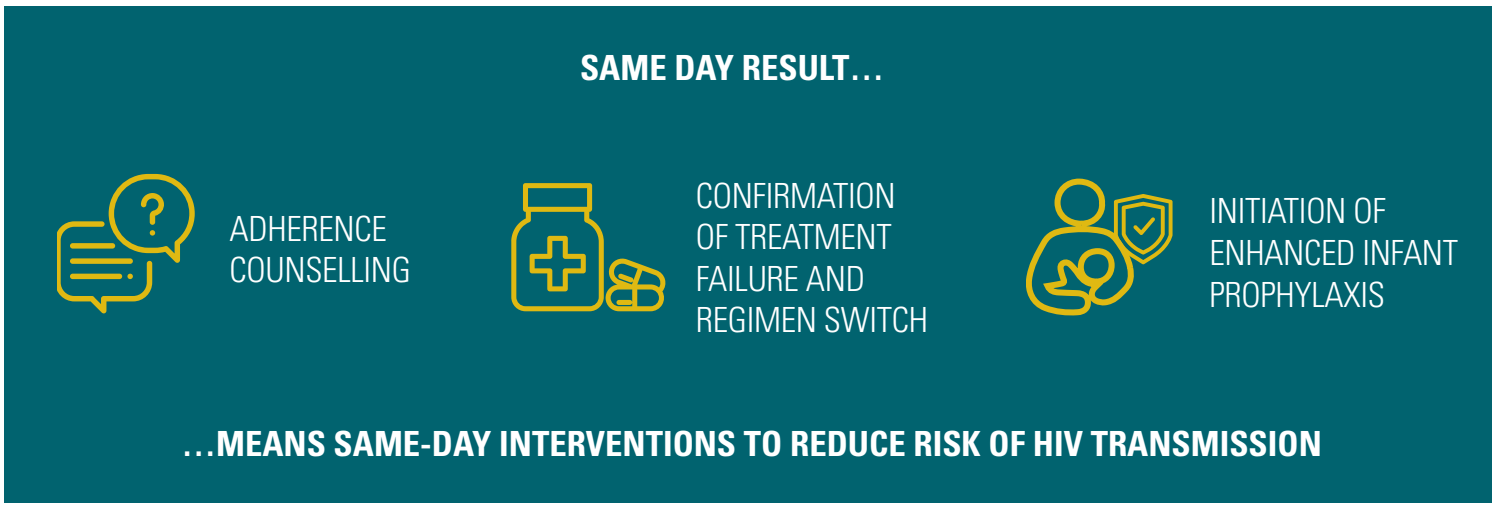
POC VL for pregnant and breastfeeding women is the future

Despite global success in reducing the number of new child infections and overall rate of vertical transmission over the last two decades, additional interventions are needed to promptly identify pregnant and breastfeeding women living with HIV, rapidly initiate them on effective treatment, retain them in care, and identify those with elevated VL to promote viral suppression to avert vertical transmission. Additional evidence is being generated to understand how POC VL can be used during the pregnancy and post-natal periods to ensure high rates of viral suppression at delivery and during breastfeeding.[26] Targeted use of POC VL, in combination with VL policies tailored to the specific needs of pregnant and breastfeeding women, has the potential to bolster PMTCT programs to achieve the elimination of vertical HIV transmission.

Box 2. PEPFAR recommendation on the use of POC VL for pregnant and breastfeeding women

PEFPAR's 2019 Country Operational Plan Guidance endorses the use of POC for pregnant and breastfeeding women:

"It is critical to ensure that diagnostic systems are in place for prompt identification of viremic women to promote re-suppression and avert vertical transmission and also to address elevated VL during pregnancy and breast-feeding. **By utilizing POC for viral load monitoring with pregnant women, there is the ability to provide an intensified prophylaxis regimen for exposed infants whose mothers have elevated viral load at delivery…in light of this, and to optimize time-sensitive VL monitoring among PBFW [pregnant and breastfeeding women], PEPFAR programs should plan to use POC for VL testing among PBFW only."**[31]



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References

1. Garcia PM, et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. N Engl J Med. 1999; 341(6):394–402.
2. Thea DM, et al. The effect of maternal viral load on the risk of perinatal transmission of HIV-1. New York City Perinatal HIV Transmission Collaborative Study Group. AIDS. 1997 Mar 15;11(4):437-44.
3. Tubiana R et al. Factors associated with mother-to-child transmission of HIV-1 despite a maternal viral load <500 copies/ml at delivery: a case-control study nested in the French perinatal cohort (EPF-ANRSCO1). Clinical Infectious Disease, 2010 Feb 15;50(4):585-96. doi: 10.1086/650005.
4. John GC, et al. Correlates of mother-to-child human immunodeficiency virus type 1 (HIV-1) transmission: association with maternal plasma HIV-1 RNA load, genital HIV-1 DNA shedding, and breast infections. J Infect Dis. 2001 Jan 15;183(2):206-212
5. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach, 2016. Pg. 120
6. UNAIDS, Global AIDS Update 2019. Available at: http://aidsinfo.unaids.org/
7. UNAIDS, 2018. Knowledge is power. Available at: https://www.unaids.org/sites/default/files/media_asset/jc2940_knowledge-is-power-report_en.pdf
8. Lecher S et al. Progress with Scale-Up of HIV Viral Load Monitoring - Seven Sub-Saharan African Countries, January 2015-June 2016. MMWR Morb Mortal Wkly Rep. 2016 Dec 2;65(47):1332-1335. doi: 10.15585/mmwr.mm6547a2.
9. Mwau M et al Scale-up of Kenya's national HIV viral load program: Findings and lessons learned. PLoS One. 2018 Jan 11;13(1):e0190659. doi: 10.1371/journal.pone.0190659. eCollection 2018
10. Minchella PA, et al. Specimen origin, type and testing laboratory are linked to longer turnaround times for HIV viral load testing in Malawi. PLoS One. 2017 Feb 24;12(2):e0173009. doi: 10.1371/journal.pone.0173009. eCollection 2017.
11. Awungafac G, et al. Viral load testing and the use of test results for clinical decision making for HIV treatment in Cameroon: An insight into the clinic-laboratory interface. PLoS One. 2018;13(6):e0198686
12. Etoori D, et al. Successes and challenges in optimizing the viral load cascade to improve antiretroviral therapy adherence and rationalize second-line switches in Swaziland. J Int AIDS Soc. 2018;21(10):e25194.
13. Katz IT et al. Factors Associated with Lack of Viral Suppression at Delivery among HAART-Naïve HIV-Positive Women in the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) P1025 Study. Ann Intern Med. 2015 January 20; 162(2): 90–99. doi:10.7326/M13-2005.
14. Myer L, et al. Differentiated models of care for postpartum women on antiretroviral therapy in Cape Town, South Africa: a cohort study. J Int AIDS Soc. 2017 Jul 21;20(Suppl 4):21636. doi: 10.7448/IAS.20.5.21636
15. WHO, 2016. Pg. 129
16. Myer L et al. Pregnant and breastfeeding women: A priority population for HIV viral load monitoring. PLoS Med 2017. https://doi.org/10.1371/journal.pmed.1002375
17. Lesosky M et al. Optimal timing of viral load monitoring during pregnancy to predict viraemia in HIV-infected women initiating ART in South Africa: a simulation study .Journal of the International AIDS Society 2017, 20(S7):e25000 http://onlinelibrary.wiley.com/doi/10.1002/jia2.25000/full
18. Lecher S et al. Progress with Scale-Up of HIV Viral Load Monitoring - Seven Sub-Saharan African Countries, January 2015-June 2016. MMWR Morb Mortal Wkly Rep. 2016 Dec 2;65(47):1332-1335. doi: 10.15585/mmwr.mm6547a2
19. Abougi LL et al. Achieving UNAIDS 90-90-90 targets for pregnant and postpartum women in sub-Saharan Africa: progress, gaps and research needs. J Virus Erad. 2018 Nov 15;4(Suppl 2):33-39
20. Sam-Agudu et al. The Impact of Structured Mentor Mother Programs on 6-Month Postpartum Retention and Viral Suppression among HIV-Positive Women in Rural Nigeria: A Prospective Paired Cohort Study. J Acquir Immune Defic Syndr. 2017 Jun 1;75 Suppl 2:S173-S181. doi: 10.1097/QAI.0000000000001346.
21. Swannet S et al. Journey towards universal viral load monitoring in Maputo, Mozambique: many gaps, but encouraging signs. Int Health. 2017 Jul 1;9(4):206-214. doi: 10.1093/inthealth/ihx021.
22. Akama E, et al. Retention and viral suppression of newly diagnosed and known HIV positive pregnant women on Option B+ in Western Kenya. AIDS Care. 2019 Mar;31(3):333-339. doi: 10.1080/09540121.2018.1524565.
23. Drain PK et al. Point-of-care viral load testing improves HIV viral suppression and retention in care. CROI 2019. http://www.croiconference.org/sessions/point-care-viral-load-testing-improves-hiv-viral-suppression-and-retention-care
24. Integrated TB-HIV testing on GeneXpert is feasible, enables increased device utilization and does not negatively impact TB service: Implementation experience in Malawi and Zimbabwe. Oral abstract: ASLM, 2018. http://aslm2018.org/wp-content/uploads/2018/12/ASLM2018abstractsLinks.pdf
25. Ndlovu Z et al. Multidisease testing for HIV and TB using the GeneXpert platform: A feasibility study in rural Zimbabwe. PLoS One 2018 Mar 2;13(3):e0193577. doi: 10.1371/journal.pone.0193577
26. CHAI and MOHCC in Zimbabwe, unpublished study; and RAPID-VL study in Uganda, clinicaltrials.gov ID: NCT03553693
27. Guidelines on the use of antiretroviral drugs for treating and preventing HIV in Kenya, 2018 Edition. National AIDS and STI Control Program, 2018.
28. National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults. April 2015. National Department of Health, South Africa.
29. Operational and Service Delivery Manual for the Prevention, Care and Treatment of HIV in Zimbabwe. AIDS and TB Programme, Ministry of Health and Child Care, Zimbabwe. February 2017.
30. Guidelines for Antiretroviral Therapy for the Prevention and Treatment of HIV in Zimbabwe, December 2016.
31. PEPFAR COP19 Guidance, p. 313. Available at: https://www.pepfar.gov/documents/organization/288160.pdf

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