Evaluation of guidelines for VL monitoring in pregnancy & breastfeeding: a simulation

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Background

- Raised maternal HIV viral load (VL) drives mother-to-child transmission (MTCT) *in utero*, intrapartum and postpartum and occurs frequently in HIV-infected pregnant and postpartum women.
- High levels of suboptimal antiretroviral (ART) adherence and disengagement from care have been widely documented among pregnant and postpartum women living with HIV globally.
- VL monitoring as part of routine care has entered low- and middle-income country (LMIC) national policies only recently.
- Intensified VL monitoring for pregnant and breastfeeding women has been proposed in guideline recommendations but not evaluated systematicially.

Guideline	Year	Continuing ART	Initiating ART
South Africa[1]	2015	1st ANC, then every 6m	3m, 6m post-ART, then every 6m
Malawi[2]	2016	Every 24m	6m post-ART, then every 24m
Kenya[3]	2016	1st ANC, then every 6m	6m post-ART, then every 6m
Zambia[4]	2018	1st ANC, then every 6m + test at 34w	6m post-ART, then every 6m + test at 34w
WHO[5]	2016	Every 12m + test at 34w	6m, 12m post-ART, then every 12m + test at 34w
US PHS[6]	2018	*As with initiating*	1st ANC, then every 1m (move to every 3m if VL <50 c/mL + test at 34w gestation

Table 1: Guidelines considered and schedule evaluated. ANC: antenatal care visit

Methods

- We developed a stochastic individual patient simulation of VL in pregnant and breastfeeding women, modelled weekly from conception through 2 years postpartum[7] with a population size of 10,000.
- The model was calibrated to parameters against data from studies of ART in pregnancy and breasfeeding (PROMISE, PROMOTE, MmaBana, MCHART)[8–11].
- We applied to the same simulated population different VL monitoring guidelines (Table 1), including adaptations for pregnant and breastfeeding women when stated and averaged over 10 independent runs for each parameter set.
- Baseline simulated population settings were that 50% of women initiated ART in pregnancy (median 22w gestation (IQR, 16-28)) and 50% were on ART prior to conception (70% $<$ 50c/mL at 1st antental care visit) with modelled ART adherence. Delivery was at median 38w (IQR, 37-40); and breastfeeding for a median duration of 40w (IQR, 29-49) (Table 2).
- Two additional scenarios are presented, holding all values the same except for setting either 20% or 80% of women to be initiating ART (Table 2).
- Guidelines were compared on coverage of VL testing in pregnancy & breastfeeding, proportion of elevated VL (eVL) successfully detected and the cumulative VL experienced by the time of detection.

	Percentage of women initiating ART in pregnancy		
	50%	20%	80%
% VL<1000 c/mL before delivery	85 (84.5, 85.2)	91.2 (91, 91.3)	78.2 (77.9, 78.5)
% eVL(≥1000) after VS	18.9 (18.6, 19.1)	10.6 (10.5, 10.9)	27.6 (27.4, 27.9)
% VL<50 c/mL before delivery	69 (68.5, 69.2)	83.8 (83.3, 83.9)	54.6 (54.2, 54.9)
% eVL(≥50) after VS	11.8 (11.6, 12)	7.3 (6.9, 7.4)	16.8 (16.6, 17)

Table 2: Selected characteristics of simulated population for each of three scenarios.

Guideline	# VL tests	Weeks to 1st VL test		% ≥ 1 VL AN	% ≥ 1 VL BF
		Initiating	Continuing		
South Africa	3 (2, 3)	13 (13, 18)	0 (0, 0)	82.8 (82.5, 83.1)	92.6 (90.9, 93.4)
Malawi	1 (1, 1)	31 (29, 33)	29 (14, 43)	13.8 (13.4, 14)	54.7 (54.3, 55)
Kenya	2 (2, 3)	31 (29, 33)	0 (0, 0)	56.3 (56, 56.8)	91.8 (90.7, 92.5)
Zambia	3 (3, 4)	14 (7, 20)	0 (0, 0)	97.8 (97.8, 97.9)	91.5 (90.5, 92)
WHO	2 (2, 3)	13 (7, 18)	10 (4, 16)	98 (97.8, 98)	80.1 (79.5, 80.9)
US PHS	6 (4, 7)	3 (2, 4)	0 (0, 0)	100 (100, 100)	37.5 (36.5, 37.9)

Table 3: Characteristics of simulation of guidelines based VL monitoring in pregnant and breastfeeding women for baseline parameters (50% inititiating ART during pregnancy). All values as median (IQR). AN: antenatal, BF: breastfeeding

Results

- Coverage of VL monitoring in pregnancy and breastfeeding varied widely by guidelines (Table 3).
- By 24m postpartum, 92% of women initiating ART achieved VL<50 c/mL, and 18% of these subsequently experienced transient or extended eVL >1000 c/mL.
- Specific recommendations for testing at either a fixed gestation (WHO, Zambia) or a short fixed period after initiation (PHS) achieved >95% testing in pregnancy; other guidelines led to 59-83% antenatal testing; and with no special stipulation only 14% of women received an antenatal test under Malawian guidelines.
- Guidelines calling for monitoring in BF (SA, Kenya) had >80% testing during BF compared to 30-60% among guidelines that did not (WHO, Malawi).
- Only a small proportion of simulated episodes of eVL>1000 c/mL were successfully detected by monitoring (range, 20-50%) among women who had reached viral suppression (Figure); guidelines with more frequent testing in pregnancy and breastfeeding led to shorter delays from the onset of eVL to detection as well as lower cumulative VL before detection (Figure).
- Larger proportions of women initiating ART during pregnancy has an impact on performance of guidelines, but does not alter the relative performance appreciably (Figure).

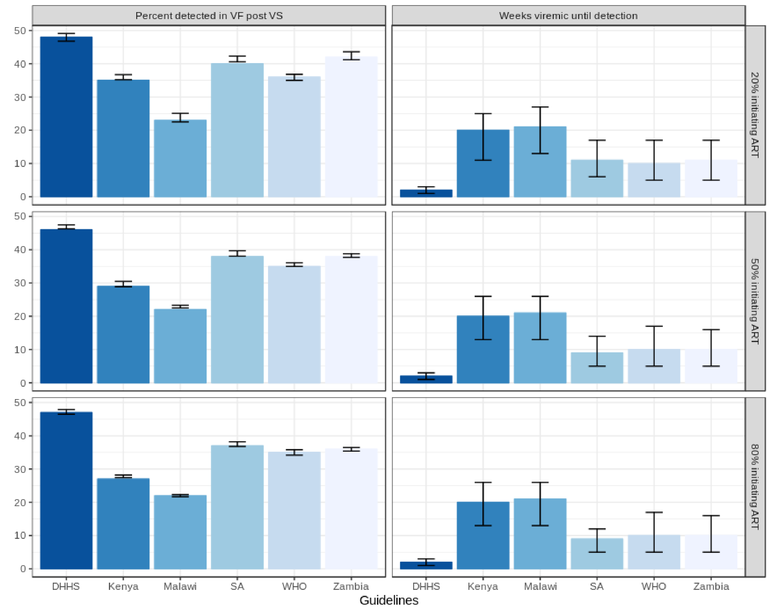

Figure 1: Simulation outcomes. Left column: percent of women detected at time of eVL given prior viral suppression. Right column: Average weeks spent viremic (1000 c/mL) until detection or end of breastfeeding. VF: elevated VL ≥1000 c/mL

Discussion

- Without guidance specific to pregnant and breastfeeding women, less than 1 in 5 women would receive antenatal or postnatal VL monitoring.
- However even with specific guidance, current guidelines yield suboptimal detection of elevated VL.
- Research is needed to optimize the timing of monitoring in pregnant and breastfeeding women to improve opportunities for intervention which will in turn improve outcomes.

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