

HEALTHCARE DELIVERY

A nurse-led intervention to improve management of virological failure in public sector HIV clinics in Durban, South Africa: A pre- and post-implementation evaluation

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Background. Identification of patients on antiretroviral therapy (ART) with virological failure (VF) and the response in the public health sector remain significant challenges. We previously reported improvement in routine viral load (VL) monitoring after ART commencement through a health system-strengthening, nurse-led ‘VL champion’ programme as part of a multidisciplinary team in three public sector clinics in Durban, South Africa.

Objectives. To report on the impact of the VL champion model adapted to identify, support and co-ordinate the management of individuals with VF on first-line ART in a setting with limited electronic-based record capacity.

Methods. We evaluated the VL champion model using a controlled before-after study design. A paper-based tool, the ‘high VL register’, was piloted under the supervision of the VL champion to improve data management, monitoring of counselling support, and enacting of clinical decisions. We abstracted chart and electronic data (TIER.net) for eligible individuals with VF in the year before and after implementation of the programme, and compared outcomes for individuals during these periods. Our primary outcome was successful completion of the VF pathway, defined as a repeat VL <1 000 copies/mL or a change to second-line ART within 6 months of VF. In a secondary analysis, we assessed the completion of each step in the pathway.

Results. We identified 60 and 56 individuals in the pre-intervention and post-intervention periods, respectively, with VF who met the inclusion criteria. Sociodemographic and clinical characteristics were similar between the periods. Repeat VL testing was completed in 61.7% and 57.8% of individuals in these two groups, respectively. We found no difference in the proportion achieving our primary outcome in the pre- and post-intervention periods: 11/60 (18.3%; 95% confidence interval (CI) 9 - 28) and 15/56 (22.8%; 95% CI 15 - 38), respectively ($p=0.28$). In multivariable logistic regression models adjusted for potential confounding factors, individuals in the post-intervention period had a non-significant doubling of the odds of achieving the primary outcome (adjusted odds ratio 2.07; 95% CI 0.75 - 5.72). However, there was no difference in the rates of completion of each step along the first-line VF cascade of care.

Conclusions. This enhanced intervention to improve VF in the public sector using a paper-based data management system failed to achieve significant improvements in first-line VF management over the standard of care. In addition to interventions that better address patient-centred factors that contribute to VF, we believe that there are substantial limitations to and staffing requirements involved in the ongoing utilisation of a paper-based tool. A prioritisation is needed to further expand and upgrade the electronic medical record system with capabilities for prompting staff regarding patients with missed visits and critical laboratory results demonstrating VF.

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The identification and management of virological failure (VF) in people living with HIV (PLWH) is a cornerstone of successful HIV care. Fortunately viral load (VL) monitoring of individuals on

therapy, recommended by the World Health Organization,^[1] has expanded vastly in the sub-Saharan African region.^[2] Despite this expansion, there remain significant weaknesses in identification

of patients experiencing VF and delays in appropriate switching to second-line ART.^[3]

Prompt response to individuals failing therapy decreases the risk of mortality, opportunistic infections, drug resistance and HIV transmission.^[4-6] Furthermore, management of VF is complex, particularly for over-burdened public sector clinics. Most guidelines recommend that individuals with VF undergo a complex series of clinical encounters. These include multiple visits for adherence support interventions, repeat VL testing, and visits to consider regimen changes to second-line antiretroviral therapy (ART). Notably, regimen changes to second-line ART often require approval from a senior clinical staff member. Moreover, individuals with VF represent an inherently complex patient population and often experience additional barriers to care.^[7] These complexities lead to low resuppression rates and poor outcomes in patients with VF.^[8-13]

Consequently, interventions to improve monitoring and management of individuals with VF are needed. We previously reported on the design of a health system-strengthening, nurse-led 'viral load champion' programme as part of a multidisciplinary team in three public sector clinics in Durban, South Africa (SA). The programme achieved a significant improvement in VL testing rates after ART initiation,^[14] but did not assess the management of patients after VF. Beginning in 2017, we piloted a paper-based tool, the 'high VL register', as part of the VL champion model to strengthen the response to VF management. We now report results of a controlled before-after study design of the pilot programme to assess whether it improved processes and clinical outcomes for PLWH with VF.

Methods

Study setting

The VL champion pilot programme was implemented at three public sector HIV clinics in Durban: Clairwood Hospital, Wentworth Hospital and King Dinizulu Hospital. Prior to the intervention in 2017, monitoring of patients with VF was expected to be conducted in accordance with SA National Department of Health guidelines.^[7] However, no specific clinic staff were delegated the tasks of identifying or monitoring patients with VF, which generally occurred on an *ad hoc* basis. A paper-based tool, the high VL register (available as a supplementary file at <http://samj.org.za/public/sup/15432.pdf>), was used in the VL champion model as part of a multidisciplinary team within a standard operating procedure (SOP) to monitor patient visits and assist in management of the VF cascade of care.

Intervention description

In January 2017, we implemented a health system-strengthening programme to manage VF at each of the three clinics. The programme included the following elements:

- Assignment of a nurse as the 'VL champion' at each clinic to supervise the staff responsible for monitoring all patients with a detectable VL.
- Development of an SOP for management of VF by clinic staff. Training on the SOP was provided to: (i) a lay counsellor or nurse assigned to adherence counselling; (ii) a nurse and/or doctor assigned to manage the VF clinic; (iii) an administrative clerk for records handling; and (iv) a data clerk to ensure same-day data entry. In brief, VL results were reviewed daily by the VL champion and filed or entered in the patient charts. Patient charts with a high VL result were identified with a sticker and filed separately from the remaining clinic charts by the administrative clerk. Upon return to the clinic, those marked with a high VL sticker were identified by the administrative clerk and referred directly

to the counsellor, who performed adherence counselling and then referred the patient to the high VL physician or nurse. The lay counsellor also managed completion of the high VL register (<http://samj.org.za/public/sup/15432.pdf>) and was expected to call patients who missed a clinic appointment within a week at any point of the follow-up period.

Study population and data sources

All adult patients on first-line ART (zidovudine or tenofovir, lamivudine and efavirenz) with a VL >1 000 copies/mL were screened for eligibility from the following data sources: TIER.net,^[15] patient clinical charts, or the weekly clinic electronic dashboard of the National Health Laboratory Service. We excluded pregnant patients and those actively participating in other research studies in the clinic. Data were abstracted at the three intervention clinics during December 2015 - December 2017. For each participant who met the inclusion criteria, sociodemographic data, laboratory data (CD4 count and HIV-1 RNA VL), dates of clinic visits and enhanced adherence counselling (EAC) events, and dates of regimen changes were obtained.

Study design and statistical methods

We evaluated the VL champion intervention using a controlled before-after observational design. The primary exposure of interest was the outcomes in the cascade in the two periods, pre-intervention (December 2015 - December 2016) and post-intervention with the VL champion model (January 2017 - December 2017). Individuals were allocated by their first clinic visit after a VL >1 000 copies/mL during 2016 as being in the pre-intervention period, and those with their first visit after a VL >1 000 copies/mL during 2017 as being in the post-intervention period. Those with a VL >1 000 copies/mL and no additional visits were included in the analysis and categorised by the year of their high VL.

The primary outcome was appropriate response completed to the repeat VL, specifically a VL <1 000 copies/mL or change to a protease inhibitor-based regimen after a repeat VL >1 000 copies/mL within 6 months of VF. Secondary outcomes included completion of at least one EAC session and completion of a repeat VL within 6 months.

Fisher's exact tests and χ^2 tests were used to compare descriptive indices of individuals in the pre- and post-intervention periods. Crude rates of outcomes by intervention period were estimated and graphically depicted the 'second-line cascade of care' to describe the proportion of people with first-line VF who successfully completed ≥ 1 EAC and a repeat VL, and had appropriate response completed. Finally, we fitted logistic regression models to identify correlates of our primary outcome with and without confounders, including age, sex, CD4 count, ART duration, ART regimen, and clinic of attendance. All data analyses were completed with Stata version 15.1 (StataCorp, USA).

Ethical considerations

The study protocol was approved by the KwaZulu-Natal Provincial Health Research Committee and the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (ref. no. BFC 377/16).

Results

A total of 116 individuals were identified as eligible for the assessment on first-line ART with a VL >1 000 copies/mL. During the observation period, 60 individuals (including 3 with no additional visit) were eligible in the pre-intervention period and 56 (including 4 with no additional visit) in the post-intervention period (Table 1). Participants in the two periods were similar in terms of sociodemographic and clinical characteristics. The primary outcome, confirmation of a

repeat VL <1 000 copies/mL or a change to second-line ART within 6 months, was similar in the pre- and post-intervention groups (11/60 (18.3%; 95% confidence interval (CI) 9 - 28) and 15/56 (26.8%; 95% CI 15 - 38), respectively ($p=0.28$)). In multivariable logistic regression models adjusted for potential confounding factors, individuals in the post-intervention period had a non-significant doubling of the odds of achieving the primary outcome (adjusted odds ratio 2.07; 95% CI 0.75 - 5.72) (Table 2).

We found similar trends across the first-line failure cascade of care (Fig. 1). In the pre- and post-intervention groups, 37/60 (61.7%) and 29/56 (51.8%) individuals, respectively, had a second VL done. Of those with a second VL result <1 000 copies/mL, only 8.3% and 10.7%, respectively, were managed as per the guidelines by continuation of first-line ART; 10.1% and 16.1%, respectively, were changed to second-line ART with a VL >1 000 copies/mL within 6 months of detection of VF.

Discussion

The VL champion model was developed to address barriers to improving routine VL testing and monitoring. We previously reported successful outcomes in improving VL completion rates utilising the VL champion model after ART initiation from 62% to >90% at 1 year and maintaining high VL suppression rates.^[14] We now report the results of adapting the VL champion model to use a paper-based 'high VL register' to manage the small but significant numbers of individuals with VF. There was no significant difference in the primary outcome for the

confirmation of a repeat VL <1 000 copies/mL or a change to second-line ART within 6 months of detection of VF in the pre- and post-intervention groups. In both groups, poor outcomes were reported at all stages of the VF cascade of care (number of EAC sessions, second VL and subsequent visit after repeat VL).

This study reinforces prior work demonstrating extremely poor outcomes after first-line ART failure in sub-Saharan Africa.^[9] Potentially more concerning than suboptimal VL monitoring is the startlingly low response to a detectable VL that we observed in this cohort in the pre-intervention and post-intervention periods.

Our findings are similar to a Mozambican study that also reported a poor cascade of care in health system response to VF.^[11] In that study, only 35% of individuals with detected VF had an appropriate repeat test, which showed 62% to have persistent VF. Only a third of those with persistent VF appropriately started second-line ART. An analysis from rural KwaZulu-Natal Province using electronic health records also reported very poor management of VF.^[10] Only 34% of patients had a VL documented 12 months after starting ART, and only 18% of these had the recommended repeat VL conducted. In total, and similar to our study, only 20% of individuals were confirmed to have

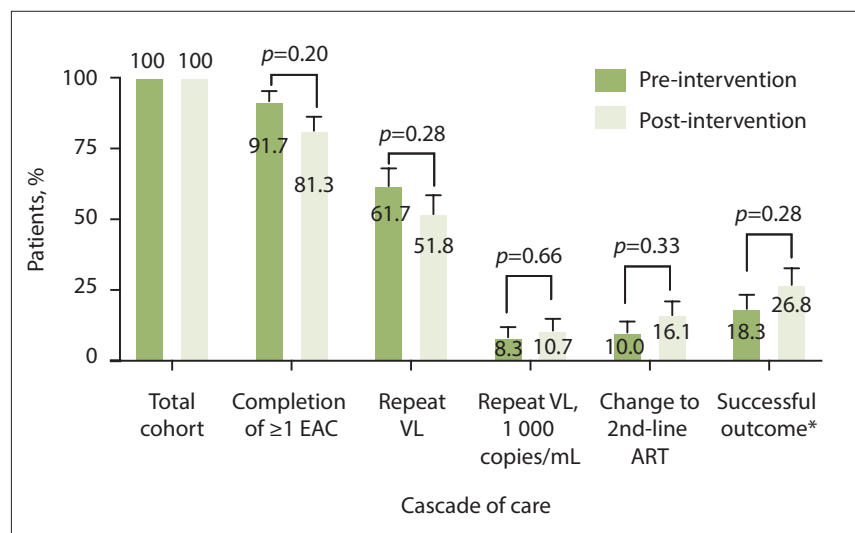


Fig. 1. Second-line cascade of care before and after implementation of a nurse-led viral load monitoring and management programme. (EAC = enhanced adherence counselling; VL = viral load; ART = antiretroviral therapy; *Successful outcome defined as a repeat VL <1 000 copies/mL or a change to second-line ART after a repeat VL >1 000 copies/mL within 6 months of first-line ART virological failure.)

Table 1. Cohort characteristics

Characteristic	Pre-intervention period (N=60)	Post-intervention period (N=56)	p-value
Age (years), median (IQR)	36 (23 - 41)	35 (30 - 39)	0.18
Female, n (%)	35 (58.3)	25 (44.6)	0.14
ART duration (years), median (IQR)	1.3 (0.5 - 3.2)	1.5 (0.5 - 3.3)	0.74
Viral load at failure (copies/mL), median (IQR)	19 443 (4 751 - 82 910)	16 963 (5 621 - 144 977)	0.64
Baseline CD4 count (cells/μL), median (IQR)	130 (38 - 223)	114 (28 - 193)	0.41

IQR = interquartile range; ART = antiretroviral therapy.

Table 2. Logistic regression model for correlates of a successful outcome after virological failure*

	Univariable models		Multivariable model	
	OR (95% CI)	p-value	aOR (95% CI)	p-value
Age (each 10 years)	0.99 (0.91 - 1.06)	0.76	1.35 (0.78 - 2.35)	0.29
Female sex	1.81 (0.86 - 3.81)	0.12	3.59 (1.21 - 10.6)	0.02
Baseline viral load (log ₁₀ copies/mL)	0.99 (0.62 - 1.59)	0.97	0.89 (0.48 - 1.65)	0.70
Pre-post intervention	1.63 (0.67 - 3.94)	0.28	2.07 (0.75 - 5.72)	0.16

OR = odds ratio; CI = confidence interval; aOR = adjusted odds ratio.

*Defined as a repeat viral load <1 000 copies/mL or a change to second-line therapy.

virological resuppression or a change to second-line therapy after VF, and those who did change therapy did so a median of 1 year after VF. These results show a consistently poor response to treatment failure in the region. Additional measures are needed to better identify, monitor, and ensure more effective clinical management for this high-risk population.

There was a drop in numbers of EAC sessions and second VLs done in the post-intervention period. If adherence counselling was not performed with sufficient expertise or if staff implementation of EAC was not consistent, the remainder of the intervention could be less effective, as reported in other studies.^[16-18] The results of our intervention demonstrate that addressing health system factors alone may not be sufficient to improve VF management. We hypothesise that failure to demonstrate improved outcomes was the result of multiple factors. Attention was directed predominantly towards SOPs, training, and support for laboratory testing and results reporting. The patient-specific factors that may need to be addressed are transportation costs, work/clinical care trade-offs, stigma and mental health issues, which have all been shown to affect outcomes in this patient population.^[19] A differentiated care model, which adds focus and resources to patients with VF, might serve to improve on-treatment HIV care in the public sector.^[20,21]

Both groups had similar rates of repeated VL testing, yet the number who returned for follow-up management was very low. Although the team contacted missing patients, additional measures for those who could not be found were limited by funds and staffing time. There is no inherent capacity in paper-based tools to prompt clinic staff to follow up missed visits. This system requires manual entry for reconciliation of laboratory results, visit schedules and clinical reporting. Additionally, the available electronic data repositories used in KwaZulu-Natal are not updated in real time and are often not available to nursing staff. We believe that a priority should be to upgrade the electronic medical record system with the capacity to prompt staff to track patients and universalise access to up-to-date electronic data repositories. Efforts to advance online medical record systems across SA, as successfully implemented in Western Cape Province, may meaningfully improve patient flow and clinical care.^[22]

Clearly, additional novel strategies are needed to more promptly identify and switch patients who qualify for second-line ART, specifically patients with advanced HIV, the group with the worst outcomes after treatment failure.^[23,24] In addition to improving online medical record systems, a greater emphasis on task-shifting to allow nurses to change patients to second-line ART with approval from a doctor is worthy of further investigation.^[25] Another strategy currently under investigation is incorporation of resistance testing into the management of VF, which may differentiate those with failure into adherence- and resistance-based causes and could encourage clinicians to respond earlier.^[26] The roll-out of dolutegravir-based ART as first-line therapy in the region, a regimen with a higher barrier to resistance and better tolerability, is also likely to change the relative importance of the workflow components for monitoring VF. It could conceivably make poor adherence rather than ART resistance the primary determinant of treatment failure.^[27] Dolutegravir-based ART may further highlight the importance of adherence counselling in the management of VF and require further optimisation of the current VF monitoring and switch guidelines.^[28]

Study limitations

Our study had limitations. The first was the small sample size, which may not have allowed sufficient power to detect a modest improvement in the outcome of interest. Second, as it was an

observational study with a historical control group, there may have been unmeasured changes in patient characteristics or management that accrued over time and also had an impact on our outcomes. Third, it was an observational study that followed very soon after the establishment of a new model of care, so there may not have been sufficient time for full uptake of the new model to affect patient care outcomes. Finally, the clinics under investigation were mainly urban, and to make the findings of future studies generalisable, it will be essential to include rural clinics with different human resource profiles.

Conclusions

In summary, this study provides a basis for more comprehensive, evidence-based, clinical operational strategies that are sorely needed to improve VF management based on implementation science research. These programmes must address both health system and individual barriers to care and consider the complex mechanisms of detection, monitoring and response to VF. Until this standard of practice is available and reflected in programmatic guidelines, high rates of losses from care, delays in appropriate switching to second-line ART, and poor outcomes among people with VF will remain unacceptably common in the region, and threaten the success and durability of global HIV treatment programmes. The VL champion model improves VL completion rates after ART commencement and may be expanded as a national public health intervention, but the model for improving VF requires further implementation research.

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Conflicts of interest. None.

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