

Research Letter

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How does population viral load vary with the evolution of a large HIV epidemic in sub-Saharan Africa?

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Using mathematical modelling, we describe the temporal evolution of population HIV-1 viral load in Tanzania throughout the epidemic. Population \log_{10} viral load was found to be stable and not sensitive to epidemic dynamics. However, even modest increases in antiretroviral therapy (ART) coverage were reflected as appreciable reductions in population \log_{10} viral load. As ART coverage expands in sub-Saharan Africa, population \log_{10} viral load will increasingly become a powerful proxy for monitoring ART implementation and HIV incidence trends.

The population plasma HIV-1 RNA viral load has become a subject of intense research [1–4]. This importance stems from findings and developments such as impact of viral load suppression on HIV transmission [5], ecological association between community viral load and HIV incidence [6–8], regional differences in population viral load [4] and availability of viral load testing and its use for clinical monitoring [9]. Yet, the evolution of population viral load in an actual epidemic in sub-Saharan Africa (SSA), with or without the impact of antiretroviral therapy (ART), remains uncertain. This contrasts with developed settings wherein empirical studies have assessed the evolution of community viral load over time [6–8].

It is not known whether population viral load varies by epidemic phase, thereby complicating the use of population viral load as a proxy of ART coverage and ART's impact on HIV incidence. The positive association between population viral load and HIV incidence following ART's expansion is not well established, though widely hypothesized on the basis of ecological evidence [6–8]. The consequences of incidence declines, as those witnessed recently in SSA [10], on population viral load are yet to be investigated.

Against this background, we attempt to answer the following questions: How did population viral load vary throughout an actual epidemic in SSA? What is the impact on population viral load of the recent reductions in incidence? Will ART scale-up in SSA lead to noticeable reductions in population viral load that are distinguished from any changes in viral load arising from

epidemic dynamics? Can population viral load be used as a proxy for ART's impact on reducing HIV incidence? To address these questions, we calculated, using mathematical modelling, the population \log_{10} viral load in a representative nation in SSA, Tanzania, to examine population viral load variation from the start of the epidemic up to today, and its future evolution with ART scale-up.

A deterministic model was used, based on earlier models [4,11] (SF Awad and LJ Abu-Raddad, unpublished observations), to describe HIV transmission in Tanzania. The model stratified the population according to HIV status, stage of infection and sexual risk group. HIV progression was divided into the three stages of acute, chronic and advanced. The model incorporated 10 risk groups, a sexual-mixing matrix and temporal changes in risk behaviour. An ART intervention was incorporated by gradually rolling-out ART among infected persons with $CD4^+$ cell count less than 200 cells/ μ l and reaching full coverage by 2020. Further details on this model type can be found in the unpublished observations by Awad and Abu-Raddad.

The model was parameterized using epidemiological and natural history data from SSA. The mean \log_{10} viral load during each of HIV stages was assumed to be 5.98 (acute infection), 4.38 (chronic infection) and 5.14 (advanced infection). These values are based on a large viral load database from SSA [4], and studies of viral load by stage of infection [12–15]. We defined population viral load, based on the Centers for Disease Control and Prevention guidance [1], as mean HIV-1 viral load among all infected persons. The term population viral load in this article refers strictly, per general convention, to population viral load transformed into the base-10 logarithmic scale.

The model was fitted to HIV prevalence time-series data [16]. Multivariate uncertainty analyses were conducted with respect to the key structural parameters and viral load level per HIV stage (Figure S1, <http://links.lww.com/QAD/A483>). Each analysis was implemented using Monte Carlo sampling from uniform probability distributions for parameter uncertainty.

The model robustly fitted HIV prevalence (Fig. 1a). HIV incidence rate peaked in the early 1990s, and HIV prevalence in the mid-1990s (Fig. 1a, b). Since then, HIV prevalence declined with the declining incidence. Despite the variations in prevalence and incidence, population viral load was virtually stable throughout the epidemic ($<0.1 \log_{10}$ variation; Fig. 1c).

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Figure 1d shows the impact of an ART intervention implemented starting from 2010. Although population viral load was stable throughout the epidemic, it was declining steadily with ART scale-up. HIV incidence rate also declined steadily with ART scale-up and declining population viral load.

The uncertainty analyses indicated that the result of stable population viral load pre-ART is not affected by parameter uncertainty (Figure S1A, <http://links.lww.com/QAD/A483>). The analyses further indicated that the considerable decline in population viral load post-ART is robust to parameter uncertainty (Figure S1B, <http://links.lww.com/QAD/A483>).

Our results show that, although the epidemic went through different phases, population viral load remained

virtually stable. The recent incidence declines had also little impact on population viral load. Epidemic dynamics does not appear to tangibly influence population viral load; observed changes in population viral load should reflect other factors. Notably, population viral load was influenced by ART scale-up and was associated with the ART-driven decline in incidence. These findings affirm the rationale for using population viral load as a proxy of ART effectiveness and the impact of ART on incidence rate. They further suggest that the empirically observed ecological association between community viral load, incidence rate and ART coverage [6–8] likely reflects a causal relationship.

The stability of population viral load pre-ART suggests that regional viral load differences, as observed recently [4], may not be explained by epidemic phase or the

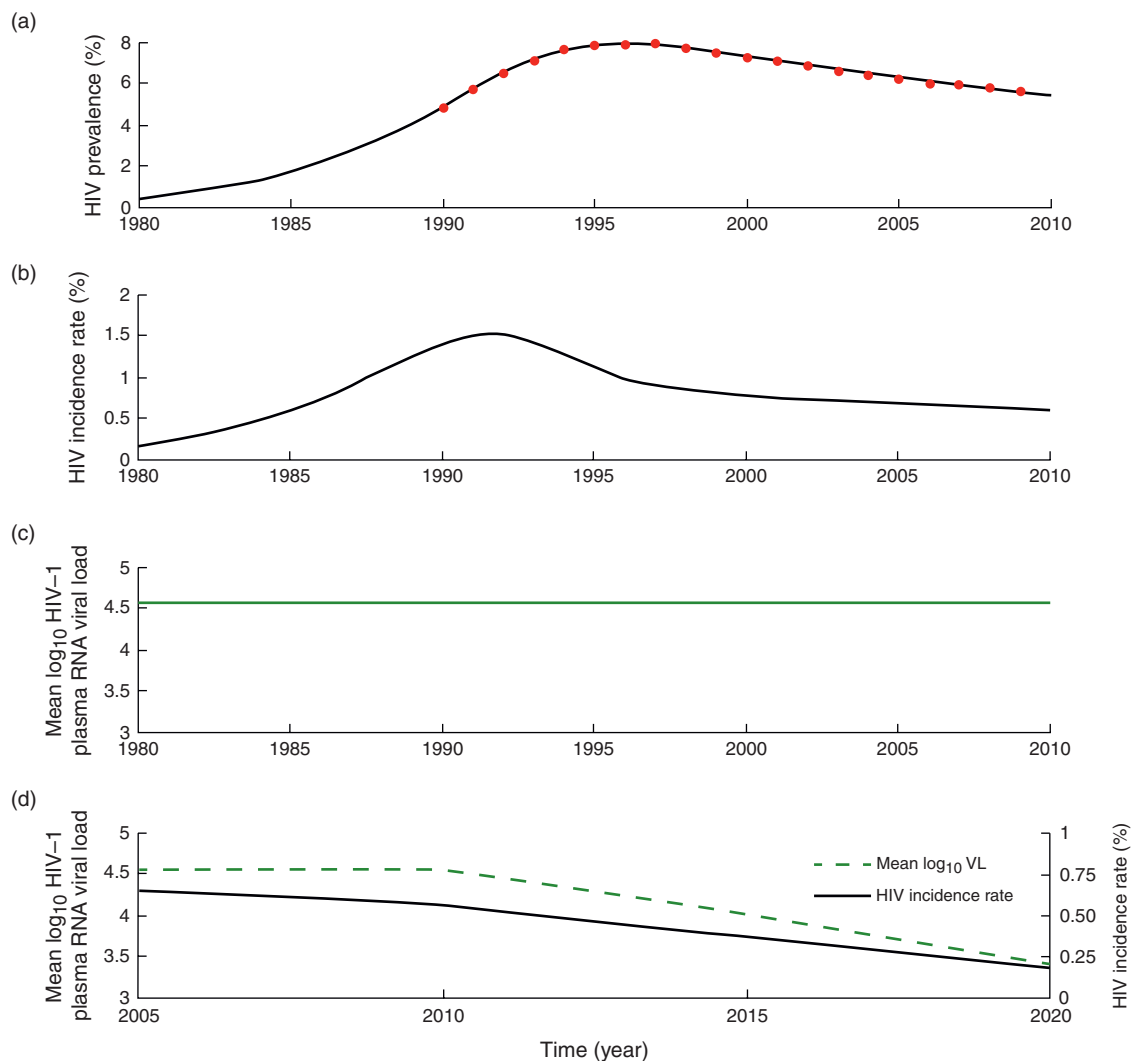


Fig. 1. Evolution of population plasma HIV-1 RNA log₁₀ viral load in a major epidemic in sub-Saharan Africa. The simulated HIV epidemic trajectory in Tanzania in terms of (a) HIV prevalence from 1980 up to 2010; (b) HIV incidence rate from 1980 up to 2010; (c) Population log₁₀ viral load from 1980 up to 2010; (d) Population log₁₀ viral load and HIV incidence rate from 2005 up to 2020 in presence of an antiretroviral therapy (ART) intervention starting from 2010.

distribution of infected persons across HIV stages. Population viral load is driven by the distribution of infected persons across stages, and this distribution varies in an epidemic. However, late-stage infection contribution tends to balance acute infection contribution with epidemic evolution leading to small overall viral load variation. The measurement of population viral load on a logarithmic scale, for statistical relevance, also minimizes population viral load variation, although viral load in its natural or low-power transformation scales also remained largely invariable (not shown).

We reported population viral load evolution only in Tanzania, and these results may not be generalizable to other countries. Nonetheless, examining the trends in Cameroon, Malawi, Mali, Togo and Zimbabwe, countries with different epidemic sizes, led to similar results (not shown). Our results may depend on the kind of mathematical model used, but our model is an elaborate one refined over multiple studies.

In conclusion, population viral load is virtually not sensitive to epidemic dynamics, but is influenced by ART. Even modest increases in ART coverage are reflected as appreciable reductions in population viral load. As ART eligibility and coverage expands in SSA over the coming years, population viral load will increasingly become a powerful tool to monitor the effectiveness of ART implementation and trends in HIV incidence.

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L.J.A. conceived the study and wrote the first draft of the article. S.F.A. conducted the bulk of the mathematical modelling analyses. Both authors contributed to the analysis, discussion of the results and writing of the manuscript.

Conflicts of interest

There are no conflicts of interest.

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