Outcomes of the Botswana national HIV/AIDS treatment programme from 2002 to 2010: a longitudinal analysis

Mansour Farahani, Anusha Vable, Refeletswe Lebelonyane, Khumo Seipone, Marina Anderson , Ava Avalos, Tim Chadborn, Hailu Tilahun, Danae Roumis, Themba Moeti, Godfrey Musuka, Lesego Busang, Tendani Gaolathe, Kolaatamo C S Malefho, Richard Marlink

Summary

Background **Short-term mortality rates among patients with HIV receiving antiretroviral therapy (ART) in sub-Saharan Africa are higher than those recorded in high-income countries, but systematic long-term comparisons have not been made because of the scarcity of available data. We analysed the effect of the implementation of Botswana's national ART programme, known as Masa, from 2002 to 2010.**

Methods **The Masa programme started on Jan 21, 2002. Patients who were eligible for ART according to national guidelines had their data collected prospectively through a clinical information system developed by the Botswana Ministry of Health. A dataset of all available electronic records for adults (≥18 years) who had enrolled by April 30, 2010, was extracted and sent to the study team. All data were anonymised before analysis. The primary outcome was mortality. To assess the effect of loss to follow-up, we did a series of sensitivity analyses assuming varying proportions of the population lost to follow-up to be dead.**

Findings **We analysed the records of 126 263 patients, of whom 102 713 had documented initiation of ART. Median follow-up time was 35 months (IQR 14–56), with a median of eight follow-up visits (4–14). 15 270 patients were deemed lost to follow-up by the end of the study. 63% (78 866) of the study population were women; median age at baseline was 34 years for women (IQR 29–41) and 38 years for men (33–45). 10 230 (8%) deaths were documented during the 9 years of the study. Mortality was highest during the first 3 months after treatment initiation at 12·8 deaths per 100 person-years (95% CI 12·4–13·2), but decreased to 1·16 deaths per 100 person-years (1·12–1·2) in the second year of treatment, and to 0·15 deaths per 100 person-years (0·09–0·25) over the next 7 years of follow-up. In each calendar year after the start of the Masa programme in 2002, average CD4 cell counts at enrolment increased (from 101 cells/μL [IQR 44–156] in 2002, to 191 cells/μL [115–239] in 2010). In each year, the proportion of the total enrolled population who died in that year decreased, from 63% (88 of 140) in 2002, to 0·8% (13 of 1599) in 2010. A sensitivity analysis assuming that 60% of the population lost to follow-up had died gave 3000 additional deaths, increasing overall mortality from 8% to 11–13%.**

Interpretation **The Botswana national HIV/AIDS treatment programme reduced mortality among adults with HIV to levels much the same as in other low-income or middle-income countries.**

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Harvard School of Public Health, Boston, MA, USA (M Farahani MD, A Vable MHP, D Roumis MSc, H Tilahun MSc, Prof R Marlink MD); **Ministry of Health, Gaborone, Botswana** (R Lebelonyane MD, K Seipone MD, M Anderson MD, A Avalos MD, T Chadborn PhD, K C S Malefho MD); **African Comprehensive HIV/AIDS Partnerships, Gaborone, Botswana** (T Moeti MBBS, G Musuka DVM, L Busang MA); **and Botswana-Harvard Partnership, Gaborone, Botswana** (T Gaolathe MD, Prof R Marlink)

Correspondence to: Dr Mansour Farahani, Harvard School of Public Health, Boston, MA 02115, USA **mfarahan@hsph.harvard.edu**

Introduction

Starting in 2002, Botswana was the first African country to establish a national HIV/AIDS treatment programme, calling it "Masa", the Setswana word for "a new dawn". Before the introduction of Masa, Botswana had one of the highest rates of HIV/AIDS in the world. By 2001, the national prevalence of HIV/AIDS had reached 27%.[1]

Key characteristics of Botswana's antiretroviral therapy (ART) programme are that it is free and universal—it is open to all citizens who meet the national guidelines; however, some of the population have not been tested for HIV, and thus their status is not known. In 2008, the eligibility criteria for ART changed from a CD4 cell count of 200 cells/μL to 250 cells/μL and, in 2013, to 350 cells/μL.[2] Since the start of the Masa programme in 2002, the national guidelines have changed to take into account the improved understanding of the biology of HIV, reduce adverse events associated with stavudine and zidovudine, and accommodate the availability of improved drugs (table). After the 2008 guideline change, tenofovir (plus emtricitabine in almost all cases) replaced zidovudine as the first-line nucleoside reverse transcriptase inhibitor in Botswana. In 2002, 3500 patients were receiving treatment. By November, 2012, that number had reached 201 822 patients treated via more than 200 clinics and 35 hospitals around the country.

To track patients eligible for ART and monitor the progress and effectiveness of the Masa programme, the Government of Botswana, with the support of the US President's Emergency Plan for AIDS Relief (PEPFAR), established a monitoring and evaluation unit within the national ART programme in the Department of HIV/AIDS Prevention and Care of the Ministry of Health. This electronic patient tracking and outcomes monitoring system has been crucial for the effective scale-up of the programme. Through capture of individual-level patient data, the system is able to generate facility-level reports that aid in both clinic management and care of patients.

	Eligible adults	First-line regimen	Second-line regimen	Summary of changes
2002	WHO stages I–II: CD4 cell count <200 cells/μL WHO stages III–IV: all patients	Zidovudine and lamivudine plus efavirenz. Zidovudine and lamivudine plus nevirapine for women of reproductive potential	Didanosine plus stavudine plus nelfinavir	..
2005	WHO stages I–II: CD4 cell count <200 cells/μL WHO stages III–IV: all patients	Zidovudine or stavudine plus lamivudine and efavirenz. Zidovudine, lamivudine, and nevirapine for women of reproductive potential	Didanosine plus stavudine or zidovudine plus lopinavir or ritonavir	Eligible adults and CD4 cell count threshold stayed the same. First-line and second-line regimen changed
2008	WHO stages I–II: CD4 cell count <250 cells/μL WHO stages III–IV: all patients	Tenofovir and emtricitabine or lamivudine with efavirenz. Tenofovir and emtricitabine or lamivudine with nevirapine for women of reproductive potential	Zidovudine plus lamivudine plus lopinavir or ritonavir	CD4 cell count threshold changed and first-line and second-line regimen changed

*Adults visit clinics every 3 months for the first 2 years, and if stable, every 6 months thereafter.

Table*: Summary of Botswana national HIV/AIDS treatment guidelines

The system allows for collection and analysis of aggregate outcome data, encourages compliance with treatment protocols, tracks pharmaceutical usage, and generates lists of patients needing home follow-up.

Assessment of national ART programmes is essential to establish whether programmes are having the desired effects and to monitor any unanticipated effects or consequences. Several studies[3–15] have shown the successful implementation of ART programmes in low-income and middle-income countries with overall outcomes that are much the same as in high-income countries. Most reports of ART outcomes, however, have come from select cohorts that might not be indicative of national programme conditions.[6,8,16–20] Additionally, most reports have captured national longitudinal outcome data for patients receiving ART for only a few years.

We analysed 9 years of follow-up data for more than 100 000 adult patients who were treated in the Botswana national HIV/AIDS treatment programme and tracked at individual level in the electronic system described above. We aimed to assess mortality, loss to follow-up, changes in CD4 cell count after treatment initiation, and other predictors of mortality including clinical and demographic factors.

Methods

Data

The Masa programme started on Jan 21, 2002. Patients who were eligible for ART had their data collected prospectively through the Botswana Ministry of Health's clinical information system. Many patients did not have an HIV medical file created until they were eligible for treatment. All hospitals and most clinics had an electronic information system by the end of 2012; at the time of our data cutoff in 2010, about 15% clinics were not integrated into the national information system.

A dataset of all available electronic records for adults (≥18 years; about 18 000 records for patients <18 years were excluded from this analysis) who had enrolled by April 30, 2010, was extracted from the Ministry of Health data warehouse and sent to the study team for this analysis. All data were anonymised before the analysis. The few patients who had started ART before the launch of the national programme in 2002 were excluded because their treatment regimen was not necessarily the same as recommended by the national guidelines. At the time the dataset was transferred from the Ministry of Health for this study, not all the available data collected from clinics from September, 2009, to April, 2010, had been integrated into the central database. However, because all available data from the clinics were collected but not yet entered into the database, we do not expect non-integrated patient data to come from patients (or clinics) whose outcomes are systematically different than those included.

This study was reviewed and approved by Harvard School of Public Health's Institutional Review Board and the Human Resource Development Committe in Botswana.

Analysis

The primary outcome measure for this analysis was mortality. For this assessment, documented death referred to a death that was recorded in the database. Deaths in hospitals or in other institutions might not be reported to HIV clinic staff and non-institutional deaths might not be reported to the health-care system as is legally required. Therefore, loss to follow-up might include patients who died without a death report captured in the database. To assess the effect of loss to follow-up on the study outcome, we did a series of sensitivity analyses assuming varying proportions of the population lost to follow-up to be dead. We used number of patients whose death was documented in the numerator and patient-years of follow-up time in the denominator to directly calculate the mortality rate.

We also recorded change in median CD4 cell count and viral load over time, for the patients for whom these data were available, and type of antiretroviral drugs used.

Role of the funding source

The funder of the study contributed to the study design, writing of the report, and the decision to submit this paper for publication. The funder was not involved in the data analysis or interpretation; all the authors had full access to the data in this study.