



World Health Organization



Case Study

Country-enhanced monitoring and evaluation for antiretroviral therapy scale-up: analysis and use of strategic information in Botswana



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Strengthening health services to fight HIV/AIDS

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CASE STUDY

COUNTRY-ENHANCED MONITORING AND EVALUATION FOR ANTIRETROVIRAL THERAPY SCALE-UP: Analysis and use of strategic information in Botswana



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ACRONYMS

Including stakeholders and description of their roles

ACHAP	African Comprehensive HIV/AIDS Partnership
ART	Antiretroviral therapy
BHP	Botswana–Harvard AIDS Institute Partnership
BOTUSA	A collaboration between the Government of Botswana and the United States Centers for Disease Control and Prevention
CDC	United States Centers for Disease Control and Prevention Collection of data on HIV/AIDS and some vertical programmes. Collection of national vital registration data, census data, hospital information system data. Conducts research on tuberculosis and HIV. Technical assistance to NACA, MOH. Coordination of all HIV/AIDS-related research, funding, laboratory, and clinical care programmes. Coordination of the comprehensive response to HIV/AIDS.
CSO	Central Statistics Office, Botswana
GIS	Geographical information systems
HSU	Health Statistics Unit, Botswana Carries out laboratory work and clinical-care systems support for MOH, NACA, and specific research projects. Management of local programmes and policies related to HIV/AIDS. Part of the Central Statistics Office/Ministry of Health
IEC	Information, education and communication programmes
IPMS	Integrated patient management systems
MCH	Maternal–child health
MLG	Ministry of Local Government, Botswana
MOH	Ministry of Health, Botswana
NACA	Botswana National AIDS Coordinating Agency Policy and management of programmes for prevention and treatment. Collection and analysis of health systems data. Provide technical support to the Ministry of Health. Coordinates international work on HIV/AIDS relevant to Botswana.
PMTCT	Prevention of mother-to-child-transmission
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UCSF	University of California, San Francisco
VCT	Voluntary counselling and testing
WHO	World Health Organization

PREFACE

National strategic information related to the scale-up of programmes on HIV/AIDS and other integrated programmes has taken an increasingly important role as countries strengthen their health systems. To support the effective use of strategic information on health, an international group of organizations has joined forces; collaborators include the World Health Organization (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), the Centers for Disease Control and Prevention (CDC), and the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM).

In this case study, we document Botswana's experience in country-enhanced monitoring and evaluation of antiretroviral therapy scale-up, and show the feasibility of applying well-known triangulation methods to integrate multiple data sets from national monitoring mechanisms. Together with capacity building, innovative approaches help to create stronger health information systems, and we hope that this case study will contribute to the adoption of bold new methods. We will summarize triangulation, and other analysis methodologies that have been effectively applied at the national and subnational levels, in a forthcoming resource manual (to be published in 2007).

The international partners and Botswana's National AIDS Coordinating Agency (NACA) wish to thank all the people who have provided valuable inputs and suggestions for this publication. In particular, we are grateful to the staff, clients and programme managers at different levels in Botswana who volunteered their experience. We are also grateful to the public health professionals who worked so hard to generate and compile these data.

We particularly wish to thank Boga Fidzani at NACA for providing leadership for this project in Botswana, and Rand Stoneburner and the University of California, San Francisco team for conceptualizing and writing this case study.

1. EXECUTIVE SUMMARY

In 2002, the Government of Botswana rolled out a national programme for the treatment of AIDS with antiretroviral therapy (ART). In 2005, the impact of this ART scale-up programme was assessed by the National AIDS Committee of the Botswana Ministry of Health (MOH), together with the World Health Organization (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), and the University of California, San Francisco's (UCSF) Institute for Global Health, using country-enhanced monitoring and evaluation methodology tailored specifically to the situation in Botswana.

Using data from multiple existing sources in a process called “triangulation,” the researchers were able to develop a model to determine the impact of ART in Botswana. Preliminary results indicate that during the 3 years since its inception, the ART programme in Botswana has achieved reductions in mortality of adults aged 25–54 years. Reduced mortality is associated with early initiation of district ART programmes and with the overall rate of ART uptake in the district.^a

Widespread application of ART has been shown to decrease mortality among individuals and constrained samples of the population. These previously stated findings are the basis for current clinical guidelines (1). This study demonstrates that in Botswana, where excess mortality attributable to AIDS has been estimated to be 83% of all deaths (2), ART has the potential to cause a population-level change in mortality rates.

The benefits of a triangulation methodology as applied in Botswana are twofold. First, the use of pre-existing data sources allows the study to be relatively rapidly executed and concluded. This is of particular importance for studies with significant policy or programmatic impact. Second, the systematic collection and examination of data from multiple sources reveals new questions to be studied, permits verification, and reduces the likelihood of data and researcher bias. The limitations imposed by the quality of the existing data remain, but are mitigated by this methodology.

The Botswana experience has also identified some of the prerequisites for the effective application of triangulation. It is necessary to be flexible during the analysis, and to consider complementing triangulation studies with additional qualitative and quantitative research, where existing data are not sufficient to answer some questions. Based upon the application of triangulation in Botswana, the engagement of high-level policy-makers and administrators throughout the early part of the triangulation process is critical to the success of data identification and collation, and remains important through the analysis phase.^b A 1-week training course for representatives from a range of institutions was initiated to build capacity in Botswana for future application of triangulation methods.

a This study was made possible by WHO under grant number WHO/SWITZERLAND A21/374/1 BOTSWANA and through the support of the European Commission funding for Second Generation Surveillance (Contract No. SANTE/2004/089-735). The participation of and support from CDC Botswana (BOTUSA project) is also acknowledged.

b Collation of data—“the detailed comparison between different items or forms of information”—was a lengthy and iterative process in which local leadership was particularly important.

2. BACKGROUND

The 1990s brought a dramatic growth in health research worldwide. Investment in research and data collection nearly doubled between 1986 and 1992, from US\$ 30 billion to US\$ 56 billion, and doubled again to US\$ 106 billion by 2001 (3). While data collection has both increased and improved in developing countries during the past 20 years, there remains a gap between research and policy implementation, and between research and programmatic improvement (4).

This gap is not easily bridged: health information systems tend to move data up from the district level and consolidate them in discrete programmatic sets, independent of other information that exists. National surveys likewise generally result in data sets that are consolidated and analysed independently from other information. Integration of different data sets, in different analytical formats, is difficult. In most instances, imperfect overlap of indicators or data points reduces the power of subsequent statistical analyses. Emphasis on best practice in analysis and the specificity of many data sets limit both the turnaround with which the results of research are obtained and their external validity.

More and more data are generated, but systemic barriers to their use limit their translation into policy-relevant formats, and impede the ability to render timely inferences that might inform policy and programme planning at the national and subnational levels.

Definition of triangulation

The term “triangulation” was originally coined for a method used in geographic surveying—the use of two known points in order to determine the location of a third point. In the social sciences, triangulation (Box 1) is often used to indicate the use of more than one method, or more than one source of data, and is used in a study as a way of verifying results.

Box 1. The four basic types of triangulation

- **Data triangulation:** linking different information sources involving persons, place and time
- **Investigator triangulation:** consists of using multiple, rather than single, observers
- **Theory triangulation:** more than one theoretical scheme is applied in the interpretation of the examined phenomenon
- **Methodological triangulation:** more than one methods (e.g. quantitative and qualitative) are combined

Applied to strategic information for health, triangulation refers to “data triangulation” (Box 1): the synthesis and integrated analysis of data from multiple sources for programme and policy decision-making. Triangulation differs from traditional analysis in four fundamental ways: (a) in its reliance on primarily non-statistical analysis; (b) in the use of multiple sources and types (quantitative and qualitative) of data; (c) in its principal focus on external validity; and (d) in the potential for rapid turnaround, from data collection to the presentation of the analysis and results. Implicit in this application of triangulation is that a lower threshold of proof is acceptable within a data set, as external sources are concurrently examined for relevance to the topic of interest and the results of the multiple viewpoints are integrated.

The advantages of triangulation are a reduction in the likelihood of bias and the ability to rapidly collect and analyse data needed for policy or programme decision-making. The emphasis implicit in the use of triangulation of data is on making the best of what data is available. The challenge of triangulation is that it is more dependent than statistical analysis on what social scientists describe as the researchers’ “capacity to organize materials within a plausible framework” (5).

3. HIV/AIDS IN BOTSWANA

The Republic of Botswana is a land-locked country in southern Africa that has a population of 1.64 million. The western part of the country is dominated by the Kalahari desert, with most of the population centres running along the eastern border, adjacent to South Africa and Zimbabwe. The democratically elected government is stable. The economy is dominated by the government and is primarily dependent upon income from diamond mining. Per-capita gross domestic income (GDI) was US\$ 4360 in 2004 (6). Unemployment is 23.8% and possibly higher, according to unofficial estimates. Politically and administratively, Botswana is divided into 9 districts and 28 subdistricts; however, a separate system in which the country is divided into 24 districts is used in the health services. This article uses the health services' system of districts throughout.

The HIV epidemic in Botswana

Botswana has one of the highest reported rates of HIV prevalence in the world. The annual HIV sentinel surveillance survey has been carried out since 1992 among a representative group of women attending antenatal care (ANC) clinics. HIV prevalence from ANC testing was 37.4% in 2003, and 33.4% in 2005 (7, 8). The adjusted national estimate accepted by UNAIDS was 24.0% in 2003 and 24.1% in 2005 (9). Migrant workers have been shown in some studies to be at a higher risk of HIV infection than the general population (10).

As a result of the HIV epidemic, life expectancy for women has declined from 66.9 years in 1995 to an estimated 36.6 years in 2005 (11, 12), and the population growth rate is zero or slightly negative. As indicated above, the prevalence of HIV appears to have reached a plateau or have declined since 2003.

The response to the epidemic

The Government of Botswana has taken a leadership role in addressing the HIV/AIDS epidemic, and since 2000 has aggressively scaled up the national response. Before 2000, the government response primarily focused on surveillance, social marketing of condoms, treatment of sexually transmitted infections (STI), blood safety, and information, education and communication programmes (IEC). Since 2000, the national response has been greatly enhanced by a public-private partnership, the African Comprehensive HIV/AIDS Partnership (ACHAP), between the Government of Botswana, the Bill & Melinda Gates Foundation, the Merck Company Foundation and the pharmaceutical company Merck, Sharp & Dohme.

Started in 2000, ACHAP was created to support the long-term mitigation of the impact of the HIV epidemic, including comprehensive nationwide prevention, care, treatment, and support. This system has been described elsewhere, particularly in *Introducing ARV therapy in the public sector in Botswana: case study* (13). Between 2000 and November 2005, more than 230 000 people were tested for HIV as part of the national voluntary counselling and testing (VCT) programme. The advanced state of treatment roll-out, evident government commitment to care, and documented data available were necessary components to piloting the triangulation studies with the Botswana Ministry of Health (MOH) and the National AIDS Coordinating Agency (NACA).

Organization of treatment

In January 2002, the Government of Botswana, with support from ACHAP, launched Africa's first national ART programme, "MASA", a Setswana word meaning "new dawn." MASA began providing treatment in 2002 in Gaborone, Francistown, and Ngami via adult care and via prevention of mother-to-child-transmission (PMTCT) programmes. Expansion to other urban centres was introduced in stages over the following years. Currently, ART is offered in 32 hospitals and clinics^c throughout the country. A small number of private treatment centres exist in Gaborone and Francistown.

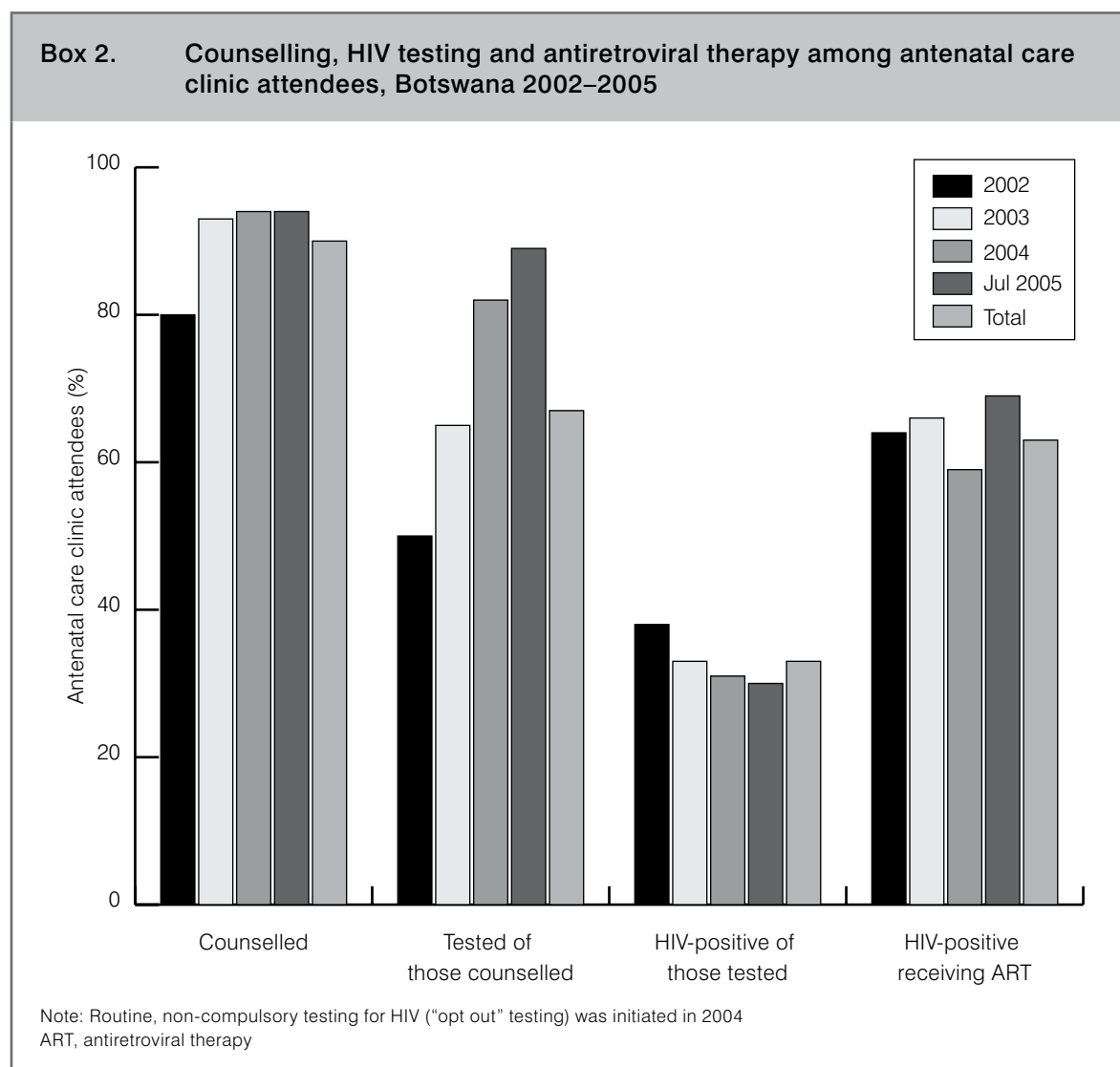
According to the MOH, 54 378 adults and 4582 children were receiving antiretroviral drugs in September 2005. This was equivalent to more than 48% of the estimated number of adults eligible for ART in Botswana (14). Of the adults receiving care, 45 554 were receiving treatment under the government MASA programme. The March 2006 WHO/UNAIDS "3 by 5" progress report gives an estimate of 67 000 to 77 000 people receiving ART in December 2005, equivalent to 85% of the estimated need (9).

^c As of mid 2005.

MASA treatment criteria give priority to pregnant women and their partners with < 200 CD4 cells per mm³ and/or AIDS-defining illnesses, to HIV-infected children aged more than 6 months in inpatient clinic wards, to HIV-infected patients with tuberculosis with < 200 CD4 cells per mm³ and then to all patients with < 200 CD4 cells per mm³ and/or AIDS-defining illnesses.

Before MASA, programmes to provide antiretroviral drugs and services to prevent mother-to-child transmission of HIV first began in 1999 and were made widely available in November 2001. Services are provided within the ANC and maternal-child health (MCH) clinic system to all pregnant women.

Roll-out of ART has been constrained owing to multiple bottlenecks in patient enrolment programmes (especially PMTCT), drug procurement, and the staffing and equipping of clinics, particularly in smaller towns and cities. Since 2001, all ANC clinics in Botswana have offered HIV screening and PMTCT. HIV testing until 2003 was performed after individual pre-test counselling, with patients actively choosing to be tested. In 2003, 60% of pregnant women receiving antenatal care were tested. In 2004, Botswana initiated a new policy for HIV testing, with routine, non-compulsory testing (i.e. patients at clinics can “opt out”) in all clinical settings. As of July 2005, 89% of pregnant women receiving prenatal care were tested (see Box 2).



Laboratory testing (for HIV CD4 count, and viral load) is largely centralized in the Gates Foundation-supported Botswana–Harvard AIDS Institute Partnership (BHP) facility attached to Princess Marina Hospital in Gaborone. The facility processes approximately 80% of all laboratory work performed in Botswana for the government. Additional laboratories exist in Francistown, and at least two private laboratories serve the private hospitals and clinics in the country. BHP processes 20 000 CD4 counts each month (July 2005).

Data sources

Many types of data are collected in Botswana. The Central Statistics Office (CSO)—a department of the Ministry of Finance and Development Planning—sets norms, consolidates data, and directly manages the Health Statistics Unit (HSU), which is located within the MOH. CSO collects census data and, through HSU, inpatient and outpatient statistics on morbidity and mortality, as well as statistics on notifiable disease, and hospital midnight census data on admissions, bed occupancy rates, and deaths.

In coordination with CSO and HSU, the MOH manages hospital data through Integrated Patient Management Systems (IMPS), and data related to HIV testing, PMTCT, tuberculosis, ANC, ART and other vertical programmes. BOTUSA, a programme run by the Government of Botswana and the United States Centers for Disease Control and Prevention (CDC), has supported the MOH in its development of an electronic registry for tuberculosis. The electronic registry and other programme databases include district-level data, which are consolidated at the ministry level. These are not linked, neither with each other nor with identification records from the Department of Home Affairs.

IMPS is a complete hospital management package, one part of which integrates electronic laboratory testing and result tracking. Approximately one third of the samples tested by BHP are linked to IMPS. As of July 2005, the software was being used by 16 sites, all of which were ART or PMTCT sites. IMPS data were not available for this analysis, but have potential for further monitoring of the impact of ART and PMTCT.

Data specific to the treatment of tuberculosis among HIV-infected patients exist both in the electronic registry for the tuberculosis programme and in treatment and research programmes jointly undertaken by the Government of Botswana and CDC via BOTUSA. A number of additional clinical studies are underway, with laboratory data consolidated at BHP.

Population survey data are principally collected and managed by CSO. The most relevant to HIV/AIDS are the Botswana AIDS Impact Survey of 2001 (BAIS I) and 2004 (BAIS II). Compilation of data from BAIS II was not yet available in the summer of 2005. Additional qualitative and quantitative data from small studies exist, but are often not centralized.

A complete list of data identified during the course of this triangulation study is given in Appendix A.

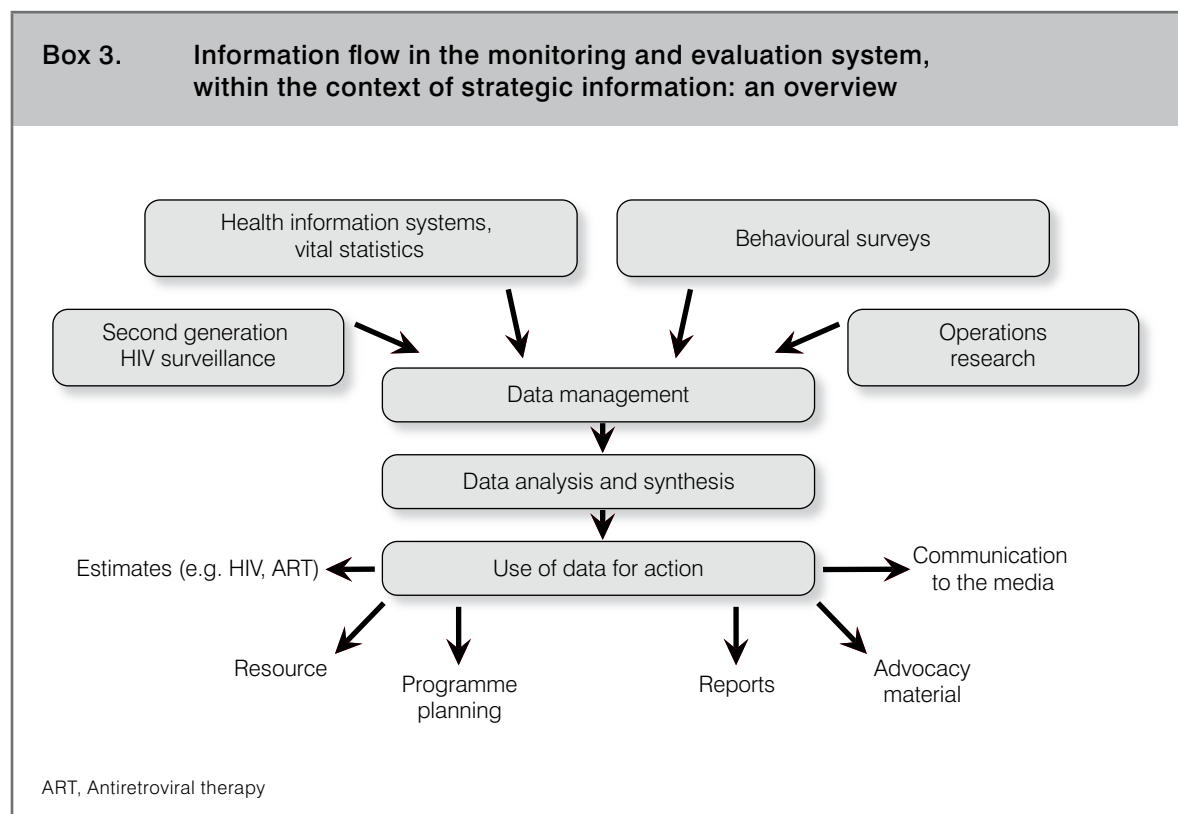
4. PLANNING THE BOTSWANA TRIANGULATION ANALYSIS

In 2005, NACA and MOH cooperated to enhance the analysis of existing data to evaluate the effectiveness of national ART and PMTCT programmes. A project was developed with the financial support of WHO, and collaborative in-country participation by WHO and UNAIDS. UNAIDS and NACA provided international and in-country coordination of triangulation planning and data collation, while the overall technical leadership came from the Institute for Global Health at UCSF.

The goals of the analysis were developed jointly in July 2005 with multiple stakeholders^d in a series of meetings to prioritize areas of study and to identify data sources. Specific study topics were revised in light of the availability or quality of data. The agreed goals were to measure the population-level effect of ART and PMTCT roll-out in Botswana. Mortality was agreed upon as the primary indicator of intervention effect, while additional measures of programme effectiveness were examined as potential modifiers and confounders.

Background for triangulation among partners

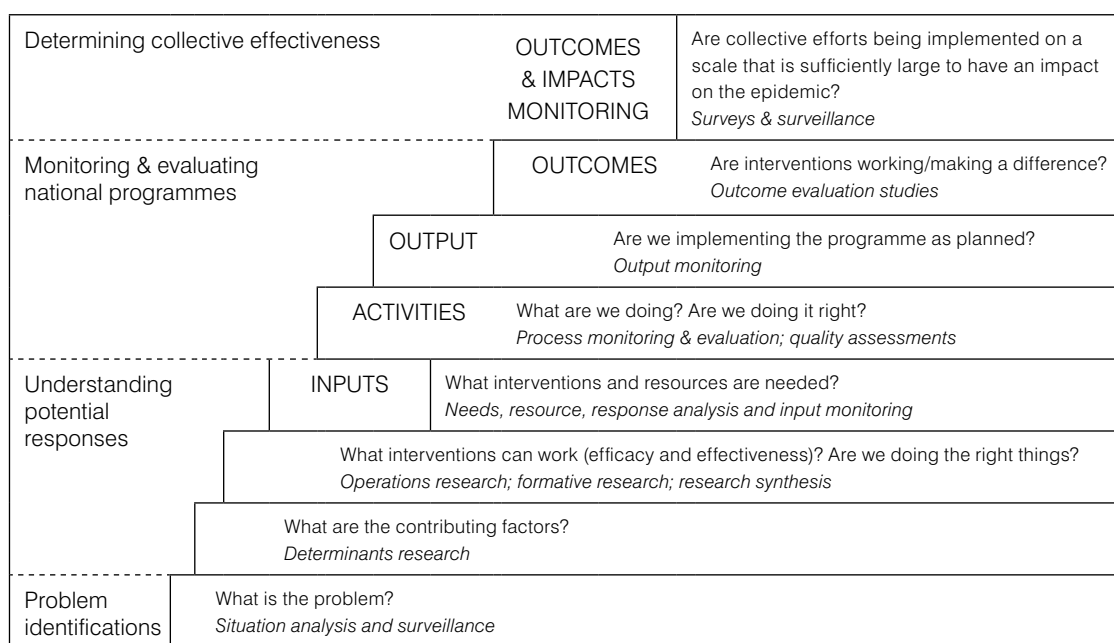
The flow of information (Box 3) in health programming is well understood. The effective use of strategic information at multiple programmatic and policy levels had been effected by many of the partners in the previous 5 years. Use of data at differing levels has been categorized in the “stair-step model” (Box 4) by CDC and applied in numerous countries.



^d MOH, NACA, the Ministry of Local Government (MLG), CSO, UNAIDS, WHO, BOTUSA, UCSF, and others were represented.

Triangulation is an established analysis methodology in the United States of America (USA), and researchers at UCSF have applied triangulation methodologies in countries around the world since 1990. The methodology has become progressively more structured and reproducible over time. The enthusiasm of participants and the demonstrated capacity of its national AIDS programme made Botswana an ideal location in which to test the application of a formal triangulation process. The high rates of HIV prevalence in Botswana and the widespread and growing coverage of ART programmes offer opportunities for obtaining unambiguous results regarding impact. Botswana, more than many countries, has large amounts of data, well-collected, often consolidated, and with sufficient overlap to allow for verification of some critical topics. HIV policy in Botswana is dynamic, as indicated by the recent decision to make HIV testing an “opt-out” standard (15). Because the Government of Botswana is small and centralized, ministries and international agencies working on service provision, data collection and management and policy and research know each other and are able to collaborate with comparative ease.

Box 4. Use of strategic information – the stair-step model



Adapted from: U.S. Centers for Disease Control and Prevention (CDC)

5. THE PLANNING PROCESS

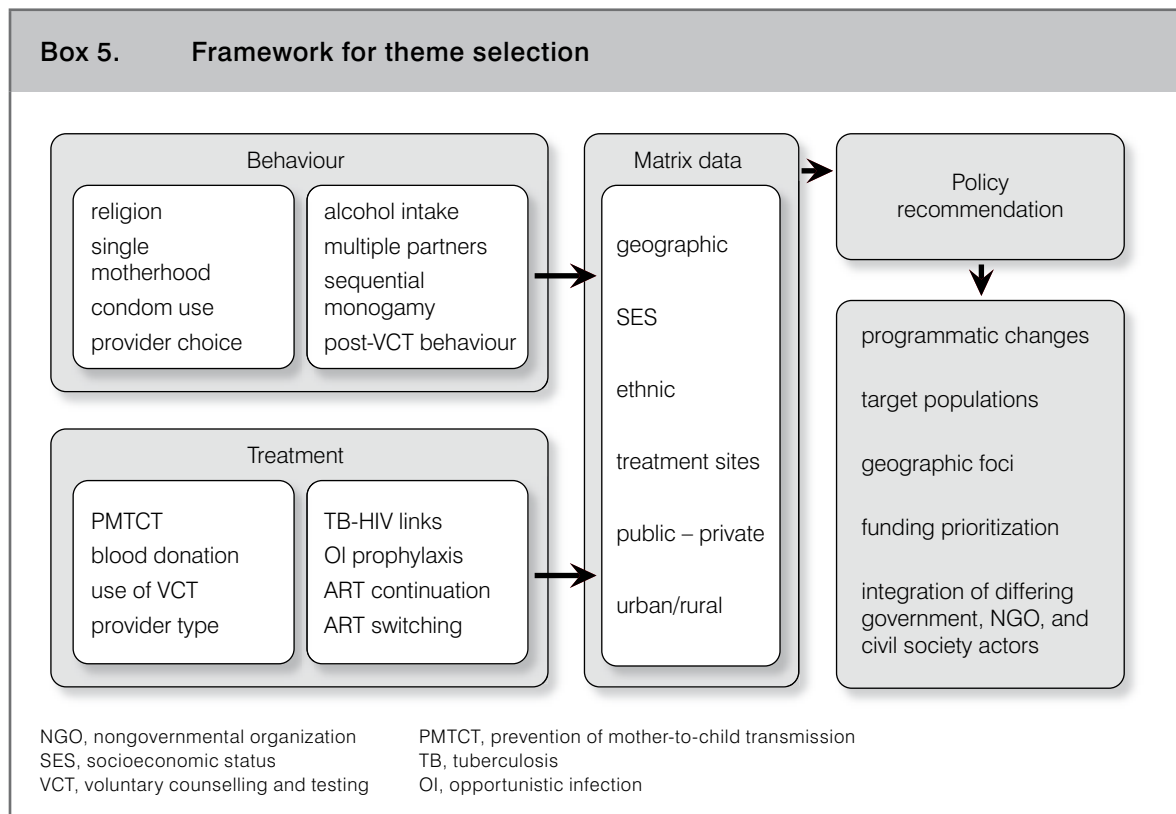
Engagement of partners began during the planning phase for the triangulation study. NACA, MOH, WHO, and UNAIDS jointly agreed on timing and identified stakeholders with interest, capacity and access to data. NACA took the lead, in close collaboration with MOH, to bring together stakeholders and assure that as wide a net as possible was cast in identifying potential data sources.

During the initial planning clinics, local geographic information systems (GIS) consulting agencies and a range of other organizations and institutions were polled for their views on current data use for themselves and for the national AIDS programme, and on the content and availability of their own data.

The principal stakeholders and an abbreviated description of their primary responsibilities relevant to HIV/AIDS are shown under Acronyms, at the start of this case study.

Planning and goal setting

In June 2005, stakeholders from Botswana national and district bureaux and international partners held a series of half-day meetings to agree on priority goals for the triangulation study. Beginning with a framework for prevention and treatment initiation and effectiveness (Box 5), based on Boerma & Weir's proximate determinants model of HIV/AIDS effect (16), the group listed and discussed a number of issues related to both behavioural and clinical inputs that were of recognized current importance.



Themes

Working from the issues enumerated, the stakeholder group produced a hierarchy of critical themes for triangulation analysis based upon the likely availability of data and the importance to setting new or revising existing policies and programmes. A number of important issues that had been cited were eliminated owing to lack of existing data, most notably the impact of religion, single mothers and changes in risk behaviour after HIV testing.

Retained on the table were the importance of behavioural issues related to condom use, alcohol intake and multiple partners and treatment effects stemming from PMTCT roll-out, the shift from routine to opt-out HIV testing, prophylaxis

with isoniazid for tuberculosis in HIV-infected patients, the direction of increased susceptibility to infection between HIV and tuberculosis, ART effectiveness, and the incidence of opportunistic infections among adults receiving ART.

Of these broad themes, isoniazid effectiveness was eliminated, as this was the subject of an ongoing large BOTUSA-led clinical trial. Lack of available data eliminated HIV–tuberculosis linkages and post-ART infection, while uncertainties about the data that would be available from BAIS II led to the decision to set aside the three behavioural questions of alcohol intake, condom use and multiple partners, and the influence of these on HIV dynamics.

Through this process of elimination, a consensus was reached that, of the issues for which sufficient data existed to allow study with triangulation methods, the effectiveness of ART and PMTCT programmes were of the highest priority for policy-makers.

Questions

Although extensively documented in small populations, clinical trials, and in developed countries as well as in Brazil, the effectiveness of ART in reducing population mortality from AIDS in sub-Saharan Africa has never been established. The priority among stakeholders was to use triangulation methods to ascertain the applicability of these methods in Botswana. It was agreed that analysis of programmatic strengths and weaknesses was important, but secondary to the broader policy questions of the impact of ART on mortality were resolved.

Morbidity, and rates of incidence for HIV and HIV-related opportunistic infections and clinical presentation were all considered for study and discarded at the present time. There was consensus that the most significant measure of programme effectiveness would be decreased mortality, both among adult recipients of ART and among neonates and infants through PMTCT programmes.

The availability of well-documented ART programmatic data, combined with credible vital registration statistics on mortality and an institutional setting (i.e. in hospitals or health-care clinics) for more than 90% of births and deaths, made it likely that if a relationship between declining mortality and ART programme roll-out existed, it could be documented.

Data identification and collection

Identification of potential data sources, database managers and actual data was an iterative process that began with the first stakeholders' meeting in July 2005 and continued until January 2006. Cleaning data—identifying gaps in data or erroneous entries—took place in Botswana and at UCSF, beginning in October 2005 when the first data were transmitted to the researchers.

While the initial identification of data sources was efficient, large investments in time and effort by researchers and officials at differing levels of authority were required to gain authorization for, and access to, the data themselves. This process was a significant challenge to colleagues within Botswana as a result of ongoing demands upon their time and the political considerations implicit in requesting data belonging to other branches of government. To access the most recently collected data required making special arrangements for CSO staff to work outside of normal hours and manually duplicate data sets. Difficulties in clarifying who had ultimate responsibility for differing data sets also led to delays in obtaining data.

Once accessed, there remained difficulties both in standardizing the data format, and in identifying and understanding problems with the data themselves. Discrepancies between, for example, national mortality figures (which dipped in 2002) and hospital mortality figures (which did not) were difficult to reconcile. Many discrepancies remained unresolved for some time because of the need for leadership by accountable officials in order to have open discussions about the possible reasons for conflicting data.

Leadership by high-level administrators from NACA, CSO, and MOH was of paramount importance throughout this period of data collection, collation and cleaning. The presence of the research team on-site and intervention by policy-level personnel were critical to assure the validity of the analysis outcomes. A timeline of data collection visits and planned checkpoints is given in Appendix B.

6. TRIANGULATION ANALYSIS AND FINDINGS

There is substantial empirical evidence that antiretroviral drugs can reverse immunodeficiency and premature mortality among patients with severe HIV-related disease, and reduce the risk of mother-to-child HIV transmission in conjunction with alternative infant feeding practices. Successful ART and PMTCT programmatic efforts are expected to lead to a reduction in adult and child and infant mortality.

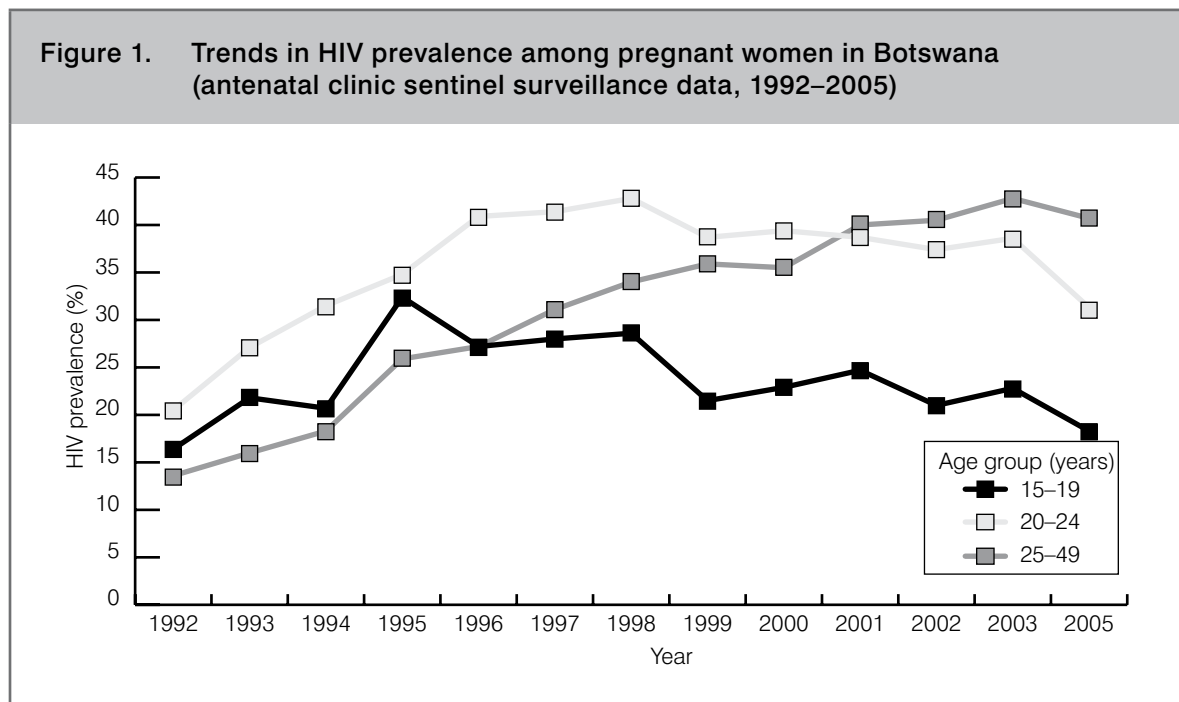
This case study provides an overview of the analysis context and findings. A more complete review of the methods used and findings (with HIV-testing data) is given in the analysis report, which is included in Appendix E.

Methodological overview

The basic analytical approach to measuring the impacts of ART and PMTCT programmes on adult and child mortality involved four stages. First, we analysed Botswana mortality statistics from the HSU to verify evidence for the impact of HIV on adult and child mortality over time and by district and in institutional settings. Secondly, we used consolidated data on hospital mortality from MOH midnight census to verify the census statistics. Next, we analysed data from the MOH ART programme, measuring cumulative numbers of persons currently receiving ART by district since 2003; and PMTCT programme indicator data from the MOH MCH unit measuring the numbers of women receiving ART during postpartum care, and infants receiving postpartum ART and formula feeding. Data were analysed overall and by district over time. The fourth analytical stage to assess potential ART impact on adult mortality involved the comparative analysis of use of antiretrovirals in adult patients and trends in adult mortality over time and by district. To assess the impact of PMTCT programmes on infant and child mortality we compared the numbers of HIV-infected women and their offspring who received ART pre- and postpartum, respectively, and trends in infant and child mortality overall and by district over time.

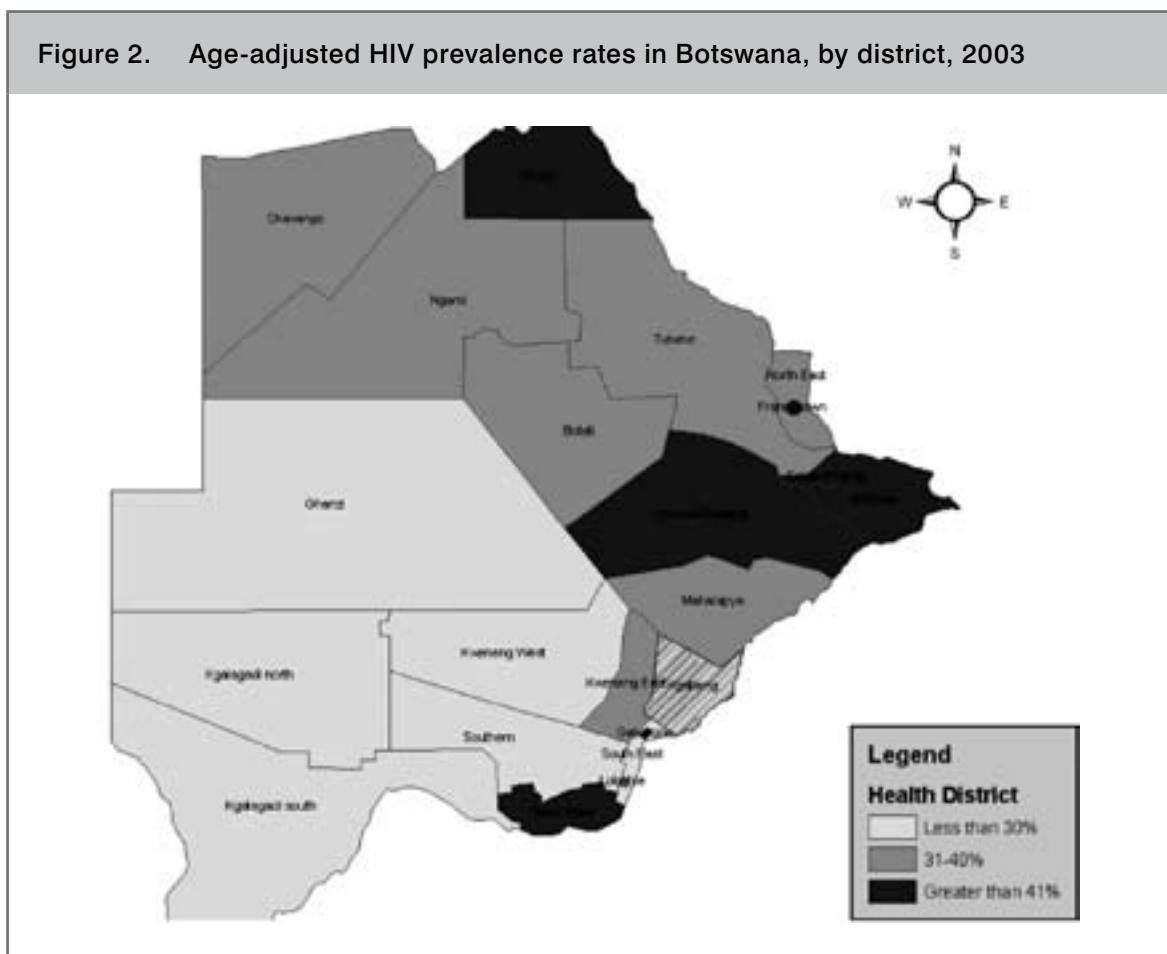
Trends from data

Trends in HIV prevalence among pregnant women surveyed through sentinel surveillance overall, and by age, from 1992 to 2005 are shown in Figure 1.



Preliminary analyses of these data suggest a significant decline in HIV prevalence, from 36.2% in 2001 to 33.4% in 2005.^e The trend between 1992 and 2003 shows rapid increases in prevalence rates across all age groups, with stabilization in prevalence among young people aged 15–24 years since the late 1990s, and continued increases in prevalence among people aged 25–49 years through 2003. However, between 2001 and 2005, HIV prevalence rates among those aged 15–19 years and 20–24 years had apparently decreased by 28% (from 24.7% to 17.8%) and 21% (from 38.7% and 30.6%), respectively. These findings suggest a recent decline in HIV incidence in younger age groups, which warrants further careful analysis to better understand the potential reasons. Age-adjusted HIV prevalence rates for 2003 varied geographically and ranged from 52% in Selibe-Phikwe district to 21% in the more rural Gantsi district. In eight districts, the prevalence was greater than 40% (Figure 2).^f

Figure 2. Age-adjusted HIV prevalence rates in Botswana, by district, 2003

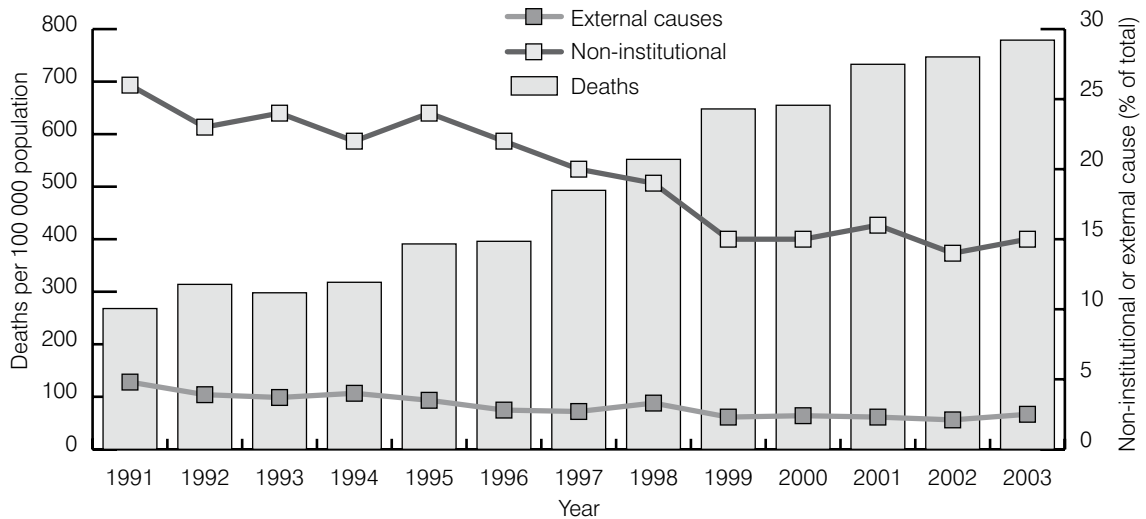


Concurrent with increasing HIV prevalence rates, crude mortality rates increased nearly threefold between 1991 and 2003, while the proportion of those deaths that were reported from non-institutional settings or attributed to external (non-natural) causes decreased from 26% to 15% and from 5% to 2.5%, respectively (Figure 3).

^e The original value for 2003 used by the MOH and UNAIDS was 37.4%. This has been revised down in the current WHO/UNAIDS “3 by 5” progress report.

^f Because the adjusted numbers were only publicly accepted for the country as a whole in March 2006, this report uses the unadjusted numbers from ANC testing throughout, in order to permit analysis of district-level data.

Figure 3. Crude mortality rates and the percentage of deaths reported from non-institutional settings or from external causes, Botswana 1991–2003



The distribution of deaths by age between 1991 and 2003 indicates that mortality increases are greatest among adults aged 25 years and older, with a fourfold increase among those aged 25–44 years (Figure 4). Mortality rates among those aged 15–64 years, stratified by sex, indicate similar trends in mortality; however, rates in males are consistently higher than in females. The average male : female rate ratio for 1991–2003 is 1.2 : 1 (Figure 5).

Figure 4. Age-specific mortality at age 5 years and above, Botswana 1991–2003

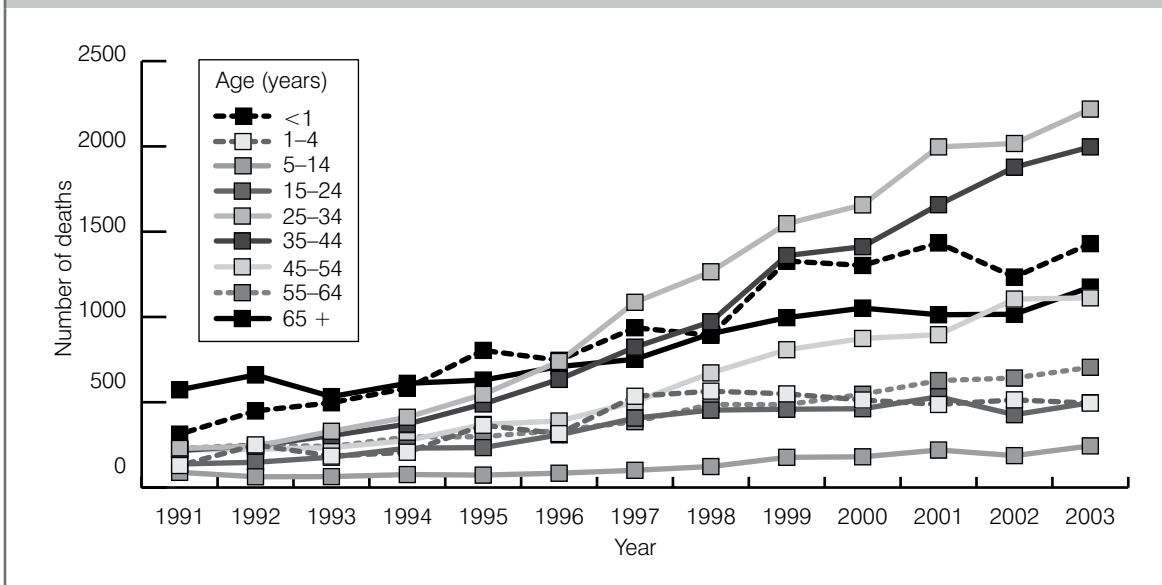
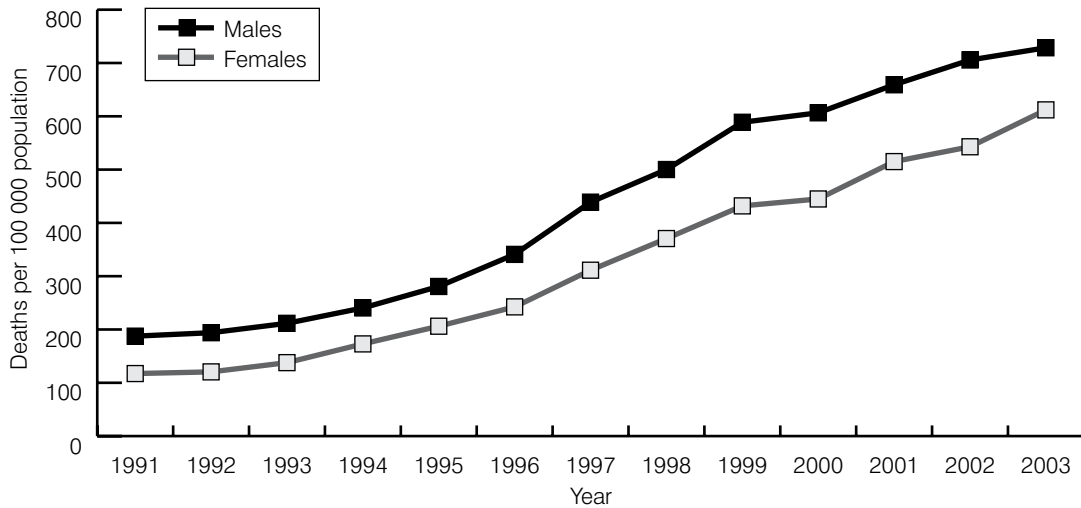
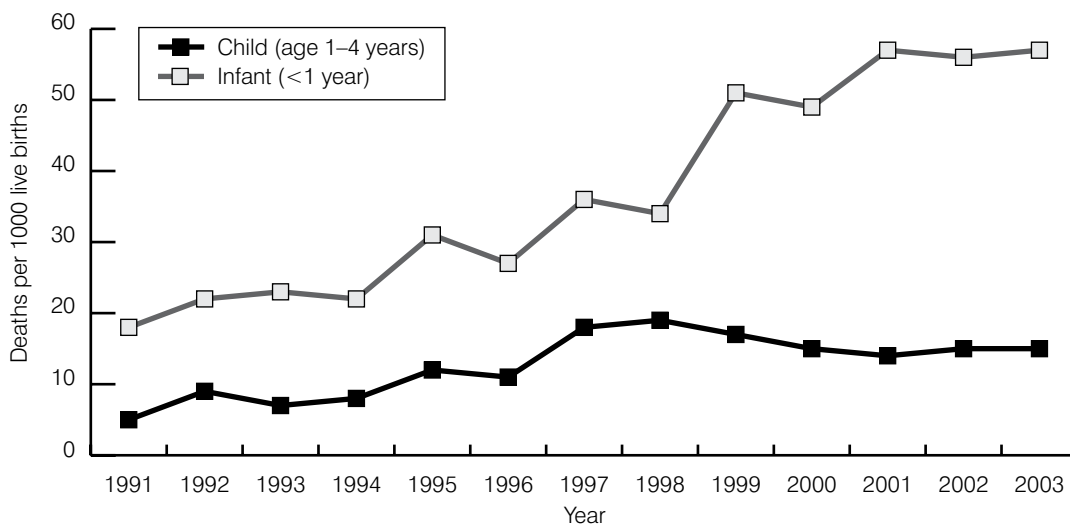


Figure 5. Mortality rates at age 15–64 years, by sex, Botswana 1991–2003



Similar increases in mortality are evident among children. Infants are defined as those aged less than 1 year and children as those aged more than 1 year and less than 5 years. Infant mortality rates increased from 17 deaths per 1000 live births in 1991, to 56 deaths per 1000 live births in 2001, and have remained stable through 2003; child mortality rates doubled during 1992–1997, and stabilized thereafter (Figure 6).

Figure 6. Infant and child mortality rates, Botswana, 1991–2003



HIV/AIDS became the leading cause of institutional deaths in 1996. Between 1992 and 2003, the proportion of deaths in which HIV/AIDS was causally implicated increased by more than sixfold, from 3.9% to 26.7%. Similarly, the number of deaths attributed to HIV/AIDS in infants and children increased from 4% to 13.4% and 4% to 9% respectively, between 1992 and 2003. Other causes of death likely to be related to HIV disease, but which were attributed to pneumonia, tuberculosis, and ill-defined conditions, also increased by similar orders of magnitude over the same period.

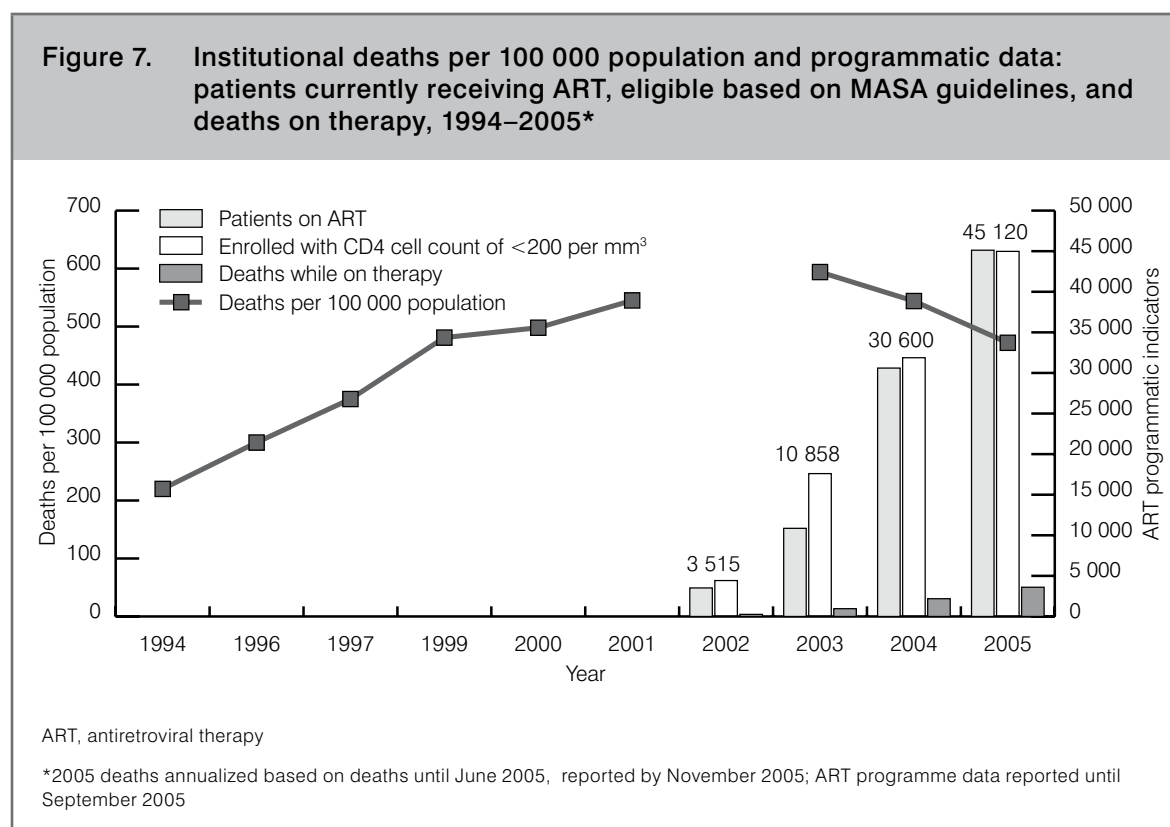
Verification of key indicators

A comparison of institutional deaths (excluding neonates) abstracted from annual health statistics reports, deaths from vital registration data files and deaths (of persons aged more than 28 days) recorded in the nightly midnight census from 1991–2003 provides a reasonable validation of the accuracy of institutional mortality trends and their potential for measuring the impact of ART or PMTCT programmes (Figures 7 and 11, Appendix E).

Empirical evidence for coincident increasing trends in mortality in children and young adults, HIV prevalence in pregnant women, and AIDS as reported cause of death, coupled with similar patterns of the impact of HIV-related mortality in neighbouring South Africa and elsewhere provides compelling evidence that the HSU-CSO vital registration system provides reasonably accurate evidence for the demographic impact of HIV/AIDS on population structure over time in Botswana (17).

ART impact on adult mortality

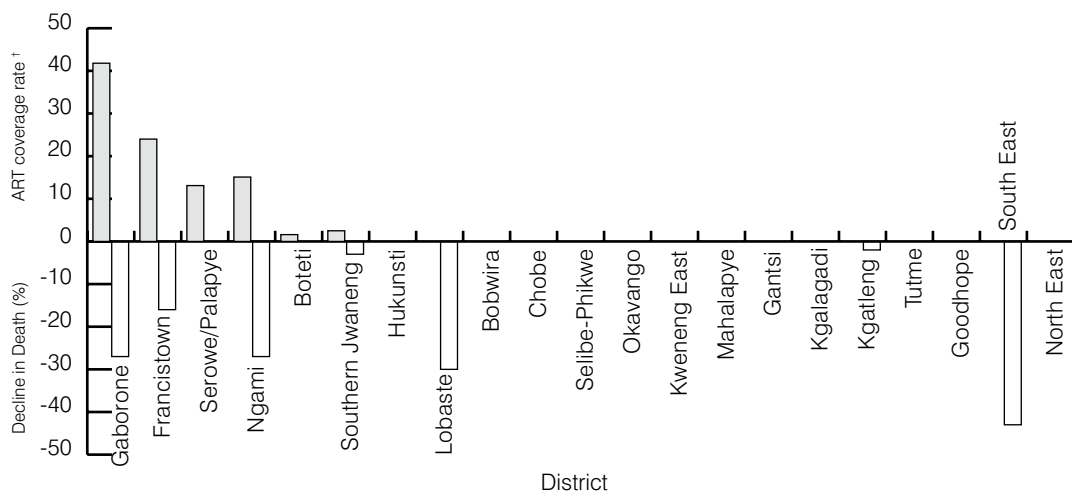
Trends in rates of institutional deaths reported from vital registration from 1994 to 2005 (incorporating updated deaths from 2004 until June 2005) are shown in relationship to ART programmatic data in Figure 7. Mortality rates stabilized in the early 2000s and decreased by 8% between 2003 and 2004, and 20% between 2004 and 2005. This decrease was coincident with increasing numbers of patients receiving ART, beginning in 2002. Data for 2002 are not shown as reporting of data in 2002 was incomplete (vital registration files were only available for 11 months). Data for 1995 and 1998 were not available for analysis.



Age-specific deaths and death rates between 2004 and 2005 declined substantially in age groups 20–49 years (Appendix E Figure 13A). This contrasts with older and younger age cohorts, for which death rates remained relatively stable during this same period.

A comparison of ART coverage rates by district and changes in mortality rates for people aged 20–49 years between 2003 and 2004 by district reveal that mortality declines were evident in 29% of districts, ranging from a 43% decline in the South East district to a 2% decline in Kgatleng (Figure 8A, 8B and Table 1). Mortality declines were associated with high rates of ART uptake (Gaborone, Francistown and Ngami) or with close geographic proximity to Gaborone (Lobatse, Southern Jwaneng, South East and Kgatleng). Mortality rates in districts without early ART sites in 2002–2003 continue to increase. This is consistent with the analysis of technical staff who were consulted regarding ART roll-out, who described a common practice of migration to treatment sites in the initial phase of the ART programme. This implies that access to care is reflected by treatment sites located in a patient’s province, or treatment sites located in an adjacent province, at least during the early years of the programme.

Figure 8A. Declines in mortality rates for people aged 20–49 years between 2003 and 2004, and 2003* ART coverage rates by district



* All data is from July 2003
 † ART coverage rate per 100 000 population aged 20–49 years
 ART, antiretroviral therapy

In Gaborone and Francistown—districts that had 36% of the cumulative national mortality burden in 1999–2004, had early site-opening dates, and had the highest rates of persons receiving ART—mortality declined by 27% and 17%. Both sites exhibit similar patterns of mortality: declines in those aged 20–49 years, and relative stability in older and younger age groups (Figure 9). In addition, overall mortality trends from vital registration and from hospital midnight census data reveal similar declines through 2004, providing some degree of validation that the trends are not related to reporting biases or inaccuracies in the vital registration system.

Figure 8B. ART coverage in patients aged 20–49 years, by district, 2003–2005

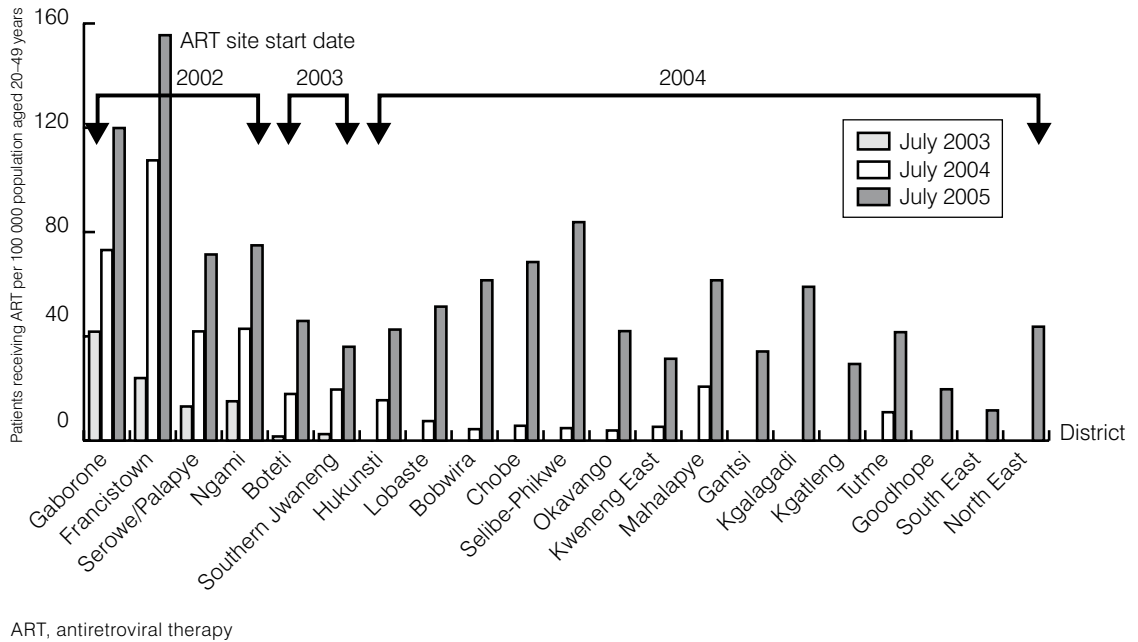
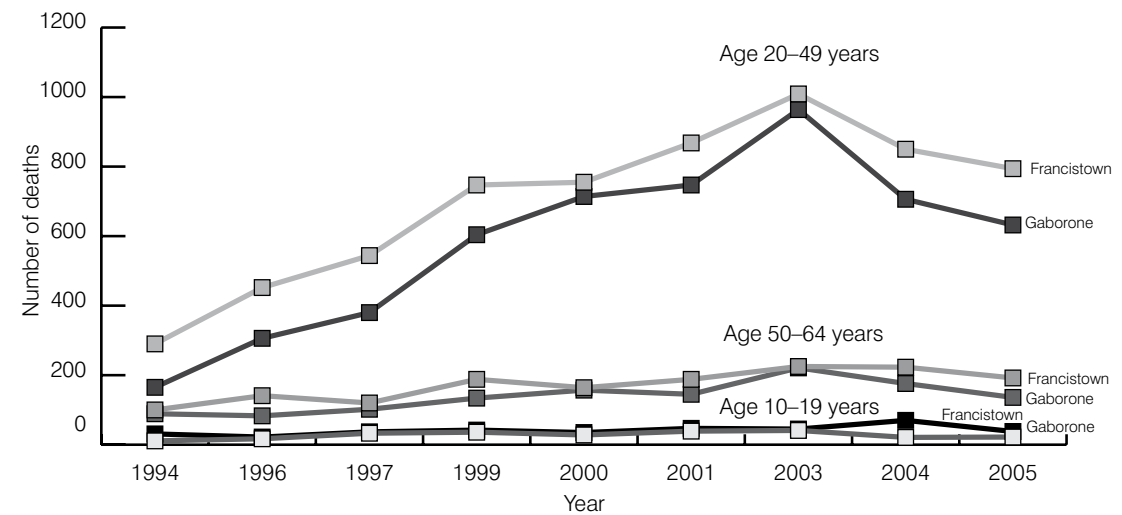


Figure 9. Trends in institutional mortality by age, from vital registration, Gaborone and Francistown, 1994–2004



We further examined the association between district-level mortality changes between 2003 and 2004 and ART initiation date and coverage rates, as illustrated in Figures 8A and 8B and in Table 1. After weighting for population size, the decline in district-level mortality is significantly correlated with the date of initiation of district ART programmes ($P < 0.05$) and with the district-level ART coverage rate in July 2004 ($P < 0.05$), although colinearity between these two prevents their integration in a single analysis.^{g, h}

Table 1. Mortality rates at age 20–49 years per 100 000 population between 1994 and 2004, and change (%) in rates between 2003 and 2004 by district relative to rates of persons on ART* and the district mortality burden[†]

District	ART rate* July 2004	Percentage of cumulative mortality 1994–2004	Deaths per 100 000 population aged 20–49 years									Change (%) 2003–2004
			1994	1996	1997	1999	2000	2001	2002	2003	2004	
South East	0	3	137	94	184	346	429	512	462	498	281	-43.5
Lobaste	7	5	430	483	860	1302	1236	1574	1375	1402	985	-29.7
Ngami	75	5	173	293	453	502	686	817	686	1029	753	-26.8
Gabrone	120	17	153	283	351	558	660	690	702	891	654	-26.6
Gantsi	0	2	173	128	488	510	315	443	398	758	630	-16.8
Francistown	156	19	693	1080	1299	1784	1803	2073	2011	2410	2030	-15.8
Southern	20	5	94	189	343	488	207	570	314	605	583	-3.7
Kgatlang	0	3	40	109	182	496	449	478	376	361	354	-2.0
Kgalagadi	0	1	106	213	319	590	513	503	435	648	658	1.5
Chobe	6	1	103	354	114	343	629	663	572	652	675	3.5
Mahalpye	21	7	184	344	493	788	831	991	880	842	891	5.8
Boteti	18	3	110	143	236	333	367	497	447	632	678	7.3
Bobwira	4	3	115	387	315	435	549	745	740	745	807	8.3
Serowe/Palapye	71	8	155	308	426	522	654	597	631	774	849	9.6
Hukuntsi	16	1	0	0	16	0	356	356	340	486	534	10.0
Kweneng East	5	6	83	127	118	236	347	354	319	379	420	10.8
Selebi Phikwe	5	5	301	270	582	683	748	887	883	822	929	13.1
North East	0	2	7	0	7	110	589	534	603	582	705	21.2
Tutume	0	3	11	159	234	276	309	309	351	482	610	26.6
Okavango	0	1	118	176	341	188	200	323	317	312	400	28.3
Goodhope	0	1	0	130	178	0	410	437	396	417	553	32.8
Total	—	100	161	271	374	533	594	687	640	773	713	-7.8

* ART rate = cumulative number of patients on ART/100 000 population aged 20–49 years

[†] District mortality burden = % of cumulative mortality 1994–2004

g "Colinearity" refers to spurious associations or lack of associations in a multivariable model that result from excessive correlation of covariates with one another.

h High variability in mortality data, particularly in districts with low populations (as in Gantsi district), is potentially the result of either true fluctuations in mortality or of problems with data quality. We have not adjusted for this variability at this stage of the analysis, except to weight by population size.

Summary: evidence for the impact of ART on adult mortality

Our country-enhanced monitoring and evaluation provide reasonable evidence of an association between ART scale-up and declines in adult mortality from 2003 to 2004. Preliminary vital registration data from 2005 provide further empirical support; however, updating the vital registration data to include reported deaths through 2005 and 2006 to date, as well as validation of mortality reporting at key hospitals and perhaps using the vital registration database in the Department of Home Affairs will be useful to confirm findings. Trends in district-level rates of mortality should also be further investigated in "outlier districts", such as Serowe/Palapye, where ART uptake is apparently quite high, yet mortality continues to increase.

Furthermore, our investigation indicates that vital registration data, if analysed in a timely manner, can provide a reasonable HIV morbidity and mortality surveillance system at the national and district level. In addition, it could be exploited to monitor the effectiveness of ART programmes and HIV dynamics overall and by district.

PMTCT impact on infant or child mortality

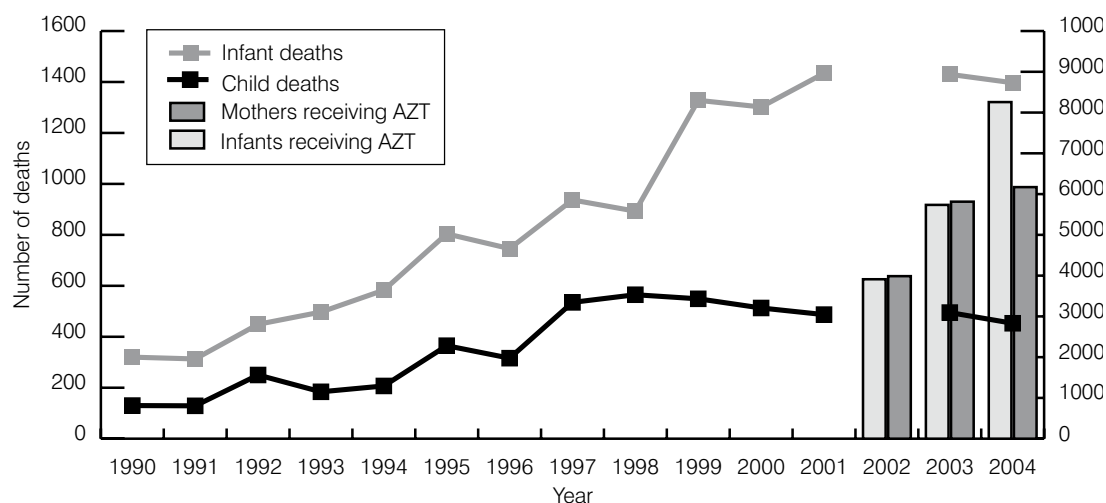
Mother-to-infant transmission of HIV at birth can be reduced from 35% in the absence of treatment to approximately 16% with the provision of single dose of nevirapine. The addition of a short course of azidothymidine (AZT) can further reduce HIV transmission rates to approximately 8%. In all cases, transmission rates increase when the mother breastfeeds, with longer duration of breastfeeding associated with increased transmission. Maternal treatment with highly active retroviral therapy (HAART) during breastfeeding is a significant barrier to mother-to-child HIV transmission (18). The effectiveness of such an intervention by PMTCT programmes should be evident in the reduction of HIV mortality among children.

According to PMTCT programme indicator data collected between 2002 and 2005, of 158 378 pregnant women presenting at ANC clinics, 90% were given HIV preventive counselling, 67% of those counselled were tested for HIV, and of these 33% (32 838) were HIV-positive. Of those infected with HIV, 64% (21 005) were provided with preventive ART (Box 2). The annual proportions of pregnant women counselled and tested have shown a steady increase between 2002 and 2005; however, the proportion of HIV-infected women receiving antiretroviral preventive interventions has remained relatively stable, between 64% and 69%. During the same period, indicators for maternity-related PMTCT interventions show substantial increases in programmatic coverage: decreasing numbers of deliveries to mothers of unknown HIV status, and increasing number of newborns treated with antiretroviral drugs.

The demographic impact of HIV on mortality is similarly evident in children: disaggregating total deaths in children aged less than 5 years shows that the proportion of deaths in neonates and infants aged more than 28 days has increased significantly since the early 1990s, most likely reflecting HIV-associated mortality.

Figure 10 shows trends in institutional deaths in infants (excluding neonates) and children aged 1–4 years from 1990 to 2004 and PMTCT indicators of AZT use in HIV-infected mothers and their newborns from 2002 to 2004. Trends in infant and child mortality show linear increases followed by stabilization in 2000 and 1998, respectively, and a modest decline of 2% in 2003–2004 for both groups. The numbers of pregnant women treated with AZT pre-partum and infants treated at birth both increased from 2002 to 2003. However, the rate of increase in numbers of mothers treated pre-partum with AZT declined sharply relative to the similar treatment of infants between 2003 and 2004.

Figure 10. Institutional infant and child mortality compared with PMTCT indicators for AZT use in mother and infants, 1990–2004*



* 2002 mortality data is incomplete and not displayed

Based on preliminary mortality data reported through July of 2005 (not shown), declines in numbers of deaths in children aged less than 5 years continue. However, high variability in reported numbers of deaths, coupled with concerns regarding reporting completeness complicates the interpretation of declining trends similar to those seen in adults. As a result of unexplained variations within data sets and between district PMTCT data sets, no firm conclusions can be drawn regarding trends in treatment.

Follow-on work from this analysis should include a complete audit of PMTCT data, with sentinel sites to include validated and active reporting of mortality.

Summary: evidence for the impact of PMTCT interventions on mortality in children aged less than 5 years

This analysis provides little evidence for substantial decline in numbers of infant or child deaths from 2002 through 2004. Preliminary analysis of mortality data for 2005 suggests that infant and child mortality have declined in some districts; however, under-reporting of deaths in 2004–2005 is a concern that may confound trend interpretation. A further validation of mortality data for 2005 and 2006, as well as audits of PMTCT indicator data, should provide insight into evidence for potential PMTCT or ART programmatic impacts, or reasons for their absence. In addition, the relative stagnation of antiretroviral preventive interventions at around 60–70% is of particular concern and requires further investigation.

Conclusions and implications

ART is reducing the rate of mortality among adults in Botswana. There are indications that the effects of ART on mortality are evident as early as 1 to 2 years after widespread availability of ART within a region. The effects of PMTCT remain unclear, although it is not certain if this is attributable to a lack of effect or limitations of the data.

From the findings of this analysis, we conclude that ART is an effective way of reducing excess mortality attributable to AIDS in Botswana, and that the protocols for prioritization of treatment that are in place in Botswana have been effective in directing care to treating patients who benefit from therapy.

The findings suggest that expansion of ART coverage will continue to reduce numbers of deaths in Botswana. Additional information is needed to determine whether the apparent lack of effect on infant mortality is a product of missing data, the result of ineffective targeting, lack of access to care for individuals most at risk or is a true finding. The lack of improvement in PMTCT treatment initiation among HIV-infected pregnant women, unchanged despite significant increases in testing during ANC visits, remains a concern and merits further exploration.

7. CAPACITY BUILDING

The analyses reported above were conducted collaboratively with partners from a number of agencies in Botswana. The methodology used to identify, collect, organize, analyse and interpret data formed the basis of a 1-week training course in Botswana for researchers, programme managers, and policy-makers from district and national stakeholder institutions, conducted jointly by researchers from UCSF and CDC in January 2006. This training was practicum-based, using data from Botswana as the basis for analyses conducted by participants. For many participants this was the first opportunity they had had to view data from other agencies, and their interpretation and insights added greatly to the researchers' understandings of what programmatic and individual behaviour lay behind the shifting numbers of testing, treatment and deaths.

As one example, participants' insights regarding migration or "commuting" for ART treatment during the early months of programme roll-out helped to explain some variability in hospital-reported ART uptake and mortality during this period.

Continued capacity building is likely to be necessary before triangulation methodologies are integrated into use at the national level in Botswana. The principal challenges to be overcome in the future have more to do with institutional comfort with data sharing than with the individual capacity of technical staff in Botswana. Data sharing is still uncommon and considerable time and energy by upper-level administrators is required to assure access to data from other departments. Once data has been accessed, the variability of triangulation methods, dependent as they are upon the kinds of data available to respond to each specific question, require flexibility in the processes used to clean individual data sets, verify specific sources through comparative indices, and methodically go through the steps of population, geographic, and temporal analysis set out in the simplified standards developed by UCSF (see draft worksheet in Appendix D). This flexibility is likely to come primarily from experience, rather than simply from training.

Building upon the concepts transferred in the January 2006 training course, the partners involved are planning future collaborative triangulation exercises, with the lead in data identification and analysis to be taken progressively by the Botswana partners. It is expected that a small number of such collaborative studies will be sufficient to ensure capacity for triangulation studies among the technical analysts involved, and an appreciation of the value of these studies among administrators and policy-makers in the respective institutions. Together, this is expected to be sufficient to assure data availability and appropriate use at the national level. Of particular interest is the potential use of IPMS data for ongoing systematic analysis. An example of this that is being planned at the present time is a cohort analysis to study survival of patients receiving ART, as a complement to this triangulation study.

The constraints of technical capacity and access to multiple data sources in useable formats are such that application of triangulation at the district level is unlikely to be developed in the near future. Notwithstanding this limitation, training of district staff in triangulation methodologies has been very useful in ensuring their ability to understand the value and limitations of this analysis and to properly interpret and communicate the results of analysis studies to their local constituents.

8. CONCLUSION

Triangulation, which has been used successfully in other countries, is well suited to investigate the impact of Botswana's HIV/AIDS programmes. This study showed that triangulation is a sufficiently mature methodology to be standardized, transferred and applied effectively in different settings. The only requirement is the existence of multiple sets of data providing insights into the programme, policy or disease under study.

The application of an integrated triangulation analysis exercise and training programme demanded coordination and scheduling, which added constraints to the normal process of data collection and analysis. This created challenges for the researchers, but paradoxically, many of the most perplexing questions raised by the data were either answered or further directions for study were suggested during discussions that took place with participants (various stakeholders, including policy-makers and analysts) during the triangulation training course. This experience made clear for all parties the need for ongoing collaboration with multiple stakeholders during the analysis and interpretation phase. Replication of the triangulation study carried out by partners is possible, but is likely to necessitate at least one additional collaborative session before triangulation can be fully institutionalized in either NACA or the MOH.

Effective triangulation requires significant commitments of time and energy by researchers, analysts and programme or policy-makers. This was underestimated in Botswana, with the result that additional time was required late in the project to follow up on commitments and support the transcription and collection of various data. At the level of programme management, both in the district and within vertical programmes, capacity for detailed analysis of data and the empowerment of analysts and managers to identify and make use of data outside of their own ministry or department are constrained. Ensuring the effective use of data at local levels will require training and leadership from central government.

Triangulation proved conceptually accessible to a range of policy-makers, programme managers and analysts at central and district levels. This was confirmed as a particular strength of this method, in particular owing to the emphasis on visual presentation of data during the analysis.

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APPENDIX A DATA AVAILABLE AS OF NOVEMBER 2005

Type of data	Used?	Source	Year
National second generation surveillance data (ANC and PMTCT programme trends)	✓	MOH	1992–2003
HIV prevalence estimates, ages 15–49 years	✓	CSO, sentinel surveillance report	2003
Vital statistics (deaths and births)	✓	MOH health statistics; and CSO vital registration annual reports and computer databases	Mid 1980s–2005 vital registration reports; 1994, 1996, 1998–2003 database
Midnight census data (admissions, live births and deaths)	✓	MOH health statistics from all hospitals	1990–2004
ART programme data (cumulative No. enrolled, cumulative No. receiving therapy, and reported deaths of those receiving therapy)	✓	MOH ART programme	2003–present
Maternal PMTCT indicators	✓	MOH MCH units; facility monthly reports from MCH units	2002–June 2005
Antenatal PMTCT indicators	✓	MOH MCH units; facility monthly reports from MCH units	2002–June 2005
No. of new ANC attendees	✓	MOH MCH units; PMTCT data facility monthly reports	2002–June 2005
Census data (population estimates)	✓	Census Bureau	1991–2001
HIV/AIDS Behavioural Survey (BAIS) relevant to HIV testing	✓	CSO	2001, 2004
VCT programme data (No. tested, No. positive, reasons for testing, much more)	✓	Tebelopele VCT centres (NGO)	2000–2005
Routine testing data (tests performed and results)	✓	MOH	2005
Hospital patient data (IPMS; available for a limited number of hospitals)		MOH	2005

APPENDIX B DATA COLLECTION SCHEDULE

Task/data	Source	Jul. 22	Aug	Sept	Oct	Nov	Dec-March 06
Work plan: anticipated <ul style="list-style-type: none"> • Key questions/data needs • Requests • Access • Analyses • Report 							
Mission to Botswana		July 9 -23		Sept 17 -26		Nov 8 -18	
Data <ul style="list-style-type: none"> • ARV • PMTCT • Mort. 91 -03 • Mort. database • Mort. 04 -05 • Census • VCT • Routine testing 	MOH MOH CSO CSO CSO Census Telep. MOH	X X X X X X X X X X	X X X X X X X X X	X X X X X X X X X	X X X X X X X X X X	X X X X X X X X X X	X X X X X X X X X X X X X X
Work plan: reality <ul style="list-style-type: none"> • Key questions/data needs • Requests • Access • Analyses • Report 							

APPENDIX C

LIST OF ILLUSTRATIONS

- Box 1. The four basic types of triangulation
- Box 2. Counselling, HIV testing and antiretroviral therapy among antenatal clinic attendees, Botswana 2002–2005
- Box 3. Information flow in the monitoring and evaluation system, within the context of strategic information: an overview
- Box 4. Use of strategic information: the “stair-step” model
- Box 5. Framework for theme selection, used by the stakeholders to set priority goals for the triangulation study
-
- Figure 1. Trends in HIV prevalence among pregnant women in Botswana (antenatal clinic sentinel surveillance data, 1992–2005)
- Figure 2. Age-adjusted HIV prevalence rates in Botswana, by district, 2003
- Figure 3. Crude mortality rates and the percentage of deaths reported from non-institutional settings or from external causes, Botswana, 1991–2003
- Figure 4. Age-specific mortality at age 5 years and above, Botswana, 1991–2003
- Figure 5. Mortality rates at age 15–64 years, by sex, Botswana, 1991–2003
- Figure 6. Infant and child mortality rates, Botswana, 1991–2003
- Figure 7. Institutional deaths per 100 000 population and programmatic data: patients currently receiving ART, eligible based on MASA guidelines, and deaths on therapy, 1994–2005*
- Figure 8A. Declines in mortality rates for people aged 20–49 years between 2003 and 2004, and 2003 ART coverage rates by district
- Figure 8B. ART coverage in patients aged 20–49 years, by district, 2003–2005
- Figure 9. Trends in institutional mortality by age, from vital registration, Gabarone and Francistown, 1994–2004*
- Table 1. Mortality rates at age 20–49 years per 100 000 population between 1994 and 2004, and change (%) in rates between 2003 and 2004 by district relative to rates of persons on ART* and the district mortality burden†
- Figure 10. Trends in institutional mortality in infants and children compared with PMTCT indicators for AZT use in mother or infant, 1990–2004*

APPENDIX D

SAMPLE TRIANGULATION CHECKSHEET FROM UCSF TRAINING COURSE

LEVEL OF ANALYSIS	Examine or Compare		By Modifying Indicator			Trend	Outlier(s)	inconclusive
	A	B	α	β	γ			
NATIONAL								
	Mortality		year					
	Mortality		sex					
	Mortality		year	sex				
	Mortality		year	age cohort				
	Mortality		year	age cohort	sex			
	Hosp admissions		year					
	Hosp admissions		year	age cohort				
	VCT testing		etc etc etc					
DISTRICT	Mortality		year					
	Mortality		sex					
	Mortality		year	sex				
	Mortality		year	age cohort				
	Mortality		year	age cohort	sex			
	Hosp admissions		year					
	Hosp admissions		year	age cohort				
	VCT testing		etc etc etc					
COMPARABLE SITES (COUNTRIES)								

ASSESSING THE IMPACT OF ANTIRETROVIRAL THERAPY PROGRAMMES AND PREVENTION OF MOTHER-TO-CHILD HIV TRANSMISSION PROGRAMMES ON ADULT AND INFANT MORTALITY IN BOTSWANA



World Health
Organization



UNAIDS
JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS

UNHCR
UNICEF
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World Health Organization (WHO)
Joint United Nations Programme On HIV/AIDS (UNAIDS)
Botswana National AIDS Coordinating Agency (NACA)
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INTRODUCTION

Substantial resources are allocated to collecting strategic information for monitoring and evaluating HIV/AIDS programmes. Monitoring and analysing programmatic data are critical for assessing and improving the effectiveness of HIV interventions. Nevertheless, these data are often under-utilized owing to the fragmented nature of the data systems and a reluctance to apply creative methods for rapidly assessing programmatic effectiveness, particularly in relation to the ultimate impacts of intervention investments.

In order to address this need, several organizations worked together to develop a project to assess the effects of national antiretroviral therapy (ART) and prevention of mother-to-child transmission (PMTCT) treatment programmes in Botswana. The collaborating organizations were the Botswana National AIDS Coordinating Agency (NACA), the Botswana Ministry of Health (MOH), the Joint United Nations Programme on HIV/AIDS (UNAIDS), and the World Health Organization (WHO), under the technical leadership of the University of California, San Francisco (UCSF).

The project was designed to evaluate multiple sources of health-related data using synthesis and triangulation, in order to answer key programmatic and policy questions. Following consultative meetings between NACA, MOH, UCSF, and other collaborators, participants in the project focused on a key issue relevant to programmatic effectiveness: ascertaining whether antiretroviral therapy (ART) programmes, which were initiated in Botswana in 2002, and programmes for preventing mother-to-child HIV transmission, initiated in 2001, have reduced HIV/AIDS-related adult and child mortality, respectively.

In collaboration with NACA and MOH, we at UCSF identified, reviewed, and analysed multiple sets of data on health information, to assess the impact of ART and PMTCT programmes. This report contains a more complete analysis of preliminary findings related to the impact of ART and PMTCT in Botswana, with the addition of a more detailed description of findings related to testing for HIV (Methods, page 36; Results, page 39; and Conclusion, page 59).

The rationale behind the implementation of ART and PMTCT stems from substantial empirical evidence that antiretroviral drugs reverse immunodeficiency and premature mortality among patients with severe HIV-related disease (1), and that ART reduces the risk of mother-to-child HIV transmission when given to pregnant women and newborns in combination with alternative infant feeding practices (2, 3). Hence, the eventual impact of successful ART and PMTCT programmes is expected to be a reduction in adult and child mortality.

To quantitatively assess such an impact, this study used the following three-pronged analytical approach. First, to validate using reduction in mortality as a measure of programme effectiveness, we analysed the impact of HIV on adult and child mortality over time, by district and in institutional settings, using mortality statistics from Botswana's Health Statistics Unit (HSU), a branch of the Central Statistics Office (CSO) of the MOH. Second, we analysed ART and PMTCT data to discern the cumulative number of people receiving treatment by district since 2002. The number of individuals receiving ART was ascertained using ART programme data. Similarly, PMTCT programme data indicated the number of women receiving ART during postpartum care and the number of infants receiving antiretroviral drugs postpartum with infant formula. Data were analysed overall, and by district over time. The third stage involved assessing the potential impact of ART and PMTCT programmes on adult and child mortality respectively. A comparative analysis of ART use by adults and trends in adult mortality over time and by district indicated the potential impact of ART on adult mortality. To assess the impact of PMTCT programmes on infant or child mortality, a comparative analysis was performed on the numbers of HIV-infected women and their offspring who received ART pre- and postpartum, respectively; as well as trends in infant or child mortality overall, and by district over time.

We reviewed vital registration, health information systems, and programmatic data that had an impact on the delivery of ART and PMTCT services. These data included the following: vital registration data including institutional and non-institutional births, deaths, and hospital admissions; ART and PMTCT programmatic data; voluntary counselling and testing (VCT) and routine testing data; HIV/AIDS behavioural surveys; and HIV antenatal sentinel surveillance data. The databases used and of the processes of acquisition and analysis are described below.

Vital registration data: HSU

The HSU has collected and published country-wide health-services statistics for measuring morbidity and mortality trends since 1980–1981. These include the following: inpatient (institutional) morbidity and mortality including births and deaths; outpatient morbidity and non-institutional births and deaths; reportable diseases; midnight census statistics on daily hospital activities including admissions, bed occupancy; admissions and discharges including deaths; and health resources statistics. These data are reported annually in a health statistics report, most of which is archived at the MOH. There is, however, a lag of several years in the collection and reporting of vital registration statistics. Hence, the most recent health statistics data that we identified were only available until 2003.

Reporting of deaths from the district to central level occurs monthly. Individual records of institutional births and discharges (alive or dead) containing demographic, diagnostic, and discharge information, and personal identification (e.g. an identification number for people aged more than 18 years), are sent to the HSU, where they are collated by institution and district. Non-institutional deaths are investigated by district welfare officers, reported to village chiefs, and then reported to the Department of Home Affairs and the HSU. The HSU codes each cause of death according to ICD-9 classification systems (International Classification of Disease, Ninth Revision). All information from death certificates, including cause of death, is entered into a computerized database, which has been maintained by the Department of Home Affairs and the HSU since the early 1990s. According to the CSO's Government Statistician (A. Majelantle, personal communication), the accuracy of the mortality reporting system was validated in 1991 (with 95% accuracy) and 2001 (with 98% accuracy), using population census data.

Data available in the archived Health Statistics Reports were used to determine whether trends in mortality reasonably reflected the impact of HIV, and to assess the validity of using mortality statistics to measure programmatic impacts. We examined adult mortality trends overall and by age and sex. We also examined neonatal, infant and child mortality rates for 1991–2003. We calculated adult and infant mortality rates using 1991 and 2001 population census data, with recorded births as denominators.

Geographic disaggregation of mortality data is important for testing associations between programmatic coverage and mortality impact. The examination of mortality trends at the district and institutional level required accessing computerized data files from 1991 to 2003; however, not all years were available for this investigation. There were technical problems in converting files to SPSS format, and we were not able to locate complete records for all years. For example, the data file for 2002 only included reported deaths for 11 months, and data for 1995 and 1998 were not available for our analysis. Nevertheless, mortality data at the district and institutional level were available for the following years: 1994, 1996, 1997, and 1999–2003. A mechanism known as the “hospital midnight census” complements the use of vital registration data for mortality reporting. In this method, deaths are recorded on a daily basis at each hospital, and a database stores monthly numbers of deaths (at age greater than 28 days) for each institution. This system provides an alternative mortality surveillance system, independent of the vital registration system. We examined mortality overall and by age, sex, district, and institution using the above-mentioned vital registration data files from 1994–2003. In addition, we compared the data from vital registration to deaths reported (overall, by district, and by institution) using the midnight census database, as well as institutional deaths recorded in the annual Health Statistics Reports, which are published annually.

The delay in the analysis and reporting of deaths by the HSU is a limitation when using the vital statistics database to assess programmatic impact. Although institutions submit morbidity and mortality statistics to the HSU on a monthly basis, there is usually at least a 1-year delay before individual records for reported deaths are encoded by cause or recorded into a HSU vital registration database. A further delay exists before data are officially reported. These delays impede the timely analysis of recent trends in mortality for 2004 or 2005. We developed a sub-study, in collaboration with the HSU, in order to address this shortcoming. A rapid epidemiological review of reported deaths by district, institution, sex, and age, for all deaths reported to the HSU by November 2005 for 2004 until June 2005 was conducted. Given time and resource restraints, the encoding of cause of death was not performed. The deaths for 2004 until June 2005 allowed the extension of the mortality analysis beyond 2003. This sub-study was completed and made available to the investigators in early January, 2006.

ART and PMTCT programmatic data

The Botswana antiretroviral programme (“MASA”), which began in January 2002, provides free ART to persons with severe HIV disease. By 2005, the programme offered ART services at 34 clinics, covering all districts in Botswana. According to the MOH, 54 378 adults and 4 582 children were receiving ART by September 2005. The MOH collects aggregate ART programmatic data from each clinic every 2 months. The key variables consistently collected and used for this investigation include the cumulative numbers of patients enrolled with CD4 counts of less than 200 per mm³ and eligible for ART, those persons currently receiving ART, and reported deaths while on therapy, articulated by sex, quarter, clinic site, and district, since January 2003. Data on the numbers of children receiving ART, by temporal and geographic distribution, were not available.

PMTCT services, including provision of ART, began in 1999, and were made widely available in November 2001. Services are provided within the antenatal care (ANC) and maternal-child health-clinic system to all pregnant women. The ART protocol includes the following for all HIV-positive pregnant women: azidothymidine (AZT) for 6 weeks pre-partum, at or around 32 weeks of gestation; 4 weeks of AZT for infants postpartum; and infant formula is provided free of charge. The key programmatic variables consistently collected and used in this study come from antenatal and maternal clinic settings at the district level. This information is reported to the MOH on a monthly basis. Since only aggregate-level data were collected, individual-level analyses of indicators across antenatal and maternal settings were not conducted.

ANC clinic variables are collected for the following types of patients: new ANC clinic visitors; visitors counselled before testing; those tested for HIV; those identified as HIV-positive; those counselled after testing, and those pregnant women who received AZT. Maternal clinic variables include: deliveries; deliveries by known HIV-positive mothers; deliveries by mothers of unknown HIV status; infants started on AZT; and infants started on infant-feeding formula.

VCT and routine HIV testing programmes

As part of the national response to HIV/AIDS, a need was identified for a VCT programme in Botswana as a prevention intervention and an entry point to other care and support services. Recognition of such a need led to the establishment of Tebelopele VCT centres in 2000. In collaboration with the MOH, Population Services International (PSI), a USA-based nongovernmental organization (NGO), the United States Embassy Office of Defence Corporation (ODC) and others, the BOTUSA project piloted the delivery of VCT services in the two major cities of Francistown and Gaborone. On the basis of this experience, VCT was later rolled out countrywide, expanding from three testing sites in 2000 to more than sixteen permanent and eight satellite testing sites by 2005.

HIV tests have been offered as a routine clinical service in public and private clinics in Botswana since the beginning of 2004. The testing is different from VCT, as HIV testing is provided routinely without counselling, but people who do not want to be tested can opt out. In the first 6 months of 2005, some 74 134 people were tested via the routine testing programme.

Since awareness of personal HIV serological status is an important determinant of early access to HIV care and support, we examined VCT data and relevant trends in testing by sex, age, district and reasons for testing over time for 2003–2005 and we examined recent routine testing data for January 2004 to June 2005, provided by the MOH. We also analysed the Botswana AIDS Impact surveys (BAIS, a population-level AIDS-related knowledge, attitudes, beliefs and practices, KABP, survey) performed in 2001 and in 2004, with special attention to variables relevant to HIV testing by age, sex and district and key variables relevant to HIV/AIDS knowledge and behaviour.

Analysis of trends in HIV testing, 2001–2005

Trends in VCT, 2001–2005

According to the VCT service-provider the NGO Tebelopole, more than 230 000 clients have sought free VCT testing services since its inception until October 2005. Client visits increased by 45% between 2003 (51 795 visits) and 2004 (75 331 visits) and preliminary data available up to July in 2005 (65 364 visits) suggests that the increase in demand and coverage continues. Of the 192 490 total visits recorded from 2002 through to the beginning of July 2005, about two thirds were persons seeking HIV testing for the first time. The distribution of total number of tests from 2003–2005 indicates that females are about twice as likely as males to seek VCT services (Figure 1) The distribution of clients tested and sero-status by administrative district reveals that HIV infection varies by district, from 28% in Ngami to 40% in Kgalega. More than 62% of clients tested were resident in the Southern and Central districts, reflecting the population distribution of Botswana. Between 2002 and 2005, the proportion of persons seeking VCT services because of self-perceived HIV-risk behaviour or that of a partner increased from 37% to 68%, while those seeking testing because of suspected HIV illness or reasons related to access to ART services remained relatively constant at around 20% (Figure 2).

Figure 1. Total number of persons tested through voluntary counselling and testing services, by age and sex, Botswana 2003–2005

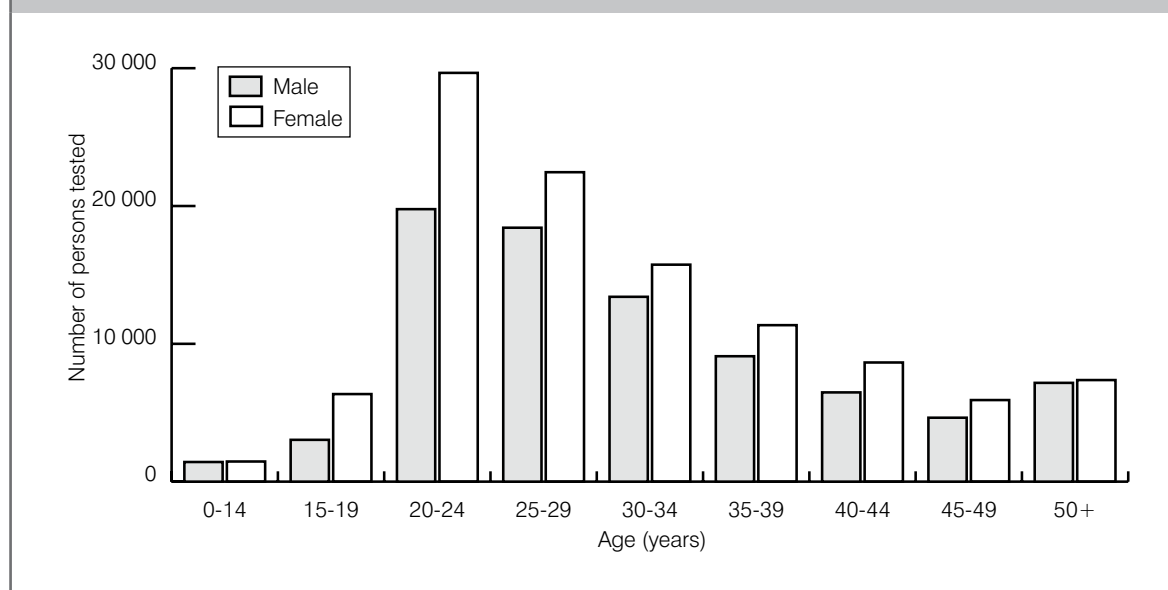
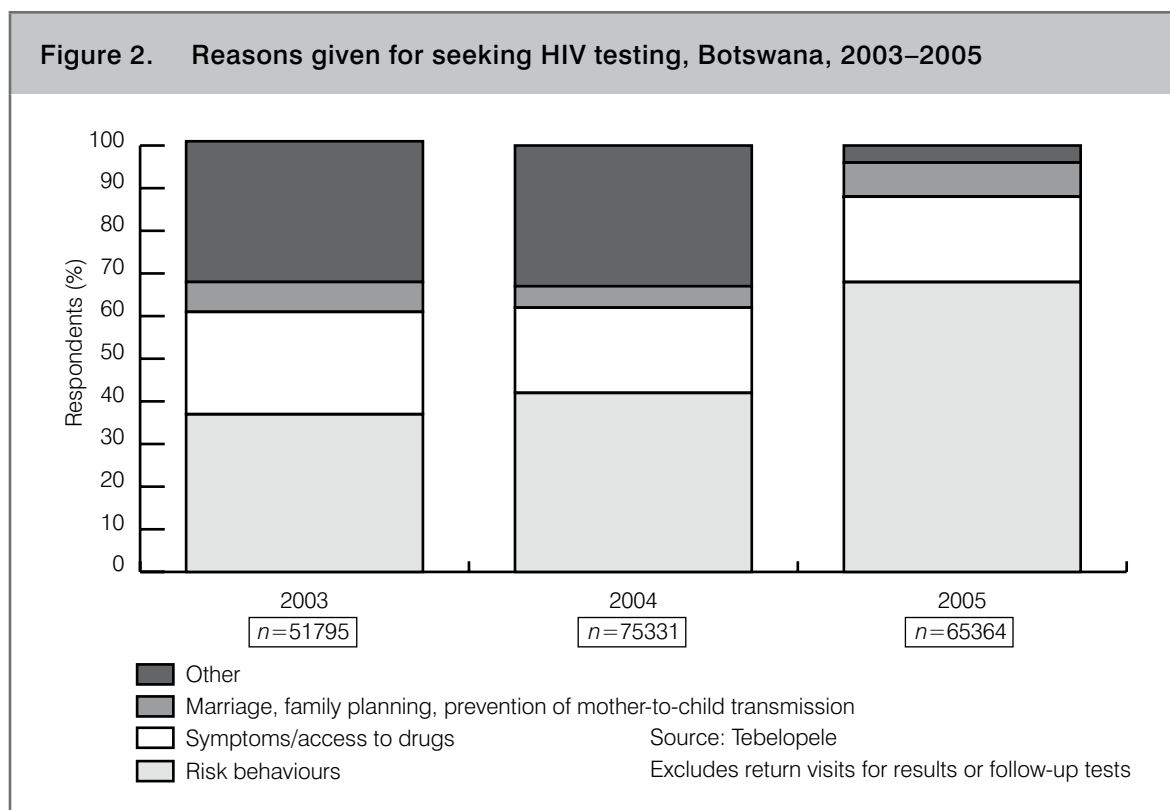


Figure 2. Reasons given for seeking HIV testing, Botswana, 2003–2005

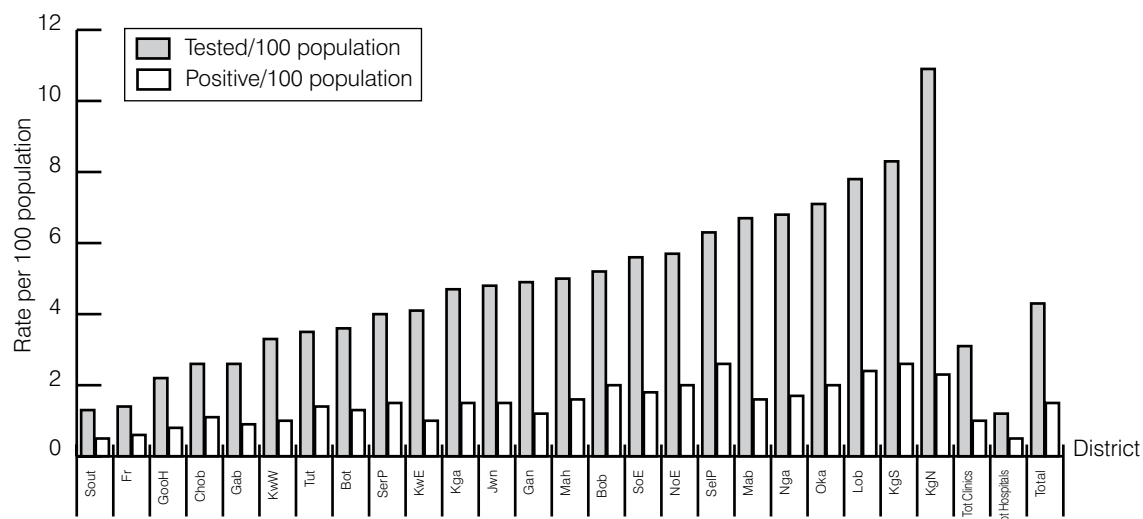


Routine HIV testing, 2004–2005

A total of 74 134 clients were tested for HIV under the routine testing programme between January and July 2005, with 22 474 (33%) testing positive. January, February and March saw all expected 51 facilities reporting. In May, 49 out of 51 (96.1%) reports were received, while June and July each had 45 (88.2%) reports. January to June 2005, reports ranged between 39.6% and 56.6% with 29 313 clients, less than half the number tested during same period in 2005. Although more clients (74 134 in 2005 compared with 29 313 in 2004) tested in 2005 than during the same period in 2004, the percentage testing positive was less in 2005 at 33% (range, 19.2–43.1%) compared with 46.7% in 2004 (range, 26.2–57.3%).

Although more tests were performed at clinics (53 390, or 72%) than at hospitals (20 744, or 28%), there are more HIV-positive clients attending hospitals (37.9%) than clinics (31.2%). Figure 3 illustrates the distribution of the overall rate of routine HIV tests performed and percentage of HIV positives from January to June 2004 by district. The proportion of HIV positives by district ranged from 36% to 63% in 2004, and 21% to 42% in 2005 and rates of HIV positives have generally declined between the 2 years, which is most likely to be related to the disproportionate number of HIV-positive patients identified and tested during the first year of the programme in 2004. With expansion of HIV testing services and knowledge of personal HIV status, the proportion of HIV-positive clients tested routinely is likely to decrease as more of the population becomes aware of their HIV status.

Figure 3. Population rate of routine HIV testing and number of positives per 100 tested by district, January–June 2005

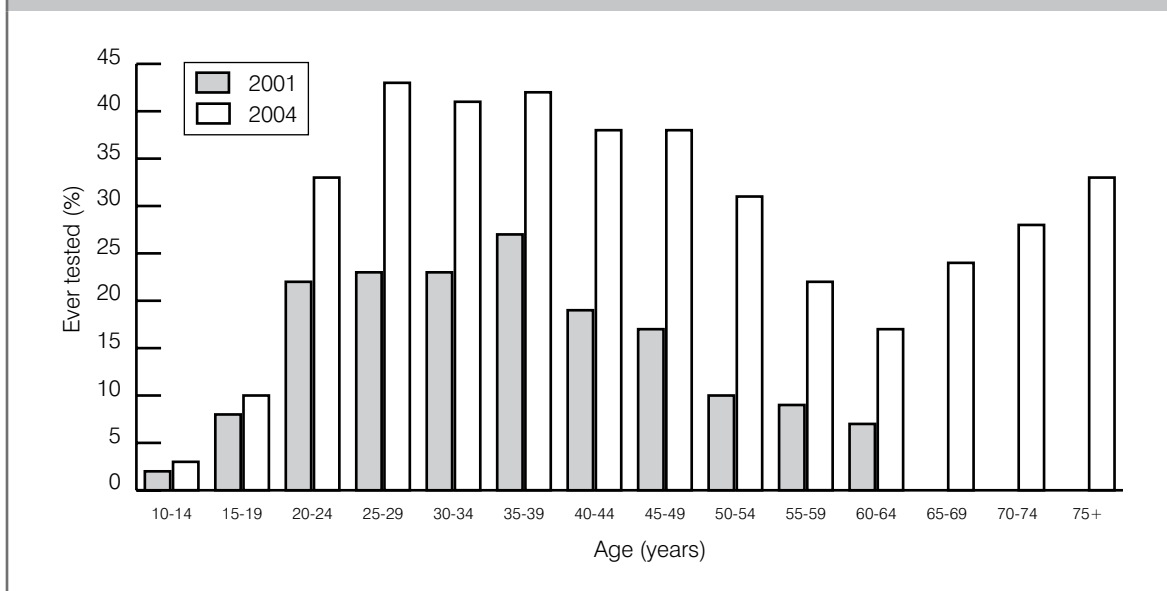


Note: The graph represents the percentage (number per 100) of the district population that was tested for HIV (shaded bar), and the percentage (number per 100) of the district population that tested positive for HIV (unshaded bar). The latter can be restated as the number of positive HIV test results per 100 people in the district. Note that this is different from the number of positive HIV results per 100 tests.

Self-reported HIV testing: Botswana AIDS impact survey (BAIS 2001 vs 2004)

Additional evidence on the impact of increases in the numbers of persons tested for HIV comes from a comparison of persons who self-reported having ever been tested for HIV and those tested during the previous 12 months, in BAIS population-based surveys in 2001 and 2004. The proportion of persons who reported ever having been tested for HIV doubled between 2001 and 2004 (from 15.4% to 30%, respectively). In 2004, 69% of persons tested were tested in the past 12 months compared with 52% in 2001; 93% of all persons tested in 2004 stated that they had received their test results, which was a similar result to that reported in 2001. Females were 1.5 times more likely to report having been tested in 2004 than were males (35% vs 23% respectively); however, in 2001 males and females were equally likely to report having been tested. The proportion of persons tested in 2001 and 2004 by age indicates that about 40% of persons aged 25–49 years report ever having been tested for HIV (Figure 4).

Figure 4. Age-specific comparison of proportion of persons self-reporting having ever been tested for HIV, 2001 vs 2004, Botswana AIDS Impact Study



Comments on HIV testing data

These three data sources provide compelling evidence of the impact of increased services for HIV testing and their uptake in the general population between 2001 and 2004. The increased number of persons tested undoubtedly has a beneficial effect on access to prevention and treatment services; however, the specificity of the testing data by district and reasons for seeking HIV testing were not sufficient to incorporate these data into the triangulation analysis to assess the impacts of ART and PMTCT on adult and infant mortality.

HIV impact overview: trends in HIV prevalence and mortality

Since being recognized in 1986, the HIV/AIDS epidemic in Botswana has proven to be one of the most severe in the world. According to the annual HIV sentinel surveillance survey, the HIV prevalence among a representative sample of women attending ANC clinics was 37.4% in 2003. As a result of the epidemic, life expectancy has declined from 66.9 years for women in 1995 to an estimated 36.6 years in 2005 (4, 5) and the population growth rate is zero or slightly negative (6).

Despite intervention efforts to implement internationally recognized “best practices,” there has been little evidence of reduction in the number of HIV infections or HIV-related deaths, according to HIV sentinel surveillance and other sources available through 2003. However, recently released antenatal HIV sentinel surveillance suggests a significant decline in HIV prevalence from 36.2% in 2001 to 33.4% in 2005. Age-specific trends in HIV prevalence among pregnant women participating in sentinel surveillance from 1992 to 2005 are shown in Figure 5. HIV prevalence peaked in 2003 at 37.4% overall, and trends since 1992 reveal rapid increases in prevalence rates across all age groups, with stabilization in prevalence among those aged 15–24 years since the late 1990s, and continued increases in prevalence among those aged 24–49 years until 2003. However, between 2001 and 2005 HIV prevalence rates among those aged 15–19 years and 20–24 years decreased 28% (from 24.7% to 17.8%) and 21% (from 38.7% and 30.6%), respectively. These preliminary findings suggest that there has been a recent decline in HIV incidence in younger age groups. Age-adjusted HIV prevalence rates varied geographically, and ranged from 52% in Selibe-Phikwe district, to 21% in the more rural Gantsi district. In seven districts, the prevalence was greater than 40% (Figure 6).

Figure 5. Trends in HIV prevalence among pregnant women in Botswana (antenatal clinic sentinel surveillance data, 1992–2005)

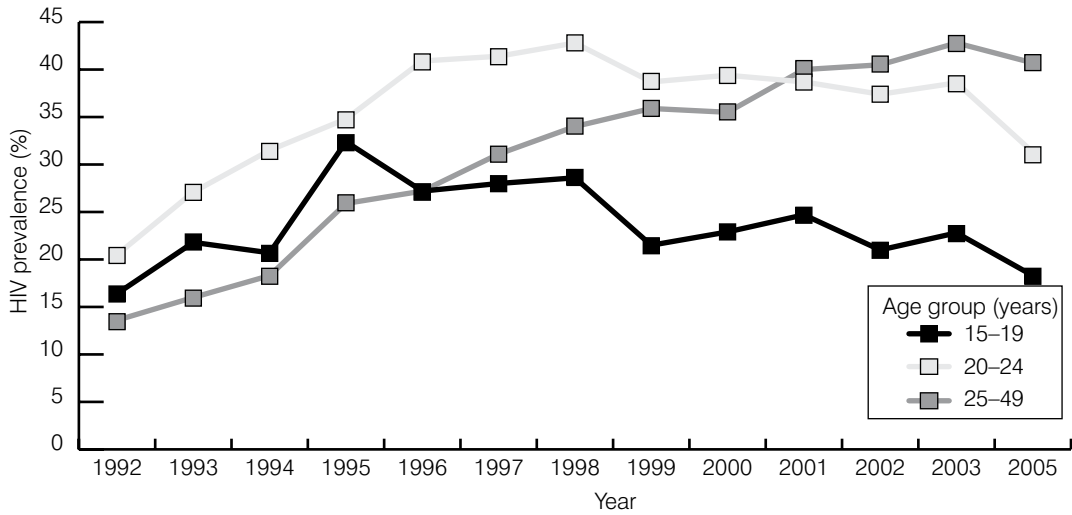
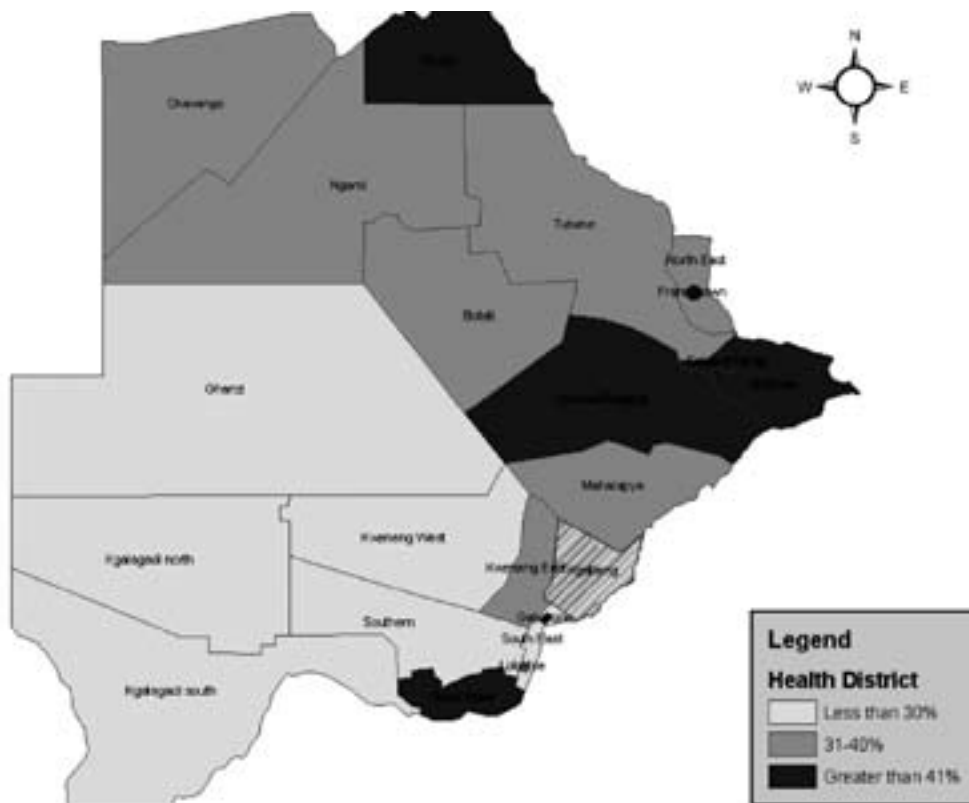


Figure 6. Age-adjusted HIV prevalence rates in Botswana, by district, 2003



Concurrent with increasing rates of HIV prevalence, crude mortality rates increased nearly threefold between 1991 and 2003. Furthermore, the proportion of deaths reported from non-institutional settings or attributed to external (non-natural) causes decreased from 26% to 15% and from 5% to 2.5%, respectively (Figure 7). The distribution of deaths by age between 1991 and 2003 indicates that mortality increases are greatest among adults aged 25 years and older, with a fourfold increase among those aged 25–44 years (Figure 8). Mortality rates among those aged 15–64 years, stratified by sex, indicate similar trends in mortality. However, mortality rates for males are consistently higher than for females, with an average male to female rate ratio of 1.2 : 1 over the period 1991–2003 (Figure 9).

Figure 7. Crude mortality rates and the percentage of deaths reported from non-institutional settings or from external causes, Botswana 1991–2003

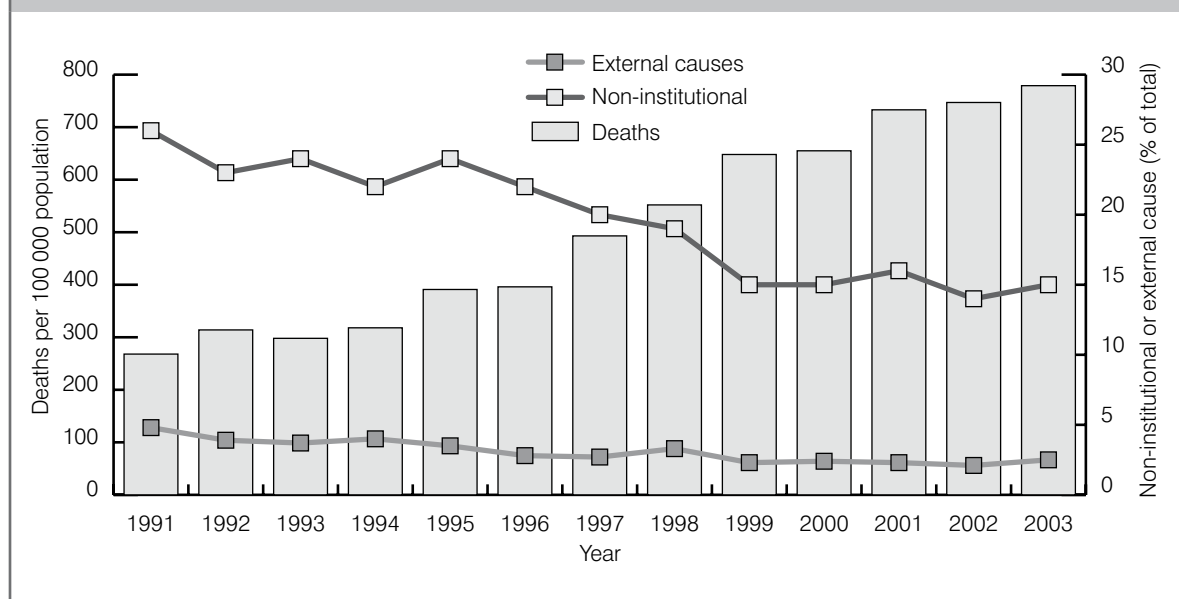


Figure 8. Age-specific mortality at age 5 years and above, Botswana 1991–2003

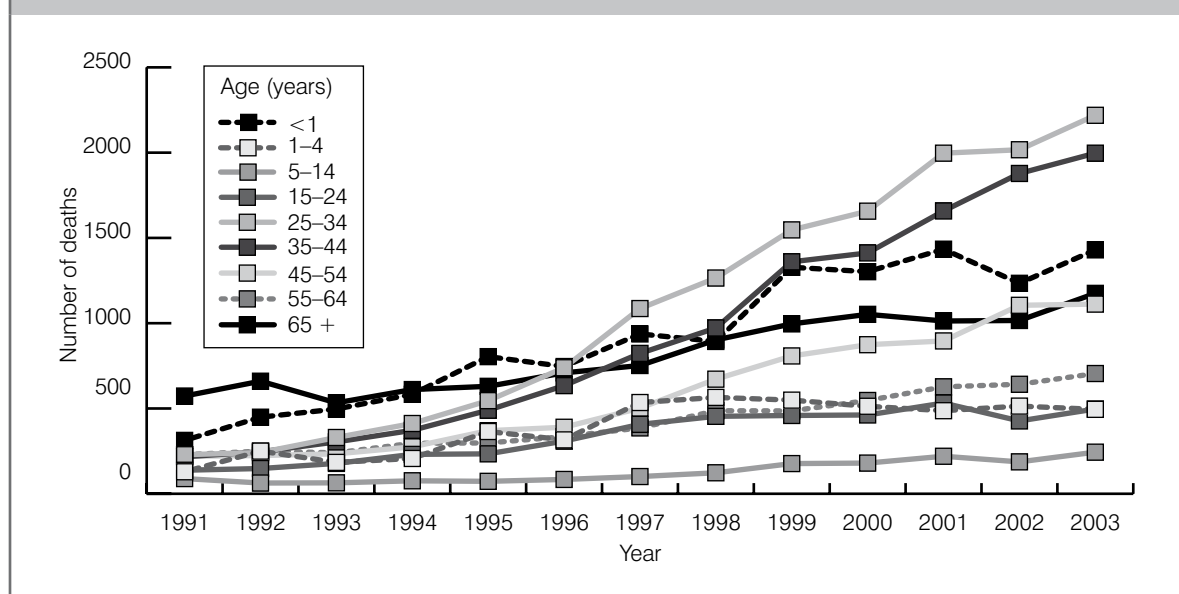
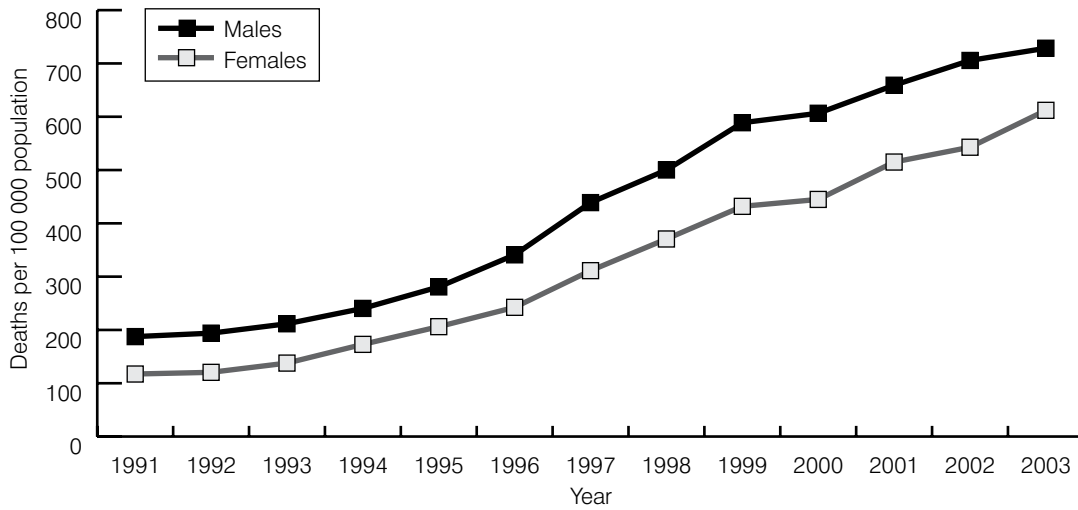
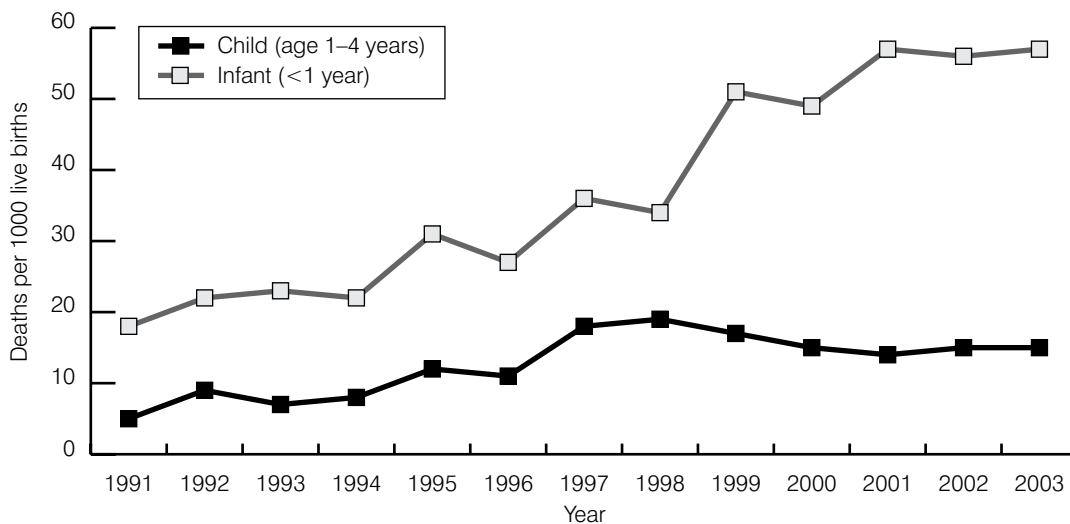


Figure 9. Mortality rates at age 15–64 years, by sex, Botswana 1991–2003



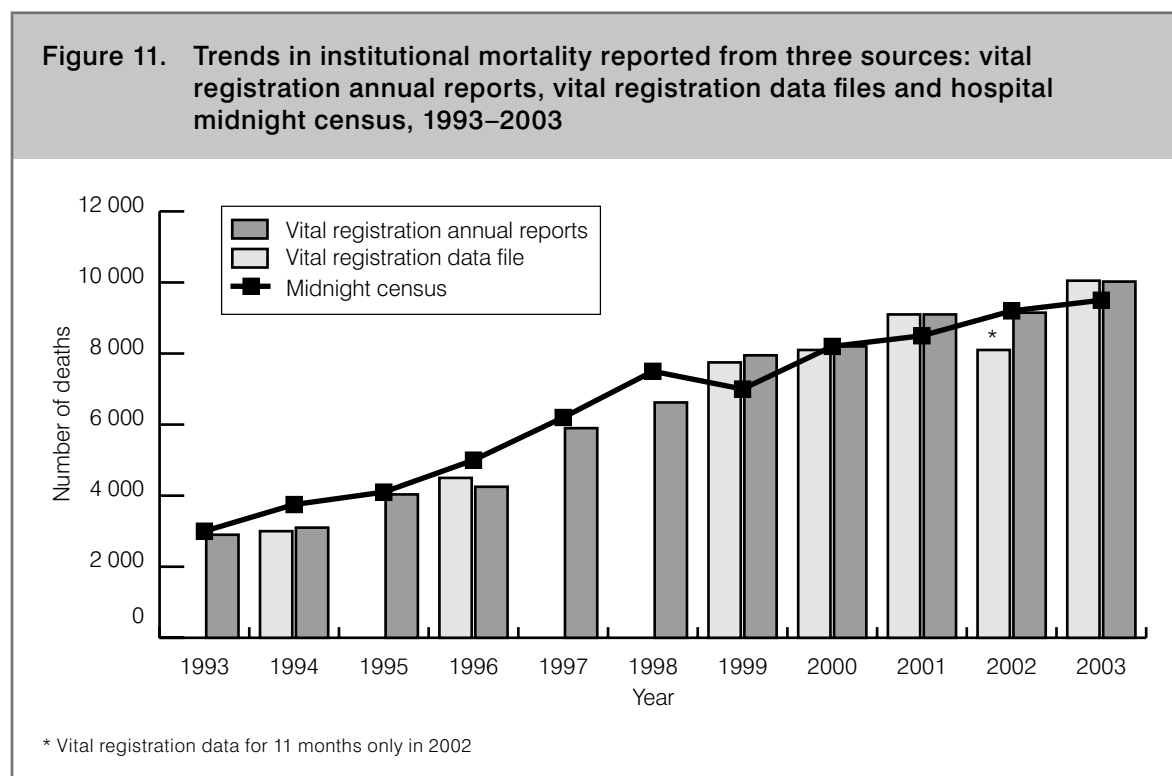
Similar increases in mortality are evident among children: infant mortality rates increased from 17 to 56 deaths per 1000 live births between 1991 and 2001 and have remained stable until 2003; child mortality rates doubled between 1992 and 1997 and stabilized thereafter (Figure 10).

Figure 10. Infant and child mortality rates, Botswana, 1991–2003



HIV/AIDS became the leading cause of institutional deaths in 1996. The proportion of deaths in which HIV/AIDS was causally implicated increased more than sixfold between 1992 and 2003, from 3.9% to 26.7%. Similarly, between 1992 and 2003, deaths attributed to HIV/AIDS increased from 4% to 13.4% in infants and from 4% to 9% in children. Other causes of deaths likely related to HIV infection—including pneumonia, ill-defined conditions, and tuberculosis—also increased, with similar orders of magnitude over the same period.

Figure 11 shows a comparison of number of institutional deaths (excluding neonatal deaths) abstracted from annual Health Statistics Reports, vital registration data files, and deaths recorded in the nightly midnight census, from 1993 to 2003. These data provide a reasonable validation of the accuracy of institutional mortality trends and the potential use of mortality indicators to measure the impact of ART and PMTCT programmes.



There is compelling evidence that HSU vital registration data provide reasonably accurate evidence for the demographic impact of HIV/AIDS on Botswana’s population structure over time. This evidence includes: co-incident increasing trends in the mortality of children and young adults; HIV prevalence in pregnant women; and AIDS as reported cause of death; coupled with similar patterns of the impact of HIV-related mortality in neighbouring South Africa and elsewhere.

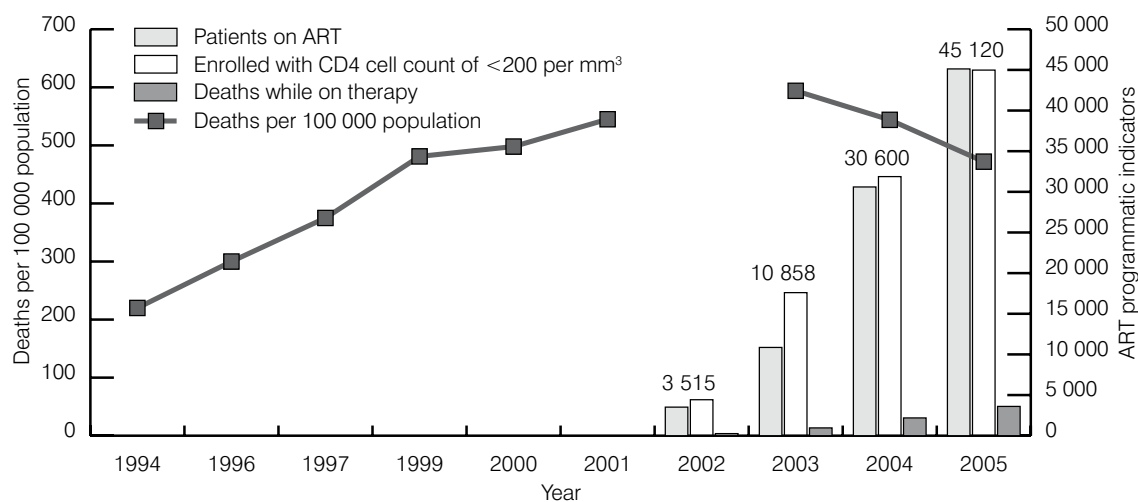
Assessment of evidence of ART impact on adult mortality

If the use of ART helps to reduce HIV mortality in Botswana, as reported in controlled trials and cohort studies, and if ART coverage is increasing over time and geographic space since 2002, then eventually a substantial decrease in HIV-related institutional deaths would be expected. Furthermore, such a decrease would be most pronounced in adults aged 25–54 years, which is the group with the highest burden of HIV mortality. Such decreases would also, perhaps, be associated with geographical areas close to sites that initiated ART at an early date, assuming minimal migration related to treatment access.ⁱ

Figure 12 shows trends in institutional death rates reported from vital registration from 1994 through June 2005, shown in relationship to ART programmatic data reported through September 2005. Mortality rates stabilized in the early 2000s and decreased by 8% and 20% between 2003 and 2004–2005 respectively, coincident with increasing numbers of patients receiving ART from 2002 to 2005. Age-specific deaths and death rates declined substantially in groups aged 20–54 years between 1994 and 2005, as trends in older and younger age cohorts remained relatively stable (Figures 13A and 13B).

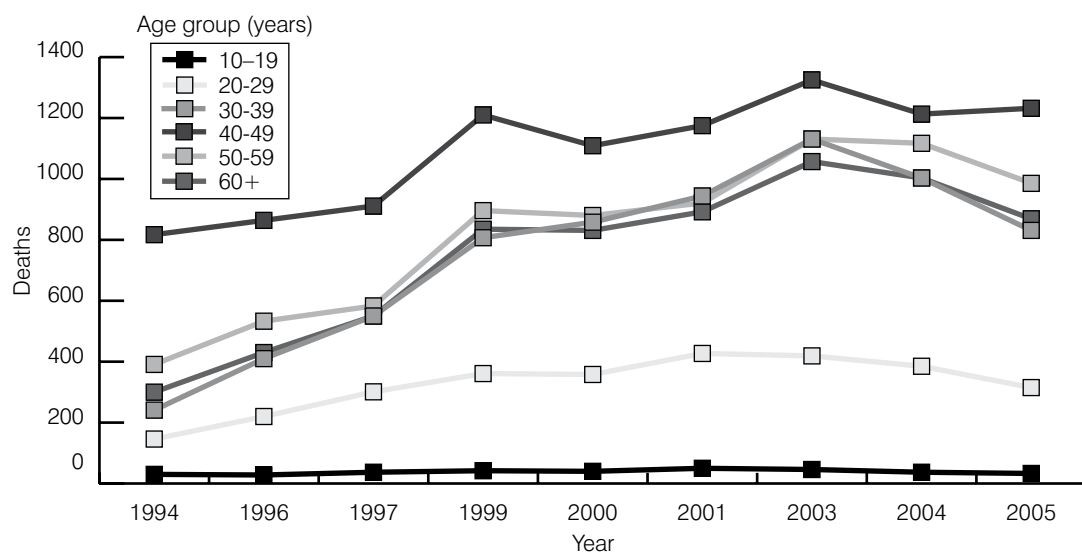
ⁱ Given the high mobility of the Botswana population, it is reasonable to assume that candidates for ART would travel to access treatment

Figure 12. Institutional deaths per 100 000 population and programmatic data: patients currently receiving ART, eligible based on MASA guidelines, and deaths on therapy, 1994–2005*



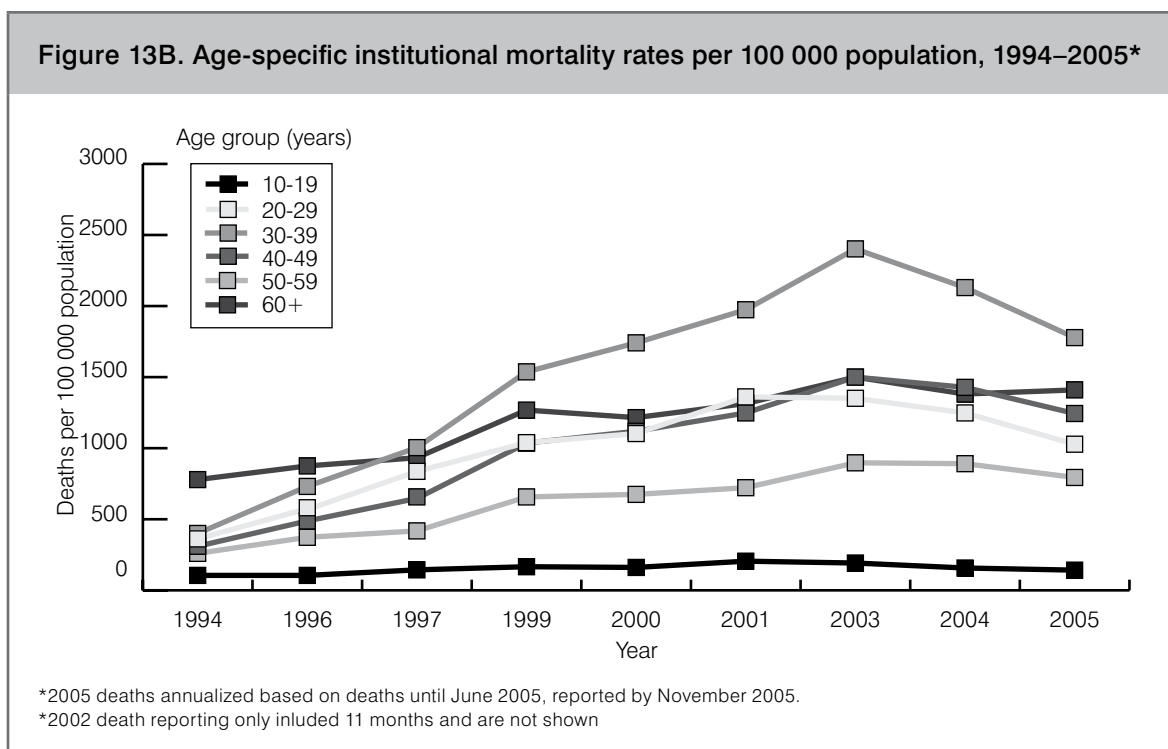
*2005 deaths annualized based on deaths until June 2005, reported by November 2005; ART programme data reported until September 2005
ART, antiretroviral therapy

Figure 13A. Age-specific incidence of institutional mortality, 1994–2005



*2005 deaths annualized based on deaths until June 2005, reported by November 2005.
*2002 death reporting only included 11 months and are not shown

Figure 13B. Age-specific institutional mortality rates per 100 000 population, 1994–2005*



The rates of ART uptake (cumulative numbers of persons aged 20–49 years currently receiving ART per population) by district, from date of programme initiation until July 2005, indicate that ART sites in Francistown and Gaborone districts had the highest rates of ART uptake throughout the period (Figure 14A). A comparison of declines in mortality rates among those aged 20–49 years between 2003 and 2004 (the most likely period to capture the effect of ART at an early stage) and ART coverage rates reported by July 2003 by district, reveal that mortality declines were evident in 29% (7 out of 24) of districts, ranging from a 43% decline in the South East, to a 2% decline in Kgatleng (Figure 14B). Mortality declines were associated with high rates of ART uptake (Gaborone, Francistown and Ngami) or in districts in close geographic proximity to Gaborone (Lobatse, Southern Jwaneng, South East and Kgatleng). Other than the Serowe/Palapye district, in which mortality apparently continues to increase despite early and relatively high rates of ART uptake, mortality rates continue to increase in districts without early roll-out of ART (in 2002–2003).

Figure 14A. ART coverage in patients aged 20–49 years, by district, 2003–2005

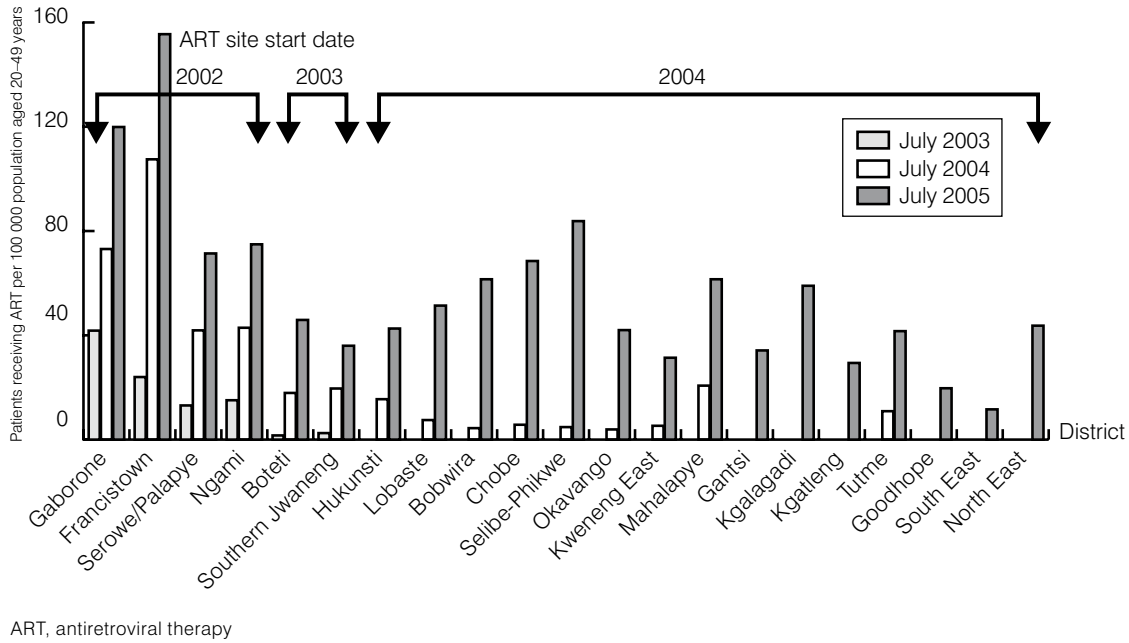
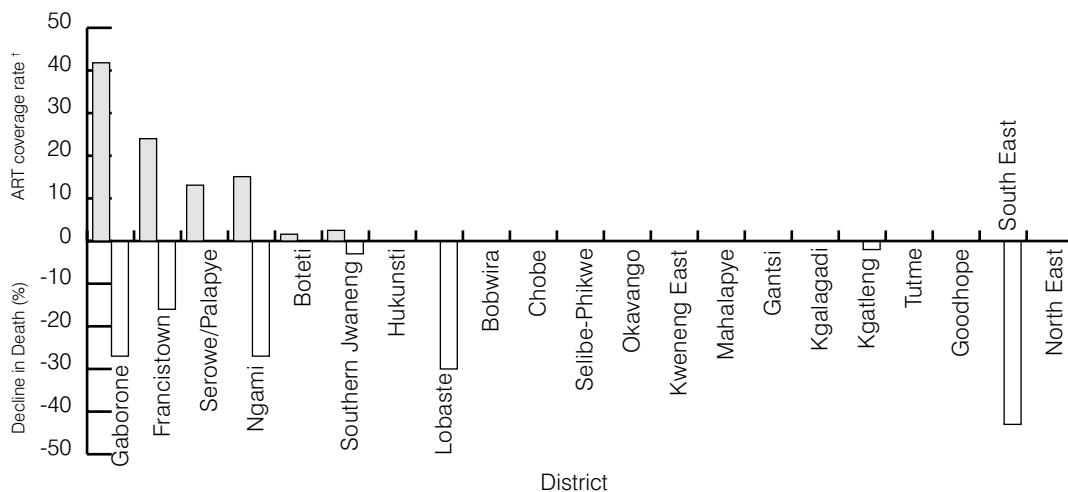


Figure 14B. Declines in mortality rates for people aged 20–49 years between 2003 and 2004, and 2003 ART coverage rates by district*



* All data is from July 2003

† ART coverage rate per 100 000 population aged 20–49 years
ART, antiretroviral therapy

The districts of Gaborone and Francistown account for 36% of the cumulative national mortality burden during 1999–2005, with early ART initiation and the highest rates of persons receiving ART. In these districts, mortality declined by 27% and 17% respectively. Both sites exhibit similar declines in mortality during 2004 and 2005, this being based on preliminary data for 2005 (Figure 15A). In addition, overall mortality trends from vital registration and from hospital midnight census mortality reveal similar declines until 2004, providing some degree of validation that the trends are not related to reporting biases or inaccuracies in the vital registration system (Figure 15B).

Figure 15A. Trends in institutional mortality by age, from vital registration, Gaborone and Francistown, 1994–2005

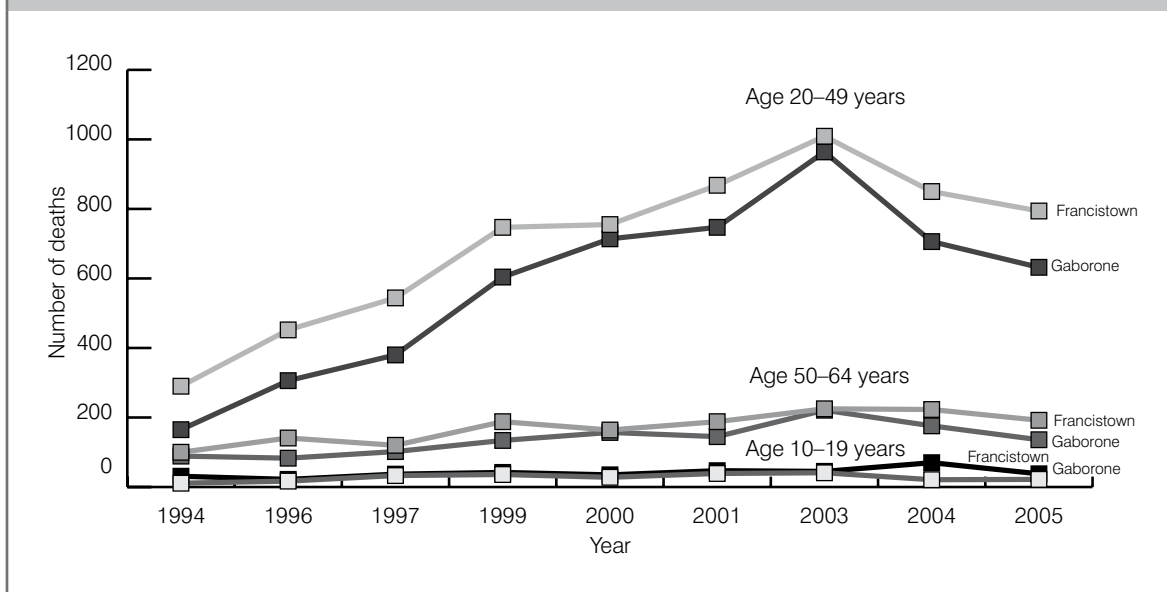
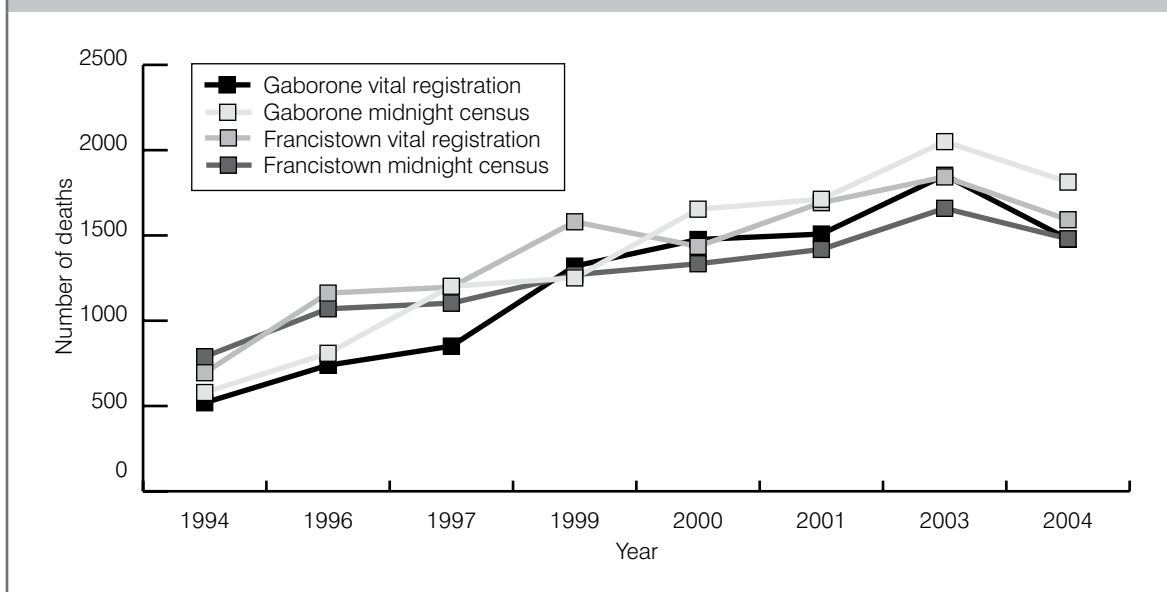


Figure 15B. Trends in mortality, overall and from midnight census, Gaborone and Francistown, 1994–2004



We further examined the association between changes in district-level mortality between 2003 and 2004 and ART initiation date and coverage rates, as illustrated in Figure 14A and in Table 1. After weighting for population size, the decline in district-level mortality is significantly correlated with both the date of initiation of district ART programmes ($P < 0.05$) and with the district-level ART coverage rate in July 2004 ($P < 0.05$). However, colinearity between these two prevents their integration in a single analysis.^j

Table 1. Mortality rates at age 20–49 years per 100 000 population between 1994 and 2004, and change (%) in rates between 2003 and 2004 by district relative to rates of persons on ART* and the district mortality burden[†]

District	ART rate* July 2004	Percentage of cumulative mortality 1994–2004	Deaths per 100 000 population aged 20–49 years									Change (%) 2003–2004
			1994	1996	1997	1999	2000	2001	2002	2003	2004	
South East	0	3	137	94	184	346	429	512	462	498	281	-43.5
Lobaste	7	5	430	483	860	1302	1236	1574	1375	1402	985	-29.7
Ngami	75	5	173	293	453	502	686	817	686	1029	753	-26.8
Gabrone	120	17	153	283	351	558	660	690	702	891	654	-26.6
Gantsi	0	2	173	128	488	510	315	443	398	758	630	-16.8
Francistown	156	19	693	1080	1299	1784	1803	2073	2011	2410	2030	-15.8
Southern	20	5	94	189	343	488	207	570	314	605	583	-3.7
Kgatlang	0	3	40	109	182	496	449	478	376	361	354	-2.0
Kgalagadi	0	1	106	213	319	590	513	503	435	648	658	1.5
Chobe	6	1	103	354	114	343	629	663	572	652	675	3.5
Mahalpye	21	7	184	344	493	788	831	991	880	842	891	5.8
Boteti	18	3	110	143	236	333	367	497	447	632	678	7.3
Bobwira	4	3	115	387	315	435	549	745	740	745	807	8.3
Serowe/Palapye	71	8	155	308	426	522	654	597	631	774	849	9.6
Hukuntsi	16	1	0	0	16	0	356	356	340	486	534	10.0
Kweneng East	5	6	83	127	118	236	347	354	319	379	420	10.8
Selebi Phikwe	5	5	301	270	582	683	748	887	883	822	929	13.1
North East	0	2	7	0	7	110	589	534	603	582	705	21.2
Tutume	0	3	11	159	234	276	309	309	351	482	610	26.6
Okavango	0	1	118	176	341	188	200	323	317	312	400	28.3
Goodhope	0	1	0	130	178	0	410	437	396	417	553	32.8
Total	—	100	161	271	374	533	594	687	640	773	713	-7.8

* ART rate = cumulative number of patients on ART/100 000 population aged 20–49 years

[†] District mortality burden = % of cumulative mortality 1994–2004

Summary: evidence for the impact of ART on adult mortality

Our analysis provides reasonable evidence for an early association between ART uptake and declines in adult mortality from 2003 to 2004. Alternative hypotheses, including the effect of other HIV interventions, population out-migration, natural dynamics of HIV, other competing causes of mortality, or artefacts of biases in mortality reporting are less plausible. Preliminary vital registration data from 2005 provides further empirical support for the continuation of these mortality declines. Before considering these conclusions as definitive, updating of the vital registration data to complement existing data on preliminary reported deaths until 2005 and into 2006, as well as studies to validate the accuracy of mortality reporting at key hospitals, are needed. A cross-validation study of data from the vital registration database in the Department of Home Affairs would also be important. District mortality trends should be further investigated in “outlier districts” such as Serowe/Palapye, where apparently ART uptake is quite

^j High variability in mortality data, particularly in districts with low population, is potentially the result of either true fluctuations in mortality or of problems with data quality. We have not adjusted for this variability at this stage of the analysis except to weight by population size.

high, yet mortality continues to increase. The strength of a geographical association between ART site opening dates, uptake rates, and declines in mortality is probably diluted by district cross-migration to access ART drugs. For example, ART sites in Gaborone district probably supplied residents from neighbouring districts (Southern, Lobatse, Kgatleng, and South East) in which mortality declines preceded ART site openings. Information about the district of residence of clients accessing ART, and careful monitoring of future district-level trends in mortality, may clarify this question.

Furthermore, this investigation suggests that if vital registration data are analysed in a timely manner, they can contribute to a reasonable HIV morbidity and mortality surveillance system at the national and district level. We believe that the vital registration system should be further used to monitor the short and long-term effectiveness of ART programmes, as well as HIV dynamics at national and district levels.

Assessment of evidence of PMTCT impact on infant or child mortality

Mother-to-infant transmission of HIV at birth can be reduced from 40% to 15–20% with a 4-week course of AZT or zidovudine (ZDV) pre-partum to the mother and post-partum to newborns (7). The addition of a single course of nevirapine and infant formula can further reduce HIV transmission rates to around 5% (8). The ultimate effectiveness of these interventions distributed in PMTCT programmes should be evident by reduced HIV mortality among children.

According to PMTCT programme indicator data collected in 2002–2005, of 158 378 pregnant women presenting at ANC clinics, 90% were provided with HIV preventive counselling, 67% of those counselled were tested for HIV, and of these 33% (32 838) were found to be HIV-positive, and 63% (21 005) of those who were HIV-positive were provided with preventive ART (Figure 16A). The annual proportions of pregnant women counselled and tested have shown a steady increase between 2002 and 2005. However, the proportion of HIV-infected clients receiving ART has remained relatively stable, ranging between 64% and 69%. During the same period, maternity-related indicators for PMTCT interventions also show substantial increases in programmatic coverage: decreasing deliveries of patients with unknown HIV status and increasing numbers of newborns treated with ART (Figure 16B).

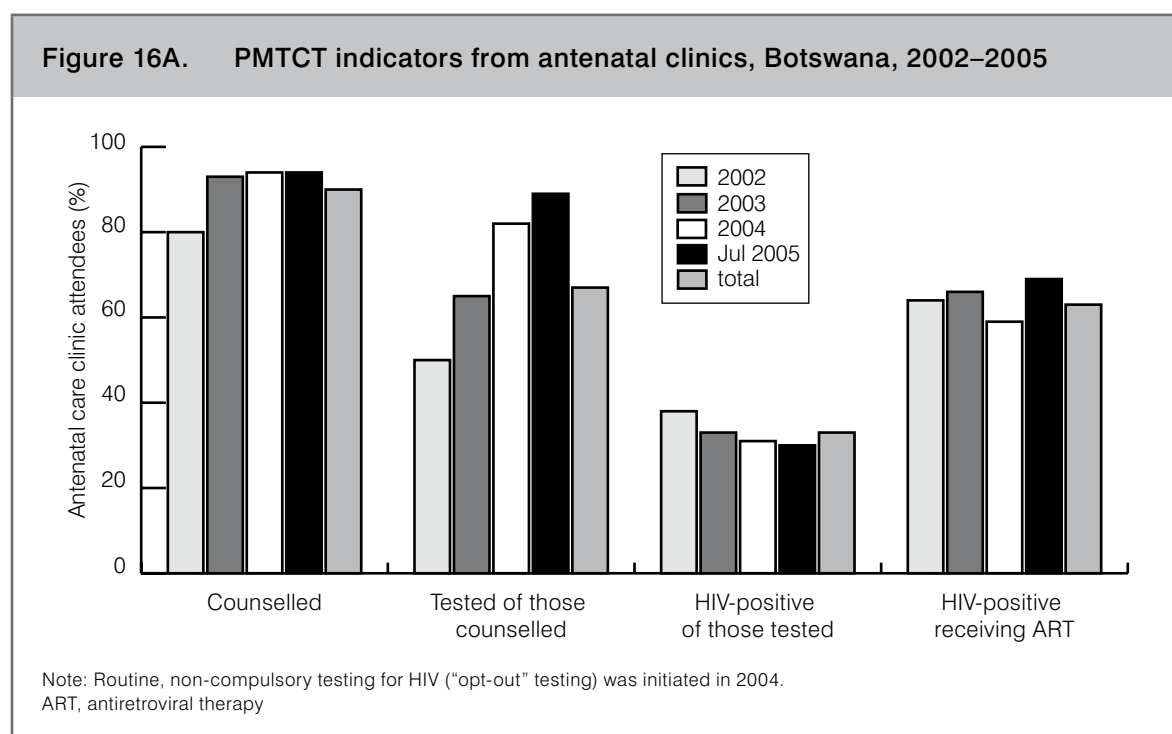
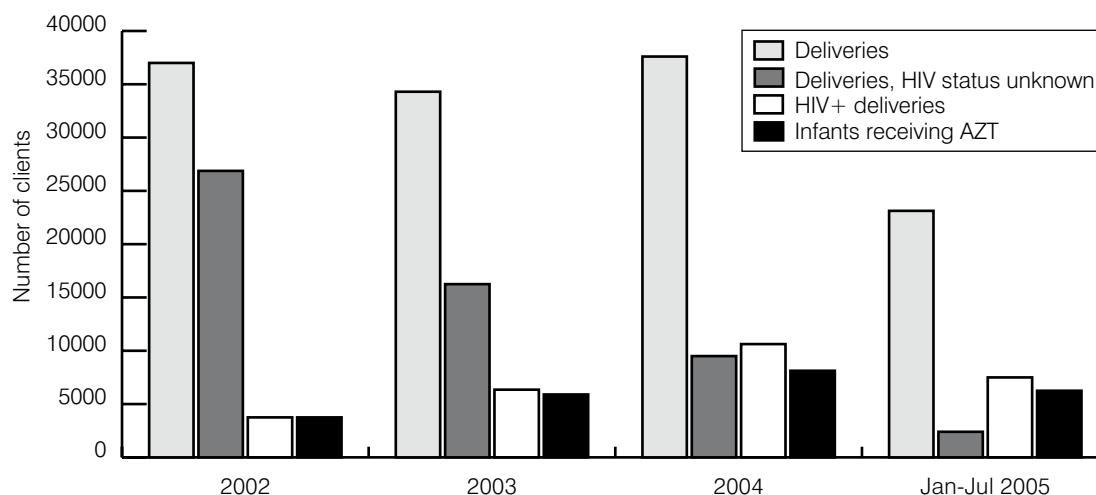


Figure 16B. PMTCT indicators from maternity clinics, Botswana, 2002–2005



AZT, azidothymidine
PMTCT, prevention of mother-to-child transmission

The approach we used to explore PMTCT impacts on child mortality was similar to that applied to assess ART impacts on adult mortality. However, assessing the impact of PMTCT on child deaths may be more complex for the following reasons: reporting of child deaths, particularly in institutional settings may be less accurate than that in adults; PMTCT programmatic indicators may be more subject to reporting inaccuracies than those for ART and are not designed to measure postpartum infant HIV transmission through breastfeeding; competing risks for child mortality are not easily dissociated from those related to HIV; and infant or child mortality may also be influenced by increasing numbers of children receiving ART, which should also substantially reduce child mortality.^k

The demographic impact of HIV on adult mortality is similarly evident in children (Figure 10). Further disaggregation of total number of deaths in children aged less than 5 years shows that the proportion of deaths in neonates and infants aged more than 28 days reflects the greatest increase since the early 1990s, and this increase is most likely reflecting HIV-associated mortality (Figure 17A). The proportion of non-institutional deaths in neonates, infants (defined as aged more than 28 days and less than 1 year in this dataset) and children aged 1–4 years, has decreased substantially since the early 1990s to relatively recent stable levels of 2.7%, 9.5%, and 14.2%. This indicates that apparent stabilization or possible declines in childhood mortality are not likely to be a reflection of increasing mortality in the non-institutional setting (Figure 17B). Hence, it is reasonable that an appropriate indicator for measuring the impact of PMTCT should include infants aged less than 1 year. However, for the purposes of this investigation, the vital registration mortality data files and the 2004–2005 mortality survey only included deaths of infants aged more than 28 days, thereby excluding institutional deaths in neonates from the analysis at the present time.^l

^k According to the Botswana MOH, nearly 5000 children are currently receiving ART, yet we have no information on the temporal or geographic distribution of its use.

^l Trends are expressed as incidence rather than death rates per 1000 live births because live-birth denominator data was not readily available for 2004 and 2005. Furthermore, rates of live births have remained relatively stable overall and by district for the past several years—changing denominators are unlikely to have an impact on trends in infant or child mortality rates.

Figure 17A. Trends in mortality rates in children aged less than 5 years and incidence of mortality for neonates, infants excluding neonates, and children aged 1–4 years, from institutional and non-institutional settings, 1991–2003

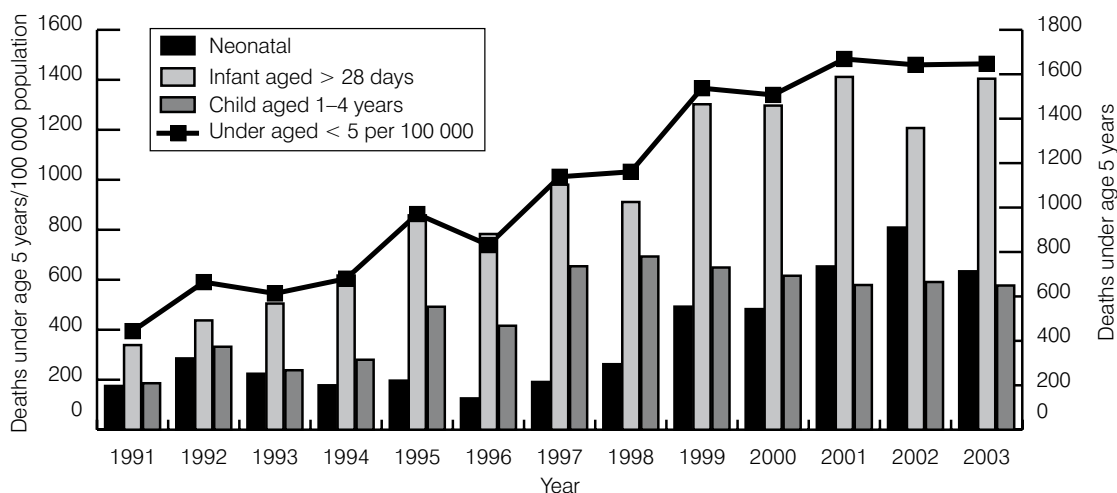
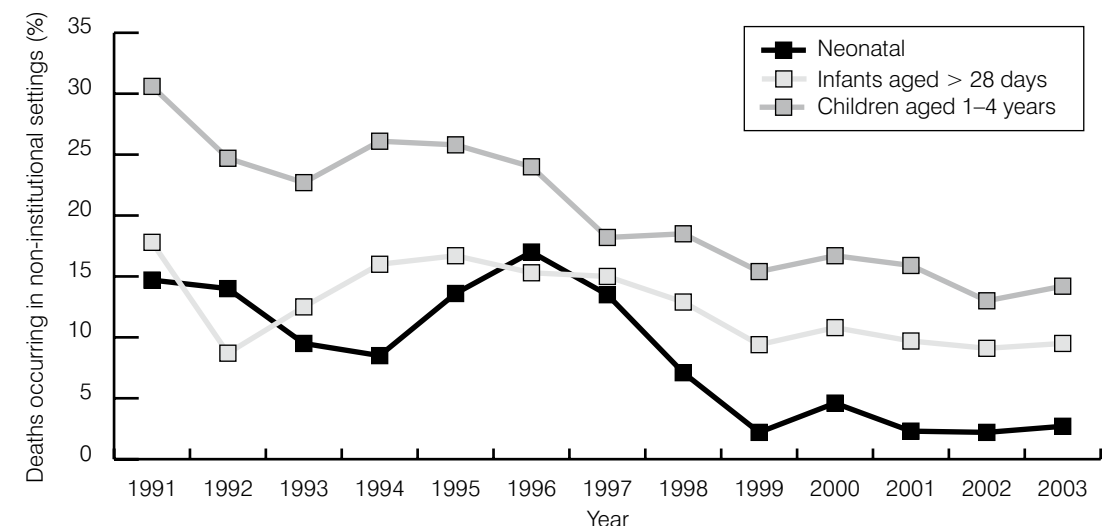
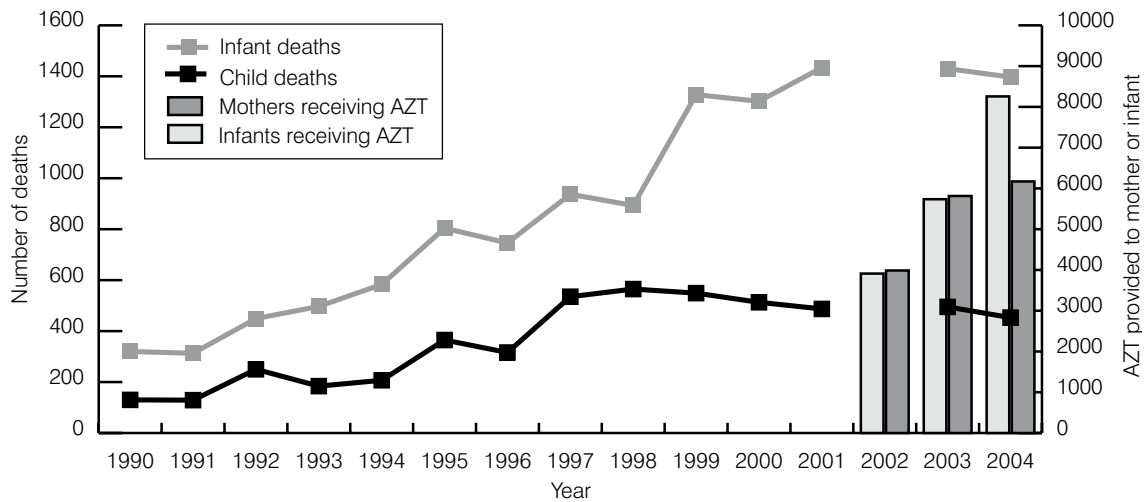


Figure 17B. Proportion of deaths of children (neonates, infants excluding neonates, and children) occurring in non-institutional settings



Trends in institutional deaths in infants (excluding neonates) and children aged 1–4 years from 1990 to 2004 and PMTCT indicators of AZT use in HIV-infected mothers and their newborns from 2002 to 2004 are shown in Figure 18. Trends in infant and child mortality show linear increases followed by stabilization in 2000 and 1998, respectively, and a modest decline of 2% in 2003–2004. Coincidentally, the numbers of pregnant women reportedly treated with AZT pre-partum, and infants similarly treated at birth, increased between 2002 and 2003. However, the rate of increase in numbers of mothers treated pre-partum with AZT declined sharply relative to the similar treatment of infants between 2003 and 2004.

Figure 18. Institutional infant and child mortality compared with PMTCT indicators for AZT use in mother and infants, 1990–2004*



* 2002 mortality data is incomplete and not displayed

Based on preliminary mortality data reported through June 2005, there is a continued decline in the numbers of deaths of children aged less than 5 years. Furthermore, there is evidence of declines in rates of institutional infant deaths (excluding neonates) between 2003 and 2004, by district. Nevertheless, high variability in reported deaths particularly in districts with lower populations, coupled with concerns of reporting completeness makes it difficult to interpret declining trends similar to that seen in adults (Table 2). For example, data comparing infant deaths and antiretroviral interventions in HIV-infected mothers and infants in Gaborone and Francistown districts (districts accounting for 42% of total infant deaths between 1999 and 2004) reveal diverse mortality trends between 2003 and 2004, coincident with increasing uptake of PMTCT interventions. This suggests that the intervention has no definitive effect (Figure 19A and 19B). Furthermore, there is a substantial decline in the reported numbers of pregnant mothers provided with AZT in Gaborone district between 2003 and 2005, which is not seen in data from Francistown or in other major districts (Figure 20). This suggests a deterioration in PMTCT services, or inaccurate monitoring data identified in Gaborone.

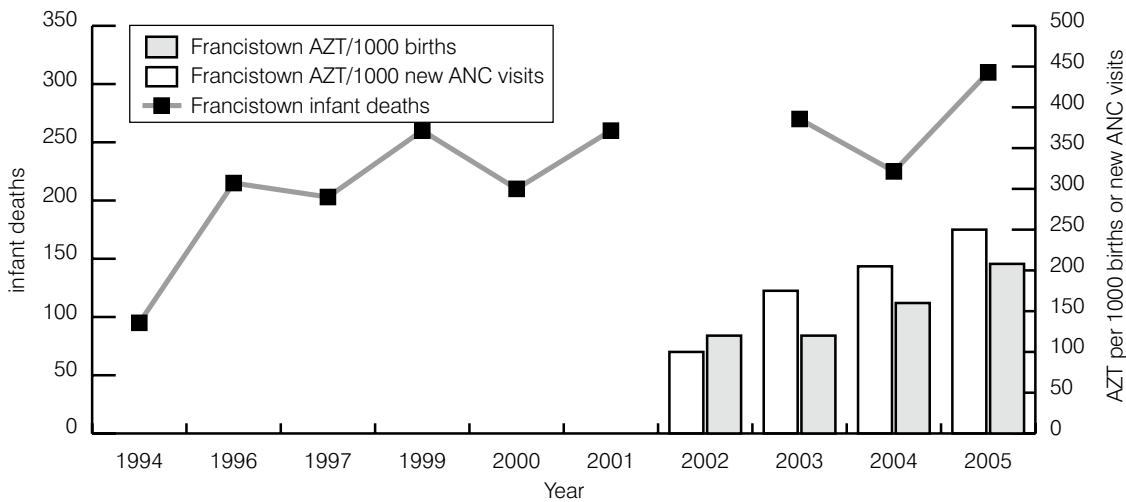
Table 2. Institutional infant* mortality by district, 1994–2004 and change in incidence between 2003 and 2004

District	Proportion of cumulated deaths (%) 1999–2004	Infant deaths									Change (%) 2003–2004
		1994	1996	1997	1999	2000	2001	2002	2003	2004	
Lobaste	2.4	15	14	28	36	37	46	18	42	11	-73.8
South East	1.8	7	12	30	17	26	24	34	25	14	-44.0
Selebi Phikwe	4.9	63	30	68	51	77	77	69	68	40	-41.2
Bobwira	3.4	15	22	39	41	51	51	35	53	37	-30.2
Ngami	5.3	24	39	71	54	61	94	48	91	67	-26.4
Francistown	18.4	96	215	201	261	209	263	209	273	223	-18.3
Gantsi	1.1	13	7	21	17	4	15	6	24	21	-12.5
Serowe/Palapye	7.3	46	38	61	77	117	83	69	115	108	-6.1
Kweneng East	5.1	19	21	19	53	55	82	42	82	82	0.0
Hukuntsi	0.6	0	2	0	0	9	7	9	10	10	0.0
North East	1.4	0	0	0	6	24	30	16	17	18	5.9
Kgalagadi	1.2	11	9	9	8	18	27	10	15	16	6.7
Gabrone	24.2	152	178	179	310	336	336	262	310	336	8.4
Mahalapye	5.9	37	51	65	66	86	73	59	83	97	16.9
Boteti	2.3	10	20	21	21	37	26	31	30	37	23.3
Tutume	3.5	3	29	28	47	33	45	48	43	57	32.6
Kgatleng	1.9	1	1	8	20	28	33	10	24	34	41.7
Okavango	2.3	11	21	28	21	27	33	16	35	50	42.9
Southern†											
Jwaneng	4.2	21	27	52	59	34	58	40	49	89	81.6
Chobe	1.0	6	0	3	12	18	12	6	11	20	81.8
Goodhope	1.1	0	10	7	0	15	18	8	13	30	130.8
Unk	0.7	0	0	0	23	0	0	15	17	0	
Total	100	550	746	938	1200	1302	1433	1060	1430	1397	-2.3

* Excluding neonates

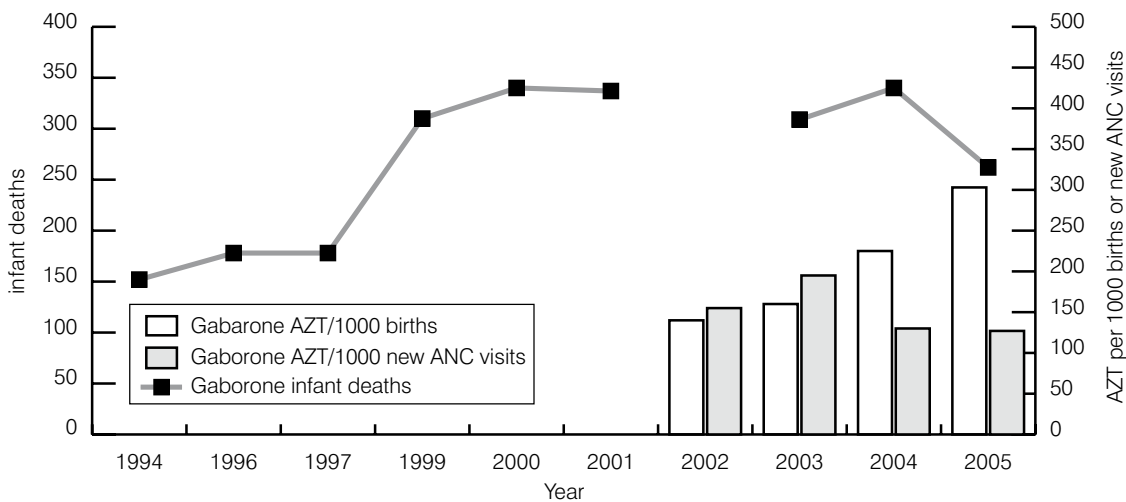
† Left empty because of border changes during the period

Figure 19A. Institutional infant mortality and reported AZT use among ANC attendees and newborns, based on PMTCT programmatic data for districts of Francistown, 1994–2005*



*Data from 2002 are incomplete and not presented, and those from 2005 are annualized based on deaths occurring until June and reported by December 2005
 ANC, antenatal care clinic
 AZT, azidothymidine
 PMTCT, prevention of mother-to-child transmission

Figure 19B. Institutional infant mortality and reported AZT use among ANC attendees and newborns, based on PMTCT programmatic data for districts of Gaborone, 1994–2005 *



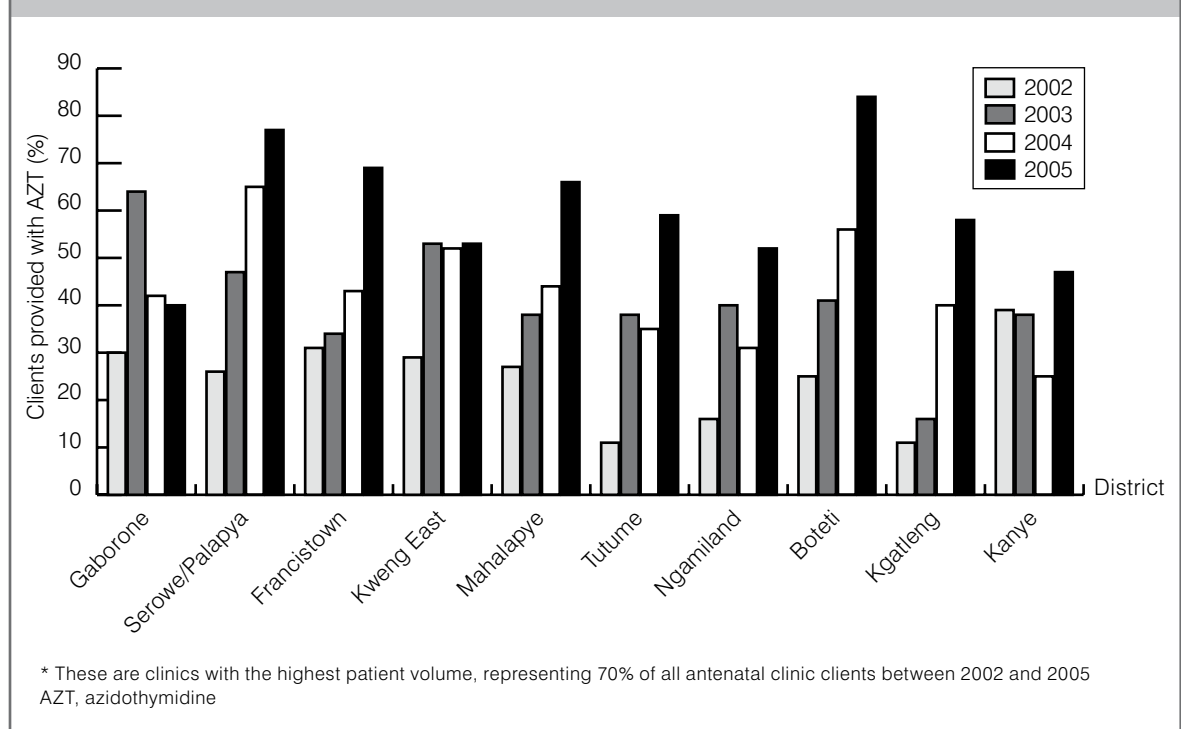
*Data from 2002 are incomplete and not presented, and those from 2005 are annualized based on deaths occurring until June and reported by December 2005
 ANC, antenatal care clinic
 AZT, azidothymidine
 PMTCT, prevention of mother-to-child transmission

Summary:

evidence for the impact of PMTCT on mortality in infants or children aged less than 5 years

This analysis provide little evidence of any substantial decline in infant or child deaths until 2004, and issues concerning data quality would be unlikely to produce biases that would mask true declines in numbers of deaths. Preliminary analysis of mortality data for 2005 suggests that infant and child mortality have declined in some districts. However, under-reporting of deaths in 2004–2005 is a major concern that may confound trend interpretation. A further validation of mortality data from 2005 and 2006, as well as audits of PMTCT indicator data, should provide insight into evidence for any potential impact of PMTCT programmes, or reasons for its absence. The relative stagnation of ART preventive interventions in HIV-positive pregnant women at levels of 60–70% is of particular concern, and requires further investigation. Finally, assuming that mortality and PMTCT indicator data are reasonably accurate, it is unclear why the impact of PMTCT interventions among nearly 10 000 HIV-infected women in 2002–2003 would not have reduced infant mortality by a measurable degree by 2004 and is worthy of further investigation.

Figure 20. The proportion of HIV infected women provided with AZT pre-partum, by district,* 2002–2005



CONCLUSION

Although controlled trials and at a population-level in North America, Europe, and Brazil have provided substantial evidence for the efficacy of ART in reversing HIV-mediated immune suppression and mortality, evidence (beyond the anecdotal) for a comparable effect on mortality at the population level in sub-Saharan Africa has yet to be confirmed. Similarly, evidence of benefits of ART to interrupt mother-to-infant HIV transmission, in combination with further postpartum interventions to prevent HIV infection through breastfeeding, are well documented in controlled trials and cohort studies. However, the population-level effectiveness of the programmatic approach has yet to document the expected impact of reductions in infant and deaths associated with HIV in children.

Our preliminary analyses indicate that death rates in adults overall, and particularly in the age group 20–49 years, have declined between 2003 and 2004, coincident with increasing exposure to ART. This suggests a causal association. There is no evidence for similar declines in infant or child mortality rates, despite increasing exposure of HIV-positive pregnant women and their newborns to PMTCT programmes.

Definitive conclusions regarding these associations will require further investigation including but not limited to the following:

- Validation of adult and child mortality reporting at district level (institutional and non-institutional settings);
- Auditing of PMTCT and ART programmatic data at the district level; analysis of mortality statistics for 2005 and 2006; and
- Qualitative research to better understand possible barriers to effectively interrupting mother-to-infant transmission of HIV transmission and resultant infant and child mortality. Of particular concern is the relative stagnation in the proportion of HIV-infected women (around 60–70%) provided with antiretroviral preventive interventions: this is a finding not restricted to Botswana, but has also been noted in numerous PMTCT programmes in sub-Saharan Africa.

Botswana policy and programme managers should note the potential benefits to public-health programme management of applying triangulation, or simply rigorous epidemiological analytical methods to multiple data sets, which are usually readily available. This study demonstrates the utility of demographic analyses of vital registration data, and the benefit of linking vital registration data to programme data in order to evaluate programmatic effectiveness. In addition it suggests the following:

- That vital registration mortality statistics can be used as an effective surveillance method to assess HIV dynamics and effects of interventions;
- That mortality statistics are of greatest value when recording, analysis, and reporting of data can be done expeditiously, for HIV as well as for other chronic or emergent diseases; and
- The need for district-level feedback of programme indicator data to assure that it is accurately and wisely used in order to assure the highest quality of public health services.

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