ORIGINAL ARTICLE

Estimates of eligibility for antiretroviral treatment (ART) and projected ART impact on AIDS mortality among South African educators

T Rehle, O Shisana

ABSTRACT

The study assessed the proportion of HIV-infected educators that need antiretroviral treatment (ART) according to current criteria, and estimated the impact of ART on AIDS mortality by modelling scenarios with and without access to ART. Specimens for HIV testing were obtained from 17 088 educators and a sub-sample of 444 venous blood specimens from HIV-positive educators was selected for a CD4 cell count analysis. The Spectrum model package was used for estimating AIDS-associated mortality and projecting the impact of ART scenarios. The results of the CD4 cell count analysis in the HIV-positive educator study population showed that 8% had fewer than 100, 22% fewer than 200, 52% fewer than 350, and 72% fewer than 500 CD4 cells/mm^3. Based on the proportion of HIV-positive educators with a CD4 cell count < 200 cells/mm^3 we estimated that in 2005 approximately 10 700 educators would need ART according to current SA government guidelines. For the baseline scenario without ART the number of AIDS deaths among HIV-infected educators was projected to increase from 1 992 deaths in 2000 to 5 260 in 2010. The number of projected AIDS deaths in the educator study population was estimated to be 4 414 in 2005, with almost 50% of the AIDS deaths occurring in the 35 - 44 age group. The estimates suggest that in 2005 9.1% of the HIV-infected educators, or 1.2% of the total educator population, will be dying of AIDS. By 2010, a reduction of almost 50% in AIDS deaths was estimated for the treatment scenario with 90% ART coverage, compared with the baseline scenario without treatment. The ART impact scenarios illustrate that a relatively high ART coverage would be needed to ensure a substantial impact of ART on HIV/AIDS-associated mortality.

Keywords: antiretroviral treatment, CD4 cell counts, AIDS mortality, impact modelling.

RÉSUMÉ

Cette étude a évalué la proportion des enseignants séropositifs qui ont besoin du traitement antirétroviral (ART) selon les critères actuels. De plus, l'étude a fait une prévision de l'impact d'ART sur la mortalité due au SIDA en présentant deux scénarios: les patients avec accès au ART et ceux sans accès. Les spécimens des essais du VIH ont été obtenu de 17 088 enseignants. En autre, avec le but de faire des analyses des comptes des cellules CD4, un sous-échantillon de 444 spécimens de sang veineux fut obtenu des enseignants séropositifs. L'ensemble de modèles Spectrum a été employé afin de faire des prévisions de mortalité liée au SIDA et aussi pour faire une projection de l'impact des scénarios d'ART. Les résultats des analyses des comptes des cellules CD4 d'une étude de population auprès des enseignants séropositifs ont montré que 8% avaient une charge virale en dessous de 100, 22% moins de 200, 52% moins de 350 et 72% moins de 500 CD4 cellules/mm^3 respectivement. Etant donné la proportion des enseignants séropositifs ayant un compte des cellules CD4 moins de 200 cellules/mm^3, nous avons prévu qu'en 2005 approximativement 10 700 enseignants auraient besoin d'ART suivant les directives actuelles du gouvernement sud-africain. Pour le scénario de référence sans l'ART, le taux de morts parmi les enseignants séropositifs fut prévu d'augmenter de 1 992 morts en 2000 à 5 260 morts en 2010. Le taux de morts de SIDA projeté dans l'étude de population auprès des enseignants fut prévu d'augmenter à 4 414 en 2005 avec environ 50% de morts de SIDA appartenant au groupe âgé de 35 à 44 ans. Les pronostiques suggèrent qu'en 2005, 9.1% des enseignants séropositifs, ou 1.2% de l'ensemble de la population enseignante, mourront de SIDA. D'ici 2010, une baisse d'environ 50% de morts de SIDA est prévue pour les scénarios sur traitement, avec une provision de 90% d'ART en comparaison au scénario de référence sans traitement. Les scénarios de l'impact d'ART démontrent qu'une provision relativement élevée d'ART serait nécessaire afin d'assurer un impact considérable d'ART sur la mortalité liée au VIH/SIDA.

Mots clés: traitement antirétroviral, comptes des cellules CD4, mortalité de SIDA, modeler l'impact.

Thomas M Rehle is a Director in HSRC's Social Aspects of HIV/AIDS and Health Programme and holds an appointment as Visiting Professor of International Health at the University of Cape Town, School of Public Health and Family Medicine. He has extensive experience in tropical public health and disease control management. He pioneered the development of innovative evaluation tools and data collection methods and was lead editor and author of the reference guide on *Evaluating Programs for HIV/AIDS Prevention and Care in Developing Countries: A Handbook for Program Managers and Decision Makers* (Family Health International, 2001).

Olive Shisana is President and CEO of the South African Human Sciences Research Council. She served as Executive Director of Social Aspects of HIV/AIDS at the same organisation. She has done extensive research on the epidemiology of HIV/AIDS in the general population and in the health and education sectors.

Correspondence to: Thomas M Rehle, Human Sciences Research Council, 69 Plein Street, Cape Town, South Africa. E-mail: trehle@hsrc.ac.za.

Introduction

South Africa has been especially hard hit by the HIV/AIDS epidemic, with over 5million people estimated to be infected with HIV at mid-2004 (Dorrington, Bradshaw, Johnson & Budlender, 2004). As a consequence, the effectiveness and functioning of the public sector is increasingly threatened by the HIV/AIDS epidemic. Multiple studies have been conducted in South Africa to examine the impact of HIV/AIDS on the economy and the health sector (Evian, Fox, Macleod, Slowtow & Rosen, 2004). These studies performed HIV testing among employees. However, there was a shortage of similar studies on the impact of HIV/AIDS on the education sector. In 2004, the South African Education Labour Relations Council (ELRC) commissioned the Human Sciences Research Council (HSRC) to undertake a study examining the impact of HIV/AIDS on the supply and demand of educators in the education sector.

The survey was carried out between April and August in 2004 and involved 21 669 public school educators from all provinces (Shisana, Peltzer, Zungu-Dirwayi & Louw, 2005). Only those who were present on the day of the survey were asked to participate. Oral fluid and blood specimens for HIV testing were obtained from 17 088 surveyed educators (78.9%). A subsequent comparison between educators interviewed and not tested and those interviewed and tested did not suggest a bias towards higher risk for HIV among teachers who refused to be tested. HIV prevalence among educators was 12.7%, a figure lower than the 15.5% found among South African adults of comparable age in the national HIV survey in 2002 (Nelson Mandela Foundation/Human Science Research Council, 2002). The HIV age distribution profile of the educator study population was, however, very similar to that of the 2002 general adult population.

In an unrelated development, the government of South Africa has, as a matter of urgency, recently started implementing a programme to provide antiretroviral therapy (ART) in the public health sector (Department of Health, 2003, 2004a). The goal of the programme is to establish at least one accredited service point in every health district by the end of the first year of implementation and within a period of 5 years to provide all South Africans eligible for ART access to comprehensive care and treatment for HIV and AIDS. Voluntary counselling and testing (VCT) will serve as a crucial entry point for this treatment programme. Once identified as HIV-positive, patients will be assessed for the stage of their illness and referred for appropriate medical care. The assessment involves a CD4 cell count and the patient's medical history and status.

In this study we will examine the proportion of HIV-infected educators who need ART according to current criteria and estimate the impact of ART on AIDS mortality in the educator population over the next 10 years by modelling scenarios with and without access to ART.

Methods

The 2004 educator survey HIV test results were based on 7 648 oral fluid specimens and 9 440 blood specimens (total 17 088). Only HIV-positive blood specimens were subjected to the CD4 cell count analysis. A total of 1 095 HIV-positive samples were initially tested for CD4 cells. A subsequent audit conducted by the laboratory revealed that 261 out of the 1 095 samples were tested after 5 days from collection (24%) and were therefore excluded from the CD4 count analysis. Of the 834 samples that had been tested within 5 days of collection, 390 were deemed to be not reliable (samples degraded/ disintegrated and poorly viable). This left a remaining 444 valid samples out of 1 095 (or 41% of total) that could be analysed for CD4 cell count. The nature of this selection process suggests that no epidemiological bias should have been introduced with regard to the human source from which the 444 samples had been selected for the CD4 cell count analysis. CD4 cell counts were performed on whole blood specimens using the PLG CD4 assay (Glencross, Scott, Jani, Barnett & Janossy, 2002). The PLG CD4 cell enumeration methodology utilises the principle of immunophenotypic lineage identification but does not rely on lymphocyte subset identification. Instead, it identifies all white blood cells as the primary reference population for CD4 enumeration. PLG CD4 tests were performed as single platform testing using FlowCOUNT beads.

The Spectrum model package (version 2.30, March 2005) was used for the modelling work. Spectrum contains two modules: DemProj for the demographic projection and AIM for the epidemiological projection. The demographic projection model projects the population by age and sex on the basis of fertility (total fertility rate and age distribution of fertility), mortality (life expectancy at birth and age-specific mortality) and migration. The demographic variables used by the model are derived from the population estimates and projections of the United Nations Population Division database. The full details of the methodology are provided in the DemProj manual (Stover & Kirmeyer, 1999). The HIVAIDS calculations are implemented by age and sex and are described fully in the AIM manual (Stover, 2002). Epidemiological assumption and patterns used in the model to determine parameters such as the progression from HIV infection to death were developed by the UNAIDS Reference Group on Estimates, Models and Projections (UNAIDS, 2003). The computer software programme and the accompanying manuals with a detailed description of the applied equations and assumptions can be downloaded from the website at The Futures Group International (www.tfgi.com).

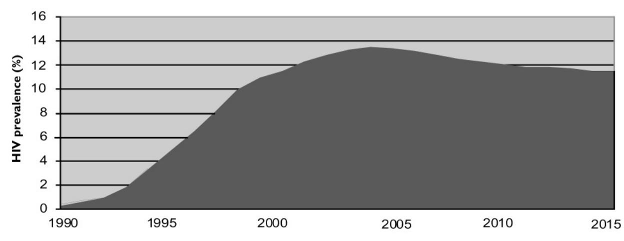
The general adult population of South Africa served as reference population for the projections in the educator study population. The average size of the educator population was assumed to be 360 000 educators during the entire modeled period. Key input parameters used in the modelling process are described.

Constructing the HIV prevalence curve for South African public sector educators

As a first step of the modelling work, HIV prevalence input values were prepared for the study population that are believed to best approximate the prevalence levels in educators in the previous time period 1990 - 2004 (Rehle & Shisana, 2003). HIV prevalence trends have been recorded among antenatal care attendees in South Africa since 1990. It was assumed that the epidemic among South African public sector educators was following a similar pattern as has been observed in pregnant women, but at a substantially lower level. HIV prevalence among educators was 12.7% (95% CI: 12.0 - 13.5) in this 2004 study, while the antenatal clinic survey of 2003 reported a prevalence of 27.9% (95% CI: 26.8 - 28.9) (Department of Health, 2004b). The ratio obtained from these two prevalence figures (12.7 / 27.9) produced an 'adjustment' factor that applied to the antenatal data, and guided the input values for the HIV prevalence curve for educators in the period 1990 – 2003.

It was further assumed that the HIV prevalence level of 2004 was slightly underestimated in the educator survey, due to the absence of sick or hospitalised educators in the surveyed population. Therefore, the value of the upper bound of the confidence interval (13.5%) was used for 2004. HIV prevalence was assumed to level off after that year and slightly fall in the following years to 11.5% in 2015 (Fig. 1), resembling an HIV prevalence pattern observed in other countries in sub-Saharan Africa with more advanced epidemics than South Africa (Asamoah-Odei, Garcia Calleja & Boerma, 2004). The obtained prevalence curve served as a baseline for the scenario without ART during the model period.

FIG. I. PROJECTED HIV PREVALENCE AMONG EDUCATORS, 1990 - 2015



Progression from HIV infection to death

The progression period describes the length of time that elapses from the time a person becomes infected with HIV until he or she dies from AIDS. The model uses the cumulative distribution of the progression period. This distribution is defined as the cumulative proportion of people infected with HIV who will die from AIDS, by the number of years since infection.

The AIM model module has two default progression patterns available: a median time from infection to death of 9 years for developing countries and 10 years for industrialised countries. These patterns are based on the assumption that better health care leads to a somewhat longer survival period in industrialised countries (UNAIDS, 2001). In this analysis the median time from infection to death is assumed to be 9 years, 8.6 years for males and 9.4 years for females. There is evidence that older people progress to AIDS and death faster than younger people; as a result, women generally progress slower than men since they tend to be infected at a younger age (UNAIDS 2001). This survival period refers to people who are not receiving treatment with antiretroviral drugs.

Modelling the effects of ART

The model calculates the effects of ART based on an assumption that the proportion of those in need of receiving ART includes those newly needing therapy and those continuing on therapy from the previous year. The calculation of the total needing therapy is as follows:

Total needing ART(t) = Number receiving ART(t-1) × % surviving on ART + Number newly needing ART(t)

ART is assumed to delay progression to death as long as it is effective. However, some people will develop resistance to ART and others may have to stop treatment because of severe side-effects. As a result, not all of those on ART in one year will continue to the next year. In the model it is assumed that 90% of those on ART survive to the following year.

The proportion of HIV-infected persons who newly need ART in a given year is linked to the evolution of the epidemic in the study population, and changes over time as the epidemic matures. In the early years of the epidemic the proportion of infected people who have progressed to AIDS is therefore smaller than in the more advanced phase of the epidemic 15 - 20 years later, when a much higher proportion of HIV-positive individuals is expected to newly need ART. For that reason, it would not be appropriate to apply in the model a fixed proportion of those who newly need ART in a given year to the entire time period. A more dynamic solution is therefore required. In the model the number of those who newly need ART in a given year is defined as the number of HIV-infected persons who are within 2 years of dying from AIDS if they do not get ART.

TABLE 1. CRITERIA FOR ART INITIATION IN ADULTS AND ADOLESCENTS

Department of Health, South Africa

- CD4 <200 cells/mm^3 irrespective of stage

or

- WHO stage IV AIDS-defining illness, irrespective of CD4 count

and

- Patient expresses willingness and readiness to take ART adherently

US Department of Health and Human Services (DHHS 2004)

- ART is recommended for all patients with history of an AIDS-defining illness or severe symptoms of HIV infection regardless of CD4 cell count
- ART is recommended for asymptomatic patients with < 200 CD4 cells/mm^3
- Asymptomatic patients with CD4 cell counts of 201 - 350 cells/mm^3 should be offered treatment

TABLE 2. CD4 CELL COUNT PROFILE IN HIV-POSITIVE EDUCATORS

CD4 (cells/mm3)	No. of samples	%
< 50	6	1
50 - 99	31	7
100 - 199	62	14
200 - 349	133	30
350 - 499	88	20
≥ 500	124	28
Sample total	444	100

Results

Eligibility for ART

Table 1 shows the selection criteria for initiating ART currently proposed by the Department of Health, (Department of Health 2004a) and the Panel on Clinical Practices for Treatment of HIV Infection convened by the US Department of Health and Human Services (DHHS 2004).

The results of the CD4 cell count analysis in the HIV-positive educator study population are shown in Table 2. The CD4 cell count profile in this sub-sample of 444 blood specimens suggests that 8% had fewer than 100, 22% fewer than 200, 52% fewer than 350, and 72% fewer than 500 CD4 cells/mm^3.

The data indicate that 22% of educators found HIV-positive in the 2004 survey would be eligible for ART under the current national criteria (Table 3). Applying the guidelines of the US Department of Health and Human services, which call for offering treatment to asymptomatic patients with a CD4 cell count of ≤ 350 cells/mm^3, would increase the proportion of HIV-positive educators eligible for ART to 52%.

Projected AIDS deaths without ART

In Table 4 the number of AIDS deaths among educators is estimated by the model for the baseline scenario without ART.

TABLE 3. PROPORTION OF HIV-POSITIVE EDUCATORS ELIGIBLE FOR ART BASED ON CD4 COUNT (REFERENCE RECOMMENDATIONS)

CD4 (cells/mm^3)	No. of samples	% eligible for ART
< 200	99	22% (national criteria)
≤ 350	232	52% (US-DHHS 2004 guidelines)

TABLE 4. ESTIMATED AIDS DEATHS WITHOUT ART

Year	Number of AIDS deaths
2000	1 992
2005	4 414
2010	5 260
2015	4 846

Table 5 shows the number and relative distribution of AIDS deaths by age in the educator study population projected for 2005. The estimates are for the baseline scenario without ART and take into account the specific HIV age distribution of the educator population as described in the 2004 survey (Shisana *et al.*, 2005). The results suggest that almost half (48.5%) of the estimated 4 414 AIDS-associated deaths in educators will be concentrated in the 35 – 44 age group.

TABLE 5. DISTRIBUTION OF AIDS DEATHS BY AGE IN 2005

Age group	Number of AIDS deaths	Percentage of total AIDS deaths
< 24	13	0.3%
25 - 34	1 483	33.6%
35 - 44	2 141	48.5%
45 - 54	653	14.8%
55 and above	124	2.8%
Total	4 414	100.0%

Projected impact of ART on AIDS mortality

Two different ART scenarios were created to model the impact of ART on AIDS mortality in the study population (Table 6). In the ART1 scenario a treatment programme is described that will expand over the next years to cover 60% in 2010 and 75% in 2015 of those who need ART. A more ambitious programme is described in the ART2 scenario, where 50% coverage is achieved in 2007. The treatment coverage is assumed to increase to 90% by 2010 and remain at this level in the subsequent years.

The estimated impact of ART on AIDS mortality in the study population over the modelled period 2003 – 2015 is presented in Table 7. The relative reduction of AIDS deaths in the treatment scenarios was calculated by comparing the modeled impact of ART1 and ART2 with the baseline scenario without access to ART.

TABLE 6. ART SCENARIOS: PERCENTAGE OF THOSE WHO NEED TREATMENT RECEIVING ART

Year	ART1	ART2
2003	0%	0%
2004	5%	5%
2005	15%	20%
2006	25%	35%
2007	35%	50%
2008	44%	65%
2009	52%	80%
2010	60%	90%
2011	66%	90%
2012	70%	90%
2013	72%	90%
2014	74%	90%
2015	75%	90%

Discussion

Our results suggest that more than a fifth (22%) of the HIV-positive educator population would need ART if health care providers use the national criteria for the initiation of ART (Department of Health, 2004a). The proportion of HIV-positive educators with a CD4 cell count < 200 cells/mm^3 (22%) is higher than those previously reported in population-based studies conducted in sub-Saharan Africa (Auvert, Males, Puren, Taljaard, Carael, & Williams, 2004; Newell, Coovadia, Cortinja-Borja, Rollins, Gaillard, & Dabis 2004; Whitworth, Morgan, Quigley, Smith, Majanja, Eotu *et al.*, 2000). However, a recent study of a cohort of HIV-infected pregnant women in South Africa found 20% with a CD4 cell count < 200 cells/mm^3, which is similar to our findings (Mtshali & Smit, 2005).

Based on the estimated proportion of HIV-positive educators with a CD4 cell count < 200 cells/mm^3 we

TABLE 7. ESTIMATED REDUCTION IN AIDS DEATHS

Year	ART1 SCENARIO	ART2 SCENARIO
2003	0.0%	0.0%
2004	4.0%	4.0%
2005	8.8%	13.0%
2006	11.1%	17.5%
2007	13.4%	23.0%
2008	15.3%	30.4%
2009	16.1%	41.5%
2010	18.6%	48.7%
2011	19.0%	38.6%
2012	17.3%	29.9%
2013	13.3%	22.6%
2014	11.1%	16.4%
2015	7.7%	10.9%

conclude that in 2005 approximately 10 700 educators would need ART according to current government guidelines (13.5%, projected HIV prevalence for 2005; 360 000, modelled total educator population: 13.5% x 360 000 x 22% = 10 692). Taking a CD4 cell count of ≤ 350 cells/mm^3 as the level for the initiation of ART, as recommended by the guidelines of the US Department of Health and Human services, would increase the number of HIV positive educators eligible to ART to more than 25 000 in the year 2005. Educators who have a CD4 count between 200 and 350 cells/mm^3 will not be able to access ART through the state health services and would either have to use their medical aids or pay out of their own pocket. Co-trimoxazole prophylaxis should be particularly recommended for these HIV-positive educators who are not yet eligible for ART under the current national policy (Benson, Kaplan, Masur, Pau, & Holmes, 2004; Mermin, Lule, Ekwaru, Malamba, Downing, Ransom *et al.*, 2004).

The number of projected AIDS deaths in the educator study population was estimated to be 4 414 in 2005, with almost 50% of the AIDS deaths occurring in the 35 - 44 age group. The estimates suggest that in 2005 9.1% of HIV-infected educators, or 1.2% of the total educator population, will be dying of AIDS. The model estimate of AIDS mortality in HIV-infected educators is in good agreement with the findings of empirical studies conducted in HIV-infected study populations in developing and industrialised countries where similar mortality rates have been reported (Porter & Zaba, 2004).

Our projections of the impact of ART scenarios on AIDS mortality show a substantial decline in deaths initially while ART coverage is increasing. By 2010, a reduction of almost 50% in AIDS deaths was estimated for the treatment scenario with 90% coverage compared with the baseline scenario without treatment. The results illustrate that the relative impact of ART programmes on AIDS deaths diminishes once the increases in coverage become smaller, as in the ART1 scenario or when coverage reaches a plateau as in ART2. Since ART is only delaying death and not averting AIDS death indefinitely, deaths due to AIDS increase over time among treated people. Once coverage stops increasing we will experience the effect of limited survivorship under ART and deaths will rise. As a consequence of these dynamics, AIDS mortality is expected to converge ultimately towards the baseline scenario.

Botswana, Namibia and Uganda now have an estimated ART coverage that exceeds one quarter of all people needing treatment, and 13 countries in the region have exceeded 10% coverage (WHO & UNAIDS, 2004). The 90% ART coverage as modelled in our ART2 scenario might be too optimistic, however. A recent assessment in the USA concluded that only 55% of eligible persons living with HIV/AIDS in the age group 15 - 49 years were receiving ART (Teshale, Kamimoto, Harris, Li, Wang & McKenna, 2005). A study among 7 812 HIV-infected adult South Africans who have been enrolled in a private-sector HIV/AIDS disease management programme revealed a relatively poor ART adherence (< 70%) in half of the patients (Nachega, Hislop, Lo, Omer, Dowdy, Regensberg *et al.*, 2005). However, increases in adherence rates should be achievable in the coming years, with improvements in case management and ART regimens with fewer side-effects.

HIV prevalence rises above baseline levels in ART scenarios with wide coverage, as longer survival for treated patients offsets reductions in new infections through reduced transmissibility (Salomon, Hogan, Stover, Stanecki, Walker, Ghys *et al.*, 2005). Increased access to ART will not only increase the survival time of HIV-infected persons, it may also have multiple, potentially altering effects on HIV transmission by increasing the pool of HIV-infected persons and by decreasing infectiousness through reduction in viral loads. As a result, the interpretation of HIV trends will be more challenging in the coming years when ART becomes more widely available for infected individuals.

Our findings have important policy implications. Firstly, the projected loss of over 4 400 educators during the year 2005 due to AIDS suggests that the educator population is seriously affected, leading to a possible shortage of educators in the public education system. Secondly, over 80% of educators projected to die of AIDS in 2005 are younger than 45 years of age, implying that the selective mortality impact is likely to exacerbate the already difficult situation. In addition, the proportion of HIV-infected educators who newly need ART will substantially increase over the next 5 years. Facing such severe challenges, it is critical that the Department of Education act swiftly to avert an acute crisis.

References

Asamoah-Odei, E., Garcia Calleja, J.M. & Boerma, T. (2004). HIV prevalence and trends in sub-Saharan Africa: no decline and large subregional differences. *Lancet*, 364, 35-40.

Auvert, B., Males, S., Puren, A., Taljaard, D., Carael, M. & Williams, B. (2004). Can highly active antiretroviral therapy reduce the spread of HIV? A study in a township of South Africa. *Journal of Acquired Immunodeficiency Syndrome*, 36, 613-621.

Benson, C.A., Kaplan, J.E., Masur, H., Pau, A. & Holmes, K.K. (2004). Treating opportunistic infections among HIV-infected adults and adolescents. *MMWR Recommendations and Reports,* 53(RR 15), 1-112.

Department of Health (2003). *Operational plan for the comprehensive HIV and AIDS care, treatment and management for South Africa.* Pretoria, South Africa.

Department of Health (2004a). *National antiretroviral treatment guidelines.* Pretoria, South Africa.

Department of Health (2004b). *National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2003.* Pretoria, South Africa.

Department of Health and Human Services (DHHS) (2004). *Guidelines for the use of antiretroviral agents in HIV-1infected adults and adolescents.* Washington, DC, USA.

Dorrington, R.E., Bradshaw, D., Johnson, L. & Budlender, D. (2004). *The demographic impact of HIV/AIDS in South Africa. National indicators for 2004.* Cape Town: Centre for Actuarial Research, South African Medical Research Council and Actuarial Society of South Africa.

Evian, C., Fox, M., Macleod, W., Slowtow, S.J. & Rosen, S. (2004). Prevalence of HIV in Southern Africa 2000-2001. *South African Medical Journal*, 94, 125-130.

Glencross, D.K., Scott, L., Jani, I.V., Barnett, D. & Janossy, G. (2002). CD45 assisted panleucogating for accurate, cost effective dual platform CD4+ T cell enumeration. *Clinical Cytometry*, 50, 69–77.

Mermin, J., Lule, J., Ekwaru, J.P., Malamba, S., Downing, R., Ransom, R. *et al.* (2004). Effect of co-trimoxazole prophylaxis on morbidity, mortality, CD4 cell count and viral load in HIV infection in rural Uganda. *Lancet*, 364, 1428-1434.

Mtshali, N. & Smit, T. (2005). HIV-1 viral load and CD4+ cell counts in a cohort of HIV-infected pregnant women at Dr George Mukhari Hospital. In: Abstracts of 2nd South African AIDS Conference, 7-10 June, 2005, Durban, South Africa; Abstract 346.

Nachega, J., Hislop, M., Lo, M., Omer, S., Dowdy, D., Regensberg, L. *et al.* (2005). Adherence to antiretroviral therapy assessed by pharmacy claims and survival in HIV-infected South Africans. In: 12th Conference on Retroviruses and Opportunistic Infections, Boston, February 22-25, Abstract 167.

Nelson Mandela Foundation / Human Science Research Council (2002). *South African national HIV prevalence, behavioural risks and mass media household survey 2002.* Human Science Research Council, Cape Town, South Africa.

Newell, M-L., Coovadia, H., Cortinja-Borja, M., Rollins, N., Gaillard, P. & Dabis, F. (2004). Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet*, 364, 1236-1243.

Porter, K. & Zaba, B. (2004). The empirical evidence for the impact of HIV on adult mortality in the developing world: data from serological studies. *AIDS,* 18 (suppl 2): S9-S17.

Rehle, T. M. & Shisana, O. (2003). Epidemiological and demographic projections: South Africa. *African Journal of AIDS Research*, 2, 1-8.

Salomon, J.A., Hogan, D.R., Stover, J., Stanecki, K.A., Walker, N., Ghys, P.D. *et al.* (2005). Integrating HIV prevention and treatment: From slogans to impact. *PLoS Med* 2 (1) e16.

Shisana, O., Peltzer, K., Zungu-Dirwayi, N. & Louw, J. (2005). *The health of our educators: A focus on HIV/AIDS in South African schools.* Human Science Research Council, Cape Town, South Africa.

Stover, J. & Kirmeyer, S. (1999). *DemProj Version 4. A computer programme for making population projections.* The POLICY Project/Futures Group, Washington, DC, USA.

Stover, J. (2002). *AIM Version 4. A computer programme for making HIV/AIDS projections and examining the social and economic impacts of AIDS.* The POLICY Project/Futures Group, Washington, DC, USA.

Teshale, E., Kamimoto, L., Harris, N., Li, J., Wang, H. & McKenna, M. (2005). Estimated number of HIV-infected persons eligible for and receiving HIV antiretroviral therapy, 2003 – United States. In: 12th Conference on Retroviruses and Opportunistic Infections, Boston, February 22-25, Abstract 167.

UNAIDS (2001). *Disease progression and survival in HIV-infected adults: Bibliographic review.* Working paper of the Reference Group on Estimates, Models and Projections. Geneva, Switzerland.

UNAIDS (2003). UNAIDS Reference Group on Estimates, Models and Projections: *Estimating and projecting national HIV/AIDS epidemics.* UNAIDS/01.83, Geneva, Switzerland.

Whitworth, J., Morgan, D., Quigley, M., Smith, A., Majanja, B., Eotu, H. *et al.* (2000). Effect of HIV-1 and increasing immunosuppression on malaria parasitaemia and clinical episodes in adults in rural Uganda: a cohort study. *Lancet,* 356, 1051-1056.

World Health Organization (2003). *Scaling up antiretroviral therapy in resource limited settings: Revision 2003.* Geneva, Switzerland.

WHO and UNAIDS (2004). '3 by 5' progress report. Geneva, Switzerland.