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

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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/mm³. Based on the proportion of HIV-positive educators with a CD4 cell count < 200 cells/mm³ 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 outre, 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/mm³ respectivement. Étant donné la proportion des enseignants séropositifs ayant un compte des cellules CD4 moins de 200 cellules/mm³, 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 apportant 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, modéliser l’impact.

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Introduction
South Africa has been especially hard hit by the HIV/AIDS epidemic, with over 5 million 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...
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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.

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.
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ARTICLE ORIGINAL

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:

\[ \text{Total needing ART}(t) = \frac{\text{Number receiving ART}(t-1) \times \% \text{ surviving on ART}}{100} + \text{Number newly needing ART}(t) \]

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

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

| Criteria | South Africa | US DHHS 2004 |
|----------|--------------|--------------|
| CD4 <200 cells/mm³ irrespective of stage | ART is recommended for all patients with history of an AIDS-defining illness or severe symptoms of HIV infection regardless of CD4 count | ART is recommended for all patients with history of an AIDS-defining illness or severe symptoms of HIV infection regardless of CD4 count |
| WHO stage IV AIDS-defining illness, irrespective of CD4 count | ART is recommended for asymptomatic patients with < 200 CD4 cells/mm³ | ART is recommended for asymptomatic patients with < 200 CD4 cells/mm³ |
| Patient expresses willingness and readiness to take ART adherently | Asymptomatic patients with CD4 cell counts of 201 - 350 cells/mm³ should be offered treatment | Asymptomatic patients with CD4 cell counts of 201 - 350 cells/mm³ 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 |

### Table 3. Proportion of HIV-positive educators eligible for ART based on CD4 count (reference recommendations)

| CD4 (cells/mm³) | No. of samples | % eligible for ART |
|-----------------|----------------|--------------------|
| < 200 | 99 | 22% (national criteria) |
| ≤ 350 | 232 | 52% (US-DHHS 2004 guidelines) |

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/mm³.

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/mm³, 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.
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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.

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.

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/mm³ (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/mm³, 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/mm³ we
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/mm³ 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/mm³ 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.

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.
ORGINAL ARTICLE

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