



Estimation of adult antiretroviral treatment coverage in South Africa

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Objectives. To estimate the annual numbers of individuals receiving antiretroviral treatment in South Africa up to mid-2008, and the coverage of antiretroviral treatment in adults according to various definitions of need.

Methods. Antiretroviral coverage is defined as the number of patients receiving antiretroviral treatment at a point in time, divided by the number needing treatment. Numbers of patients receiving antiretroviral treatment are estimated from public sector data, and data provided by disease management programmes and NGO programmes. The unmet need for treatment in adults is estimated using a Markov model of HIV progression in adults, combined with estimates of annual new HIV infections from a national AIDS and demographic model.

Results. By the middle of 2008, 568 000 adults and children were receiving antiretroviral treatment in South Africa, with

the public health sector accounting for 79% of this total. Using the current Department of Health criteria for defining antiretroviral eligibility (CD4+ count <200/ μ l or World Health Organization (WHO) stage 4), antiretroviral coverage in adults was 40.2% in 2008 – up from 4.9% in 2004. Coverage increases to 54.2% if eligibility is based on WHO stage 4 only, but falls to 22.2% if the Southern African HIV Clinicians Society guidelines are used to define eligibility. Coverage in 2008 varied between provinces, from 25.8% in the Free State to 71.7% in the Western Cape.

Conclusions. Significant progress has been made in expanding access to antiretroviral treatment in South Africa since 2004, but a substantial unmet need for treatment in adults remains.

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Death notification statistics confirm that AIDS is dramatically affecting mortality in South Africa.¹ Demographic and epidemiological models suggest that antiretroviral treatment is the only intervention that can achieve a substantial reduction in AIDS mortality in South Africa in the short term.^{2,3} South Africa therefore urgently needs to expand and strengthen services providing antiretroviral treatment. Before 2004, access to antiretroviral drugs was limited mainly to medical scheme beneficiaries. However, following the announcement of a comprehensive care, management and treatment programme by the Department of Health (DoH) in late 2003,⁴ antiretroviral treatment has become increasingly accessible, and significant progress has been made in enrolling patients onto the public antiretroviral treatment programme.

Despite this progress, there remains a significant unmet need for antiretroviral treatment in South Africa; monitoring of antiretroviral coverage is therefore important to identify where the shortfall is greatest and to quantify coverage according to different definitions of 'need'. However, monitoring of antiretroviral coverage in South Africa is challenging for

several reasons. Although the DoH regularly co-ordinates data collection for the public health sector, there is no centrally co-ordinated data collection system for the private sector and non-governmental organisations (NGOs). In addition, the numbers routinely reported by the DoH are the numbers of patients **cumulatively** enrolled on antiretroviral treatment, and there are no estimates of public-sector patients **currently** receiving antiretroviral treatment, except in the Western Cape. Coverage is also difficult to estimate because demographic projection models usually estimate only the numbers of individuals in different WHO clinical stages,^{2,5} whereas definitions of eligibility are usually based on a combination of clinical and CD4+ criteria.^{4,6,7} This makes it difficult to estimate the denominator in the antiretroviral coverage calculation.

Much is unknown regarding antiretroviral coverage in South Africa. The aim of this paper is to quantify the coverage in South Africa up to the middle of 2008, according to various definitions of antiretroviral treatment eligibility, and to quantify the relative levels of coverage in the nine provinces and the changing contribution of different providers to the antiretroviral rollout in South Africa.

Method

Following the convention of UNAIDS and the World Health Organization (WHO), antiretroviral coverage is calculated as the number of individuals receiving antiretroviral treatment, divided by the sum of the number of untreated individuals needing treatment and the number of treated individuals.^{8,9} Estimates of the numbers receiving treatment are obtained

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from public sector programme reports and data collected from the private sector, while estimates of the unmet need for treatment are derived from a model of HIV progression in HIV-infected individuals. Although numbers receiving treatment are calculated for both adults and children, antiretroviral coverage is calculated for adults only, since definitions of antiretroviral eligibility and rates of HIV progression differ between children and adults.

Estimation of numbers receiving antiretroviral treatment

Estimates of the numbers of patients starting antiretroviral treatment each year in public health facilities are obtained from unpublished reports of the cumulative numbers of patients who have started antiretroviral treatment at different times (Department of Health internal report dated 7 May 2009: National Strategic Plan for HIV and AIDS/CCMT monthly statistics, March 2009).¹⁰ To allow for mortality and loss to follow-up after starting treatment, rates of retention are applied to these annual numbers of individuals starting therapy. Based on estimates of retention in the Western Cape,¹¹ it is assumed that the probability of remaining on treatment for the first 6 months after starting therapy is 0.895, and the annual probability of remaining on treatment thereafter is 0.935. The number of individuals receiving treatment at time t (in years) is thus calculated as:

$$N(t) = N(t-1) \times 0.935 + S(t-1) \times 0.895 \quad (1)$$

where $S(t-1)$ is the number of individuals starting treatment between time $t-1$ and time t . It is assumed that individuals starting treatment between time $t-1$ and time t do so, on average, at time $t - \frac{1}{2}$.

Estimates of the numbers of patients receiving antiretroviral treatment through disease management programmes (DMPs), workplace treatment programmes (WTPs) and NGO programmes operating outside of public health facilities are based on three data sources:

1. early published data from Aid for AIDS,¹² which was treating approximately 80% of all antiretroviral patients in 2002¹³
2. early data on NGO programmes operating before 2004¹⁴
3. more recent data collected from individual programmes from 2005 to 2008.¹⁵

Since programmes do not provide estimates at regular intervals, and since information is missing for some programmes during certain periods, estimates of numbers of patients receiving treatment at the middle of each year are obtained by using linear interpolation and extrapolation of estimates at other time points. The number of individuals starting treatment between time $t-1$ and time t , $S(t-1)$, is estimated by entering the private sector estimates of $N(t-1)$ and $N(t)$ into equation (1) and assuming that the rates of retention

in the private sector^{16,17} are the same as those in the Western Cape.

For some years, data on the provincial distribution of treatment numbers are not available. In these years, we assumed that the proportion of individuals treated in a particular province, and for a given sector (private/public/NGO), was the same as that estimated in the most recent year. For the public and NGO sectors, the most recent provincial distributions are for 2008. For the private sector, a provincial distribution could be obtained only for 2003, based on a weighting of the 2003 population⁵ by the proportion of the population with medical cover¹⁸ and the proportion of medically insured individuals on antiretroviral treatment.¹²

Estimation of unmet need for treatment

The unmet need for treatment was estimated by using a Markov model of HIV progression that divides HIV-infected adults into compartments based on their current CD4+ count, clinical status and current receipt of antiretroviral treatment (Fig. 1). The initial CD4 distribution of HIV-infected adults, at the time they acquire HIV, as well as the probabilities of transition between the HIV stages in Fig. 1, are set at the rates estimated by Hendriks *et al.*¹⁹ from men in Amsterdam from 1990 to 1996. These rates were selected from several other possible sources,¹⁹⁻²² because they produced an estimated median HIV survival time consistent with medians estimated for South Africa in other studies^{23,24} and because they produced a distribution of CD4+ counts in HIV-infected adults roughly consistent with the distributions observed in South African surveys.²⁵⁻²⁷

Assumptions about the annual number of new adult HIV infections were obtained from the ASSA2003 AIDS and Demographic model.⁵ The model projects the change in the number of infected individuals in the different CD4 stages at monthly intervals, adding new infections and removing individuals who die or start antiretroviral treatment. Non-HIV mortality is set at a rate of 0.005 per annum, equal to the average non-HIV mortality rate in HIV-positive South African adults estimated by the ASSA2003 model. The numbers of adults starting antiretroviral treatment in each period are set at 90% of the $S(t)$ estimates obtained previously, since

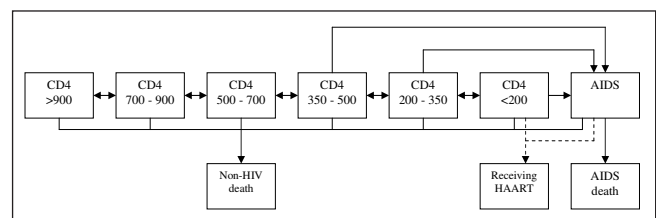


Fig. 1. Model of HIV progression in HIV-infected adults. Transitions represented by solid lines are calculated using specified transition probabilities, while transitions represented by dashed lines are calculated using specified numbers starting antiretroviral treatment.



approximately 10% of those receiving antiretroviral treatment are children. Based on data from South African treatment programmes,^{17,28,29} we assumed that 35% of adults starting treatment had already progressed to AIDS and the balance started therapy when their CD4+ count was <200/ μ l, prior to the development of clinical AIDS.

Estimates of unmet need are calculated according to three definitions:

1. conservative criteria that include only adults with untreated AIDS
2. current criteria used by the DOH,⁴ which include all adults with untreated AIDS or a CD4+ count <200/ μ l
3. criteria recommended by the Southern African HIV Clinicians Society,⁷ which include all adults with untreated AIDS or a CD4+ count <350/ μ l.

Sensitivity analysis

To assess the sensitivity of the unmet need estimates to key variables, the following plausible ranges of parameter values are considered. The proportion of adults starting treatment who have already progressed to AIDS is varied between 20% and 50%,^{17,28,29} and the rate at which individuals discontinue treatment owing to death or loss to follow-up is varied between 0.7 times and twice the rates estimated from the Western Cape data, based on variability in rates of retention observed within South Africa.^{28,30,31} The annual numbers of new HIV infections in adults are varied between the upper and lower limits of the 95% prediction intervals calculated in a previous uncertainty analysis.²⁴ In addition, alternative estimates of rates of transition between CD4 stages are considered.¹⁹⁻²²

Results

By the middle of 2008, an estimated 568 000 adults and children were receiving antiretroviral treatment in South Africa, which is more than twice the number 2 years previously, and more than 10 times the number at the middle of 2004 (Table I). Although 72% of patients in 2004 were receiving treatment through DMPs or WPTPs, this proportion declined to 15% by mid-2008, following the rapid scaling up of antiretroviral access in the public health sector (Fig. 2a). The proportion receiving treatment through NGO programmes has remained stable at around 6%, though this figure varies substantially between the provinces (Fig. 2b).

Over the years 2000 - 2008, the estimated CD4 distribution of the HIV-infected adult population changed substantially (Fig. 3a). The proportion of infected adults who have a CD4+ count >350/ μ l and are not on treatment has decreased from 70% in 2000 to 54% in 2008, and the proportion of infected adults in need of treatment, by current DoH eligibility criteria, has increased from 13% to 25% over this period. However, the proportion of infected adults who have CD4+ counts >350/ μ l and are not on treatment was relatively uniform across the provinces in 2008, at between 53% and 57% (Fig. 3b).

Antiretroviral coverage in adults has improved substantially, rising from 4.9% in 2004 to 40.2% in 2008, according to DoH eligibility criteria (Table II). Estimates of coverage change substantially when different definitions of treatment eligibility are used; when 'unmet need' is defined only as untreated AIDS, antiretroviral coverage in 2008 is estimated at 54.2%, but when 'unmet need' is defined according to the Southern African HIV Clinicians Society guidelines, coverage is

Table I. Estimated numbers of adults and children receiving antiretroviral treatment in South Africa, 2001 - 2008

	2001	2002	2003	2004	2005	2006	2007	2008
Cumulatively enrolled in public sector	0	0	0	11 000	66 000	180 000	327 000	539 000
Currently enrolled in public sector	0	0	0	9 000	59 000	157 000	278 000	449 000
NGO programmes	0	0	1 000	4 000	6 000	14 000	23 000	32 000
DMPs, WPTPs	6 000	15 000	25 000	34 000	44 000	57 000	70 000	86 000
Total currently enrolled	6 000	15 000	26 000	47 000	109 000	229 000	371 000	568 000
Total, by province								
Eastern Cape (EC)	700	1 700	2 800	5 000	12 100	25 300	41 000	62 000
Free State (FS)	400	900	1 500	2 200	4 800	9 500	17 000	28 000
Gauteng (GA)	1 500	3 900	6 400	13 600	30 100	60 000	92 000	139 000
KwaZulu-Natal (KZ)	2 000	5 100	8 500	12 800	29 800	65 000	107 000	167 000
Limpopo (LP)	300	700	1 200	1 900	4 600	11 500	20 000	34 000
Mpumalanga (MP)	500	1 200	2 000	3 100	5 600	11 900	23 000	37 000
Northern Cape (NC)	100	100	200	400	1 500	3 200	6 000	10 000
North West (NW)	400	1 000	1 600	2 600	8 500	20 500	33 000	46 000
Western Cape (WC)	300	800	1 600	5 700	12 000	21 600	31 000	45 000

Figures are rounded to the nearest 1 000, except in the case of the pre-2007 provincial estimates, which are rounded to the nearest 100. All estimates relate to the middle of the specified calendar year.

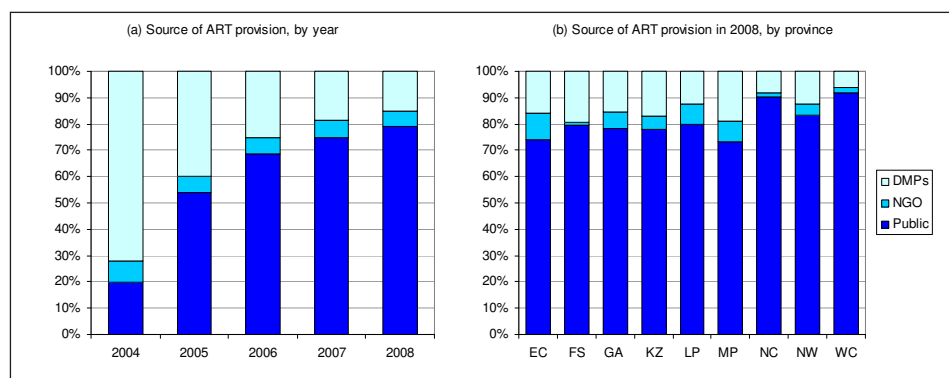


Fig. 2. Proportions of adults and children treated by different providers. ART = antiretroviral treatment; DMPs = disease management programmes (including workplace treatment programmes); NGO = non-governmental organisation. Provincial abbreviations are given in Table I. All estimates relate to the middle of the specified calendar year.

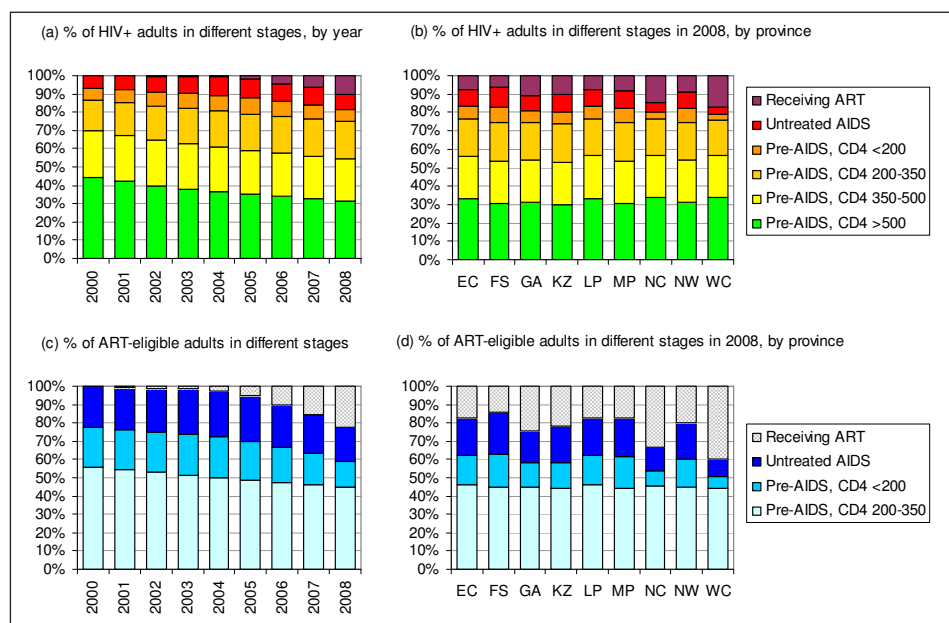


Fig. 3. Proportions of adults in different CD4 and antiretroviral eligibility stages. ART = antiretroviral treatment. Provincial abbreviations are given in Table I. All estimates relate to the middle of the specified calendar year.

estimated at only 22.2% (Fig. 3c). Adult antiretroviral coverage also varies greatly between provinces, ranging from 25.8% in the Free State to 71.7% in the Western Cape in 2008. Similar variability is observed when using the HIV Clinicians Society guidelines to define unmet need (Fig. 3d).

The total number of untreated adults needing antiretroviral treatment, at the middle of 2008, is estimated to be around 760 000 using the DoH eligibility criteria, 430 000 using the AIDS sick criterion, and 1.79 million using the HIV Clinicians Society criteria (Table III). These estimates of unmet need are relatively insensitive to changes in the assumed rates of retention on antiretroviral treatment and the assumed proportion of those starting treatment who have already progressed to AIDS. However, the estimates are very sensitive

to the uncertainty regarding the annual numbers of new HIV infections in South Africa; the estimated total number of untreated adults who are sick with AIDS or have a CD4+ count $<200/\mu\text{l}$ changes to 480 000 and 1.01 million when the lower and upper estimates of the annual new adult HIV infections are substituted into the model. The estimates of unmet need are also quite sensitive to the choice of HIV progression parameters. Using the progression parameters estimated by Hendriks *et al.*¹⁹ for men in Amsterdam over the 1985 - 1990 period, the unmet need reduces to 600 000, but using the progression parameters estimated by Longini *et al.*²¹ for USA military personnel, the unmet need increases to 990 000.

Discussion

This study demonstrates significant progress in the provision of antiretroviral treatment in South Africa, particularly after the phasing in of antiretroviral treatment in the public health sector after 2003. However, a large unmet need for antiretroviral treatment remains and, by the middle of 2008, only 40.2% of adults needing antiretroviral treatment were receiving it. A significant barrier to the expansion of the antiretroviral treatment programme is the limited number of public health facilities providing treatment and

their shortage of health workers. An urgent need therefore exists for greater decentralisation of antiretroviral treatment services³² and greater recruitment and retention of health workers in the public health sector.³³⁻³⁶ A further barrier to improving antiretroviral coverage is the high proportion of eligible individuals who are unaware of their HIV status; in the 2005 HSRC household survey, for example, only 36% of HIV-infected adults had ever been tested for HIV.³⁷ Stigma and confusion regarding the efficacy of antiretroviral treatment relative to traditional medicines are also significant factors inhibiting access to antiretroviral treatment;³² leaders at all levels must present clear and consistent messages to overcome these barriers.


Table II. Estimated antiretroviral coverage in adults (%), according to different definitions of treatment eligibility

	Definition of eligibility		
	AIDS sick	DOH criteria	SAHIVCS criteria
National estimates (by year)			
2001	1.9	1.0	0.5
2002	3.9	2.1	1.0
2003	5.6	3.0	1.5
2004	8.8	4.9	2.4
2005	17.1	10.0	5.1
2006	30.1	19.1	10.0
2007	41.6	28.3	15.2
2008	54.2	40.2	22.2
2008 estimates (by province)			
Eastern Cape	46.4	32.4	17.5
Free State	38.4	25.8	14.2
Gauteng	57.6	43.5	24.0
KwaZulu-Natal	53.3	39.4	22.1
Limpopo	45.9	32.2	17.4
Mpumalanga	44.6	31.2	17.3
Northern Cape	72.5	61.1	33.3
North West	49.6	35.4	19.6
Western Cape	80.9	71.7	39.9

DOH = Department of Health; SAHIVCS = Southern African HIV Clinicians Society.
All estimates relate to the middle of the specified calendar year.

Table III. Sensitivity analysis of the total unmet need for antiretroviral treatment in adults at the middle of 2008

	Definition of eligibility		
	AIDS sick	DOH criteria	SAHIVCS criteria
Baseline estimate	432 000	760 000	1 795 000
Percentage of adults starting ART with AIDS = 50%	417 000	801 000	1 836 000
Percentage of adults starting ART with AIDS = 20%	457 000	745 000	1 780 000
Rate of death/discontinuation on ART = 0.7 × baseline	437 000	773 000	1 808 000
Rate of death/discontinuation on ART = 2 × baseline	421 000	741 000	1 777 000
New adult HIV infections = lower limit of 95% interval	278 000	476 000	1 227 000
New adult HIV infections = upper limit of 95% interval	568 000	1 011 000	2 226 000
Alternative estimates of HIV progression parameters			
Longini <i>et al.</i> , USA army personnel, 1985 - 1990 ²²	580 000	992 000	1 769 000
Satten & Longini, men in San Francisco, 1984 - 1992 ²³	403 000	695 000	1 427 000
Hendriks <i>et al.</i> , men in Amsterdam, 1984 - 1993 ²¹	467 000	802 000	1 667 000
Hendriks <i>et al.</i> , men in Amsterdam, 1985 - 1990 ²⁰	406 000	604 000	1 429 000
Hendriks <i>et al.</i> , men in Vancouver, 1985 - 1990 ²⁰	478 000	622 000	1 341 000
Hendriks <i>et al.</i> , men in Vancouver, 1990 - 1996 ²⁰	565 000	948 000	1 779 000

ART = antiretroviral treatment; DOH = Department of Health; SAHIVCS = Southern African HIV Clinicians Society.

Our analysis also demonstrates significant inequality in access to antiretroviral treatment in South Africa, with coverage in mid-2008 ranging from 25.8% in the Free State to 71.7% in the Western Cape. This appears to be mostly owing to variability in the performance of the public health sector, since the provinces with the highest coverage (Western Cape and Northern Cape) have the highest proportions of patients managed in the public sector, and the provinces with

low coverage (Free State, Eastern Cape, Mpumalanga and Limpopo) have low proportions of patients managed in the public sector. The high coverage in the Western Cape and Northern Cape could also reflect their relatively low HIV prevalence.

We present a novel approach to estimating the unmet need for antiretroviral treatment. Although it is possible to conduct surveys to measure the unmet need for treatment at



a given time,^{25,38} this analysis shows that the CD4 distribution in the HIV-infected population can be expected to change substantially over time. Since it is costly to conduct surveys, mathematical models provide a simple alternative method for estimating the change in the unmet need for treatment as the epidemic progresses. The Spectrum model employed by UNAIDS, for example, estimates unmet need in adults by assuming that the CD4+ count in infected adults falls below the 350 and 200 thresholds at specified rates, based on CD4 data from Africa.³⁹ The ASSA2003 model, which is commonly used in setting antiretroviral treatment targets in South Africa, quantifies unmet need in terms of WHO clinical staging,² although this is a poor indication of unmet need according to combined CD4 and clinical criteria.^{38, 40-42} A mathematical model proposed by Williams *et al.*⁴³ estimates unmet need based on local CD4 data, but does not incorporate clinical criteria. It would therefore appear that few mathematical models exist for estimating unmet need according to the combined clinical and CD4 criteria that are commonly used in defining antiretroviral eligibility.^{4,6,7}

Although our model has the advantage of quantifying unmet need in terms of various combinations of clinical and CD4 criteria, it is, like other models,^{3,44} parameterised using data that are not local to the setting in which the model is applied. Since distributions of CD4+ counts in HIV-negative adults and rates of CD4 decline in HIV-infected adults differ substantially between populations,^{43,45} the HIV progression parameters that have been calculated from men in Amsterdam could be inappropriate for South Africa. We chose the progression parameters estimated from men in Amsterdam because they yielded the model results most consistent with South African data. For example, the model estimates of the proportion of untreated adults with CD4+ counts <200 (19%), 200 - 349 (20%), and 350 - 499 (25%) in 2004, are roughly consistent with the ranges measured in South African surveys between 2002 and 2005 (10 - 22%, 19 - 28% and 18 - 26% respectively).²⁵⁻²⁷ In addition, the median survival time estimated using the Amsterdam cohort data (10.8 years in the absence of highly active antiretroviral treatment) is roughly consistent with the median of 10.5 years estimated for South African gold miners aged 25 - 34 at the time of HIV acquisition²³ and the median of 10.8 years estimated for adults aged 29 at the time of HIV acquisition, based on South African mortality data and HIV prevalence data.²⁴ This suggests that the HIV progression parameters estimated from the Amsterdam cohort serve as a reasonable approximation to those in South Africa.

A potential concern is that data on the numbers starting treatment in the public sector could be subject to significant double-counting,⁸ and the rates of antiretroviral retention estimated from the Western Cape public health sector¹¹ might not be applicable to other provinces. However, the estimates of numbers currently receiving antiretroviral treatment in the public health sector (Table I) are consistent with unpublished

public sector drug distribution estimates produced by Aspen Pharmacare, which suggests that bias owing to double-counting and inter-provincial differences in antiretroviral retention is not substantial. Another limitation is the absence of data from some of the smaller DMPs and from individuals paying for their own treatment outside of DMPs,¹⁵ which may result in some under-estimation of antiretroviral coverage. Further work is needed to explore definitions of antiretroviral coverage other than the standard UNAIDS/UNGASS indicator, e.g. the proportion of newly eligible individuals in a given year who start treatment. Such measures may provide a more accurate indicator of recent programme performance, as they are not affected by the numbers of patients enrolled in the past. Further work is also required to produce separate estimates of antiretroviral coverage in men and women and to develop a separate model for estimating antiretroviral coverage in children.

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