

National HIV incidence measures – new insights into the South African epidemic

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Background and objectives. Currently South Africa does not have national HIV incidence data based on laboratory testing of blood specimens. The 2005 South African national HIV household survey was analysed to generate national incidence estimates stratified by age, sex, race, province and locality type, to compare the HIV incidence and HIV prevalence profiles by sex, and to examine the relationship between HIV prevalence, HIV incidence and associated risk factors.

Method. The detection of recent infections was performed on confirmed HIV-positive samples, using the BED capture enzyme immunoassay optimised for dried blood spot (DBS) specimens. BED HIV incidence calculations applied adjustment procedures that were recently revised and approved by the Centers for Disease Control and Prevention for subtype C blood specimens.

Results. HIV incidence in the study population aged 2 years and older was 1.4% per year, with 571 000 new HIV infections estimated for 2005. An HIV incidence rate of 2.4% was recorded for the age group 15 - 49 years. The incidence of HIV among females peaked in the 20 - 29-year age group at 5.6%, more than six times the incidence found in 20 - 29-year-old males (0.9%). Among youth aged 15 - 24 years, females account for 90% of the recent HIV infections. Non-condom use among youth, current pregnancy and widowhood were the socio-behavioural factors associated with the highest HIV incidence rates.

Conclusions. The HIV incidence estimates reflect the underlying transmission dynamics that are currently at work in South Africa. The findings suggest that the current prevention campaigns are not having the desired impact, particularly among young women.

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Monitoring the spread of HIV in populations would greatly benefit from a practical method that could identify recently infected persons. Ideally, HIV spread and changes over time should be tracked through measuring the number and distribution of new infections, i.e. incidence, in a population. Incidence measures are generally better than prevalence measures for assessing the dynamics of HIV transmission in different populations.¹ Incidence is the key indicator of the rate of HIV transmission and provides the most direct means of assessing the impact of HIV prevention programmes.

True incidence data, however, can only be obtained through large-scale cohort studies. Such studies have many drawbacks, including cost, ethical considerations, participation and/or selection biases and the fact that those included in a cohort will inevitably have more exposure to HIV programmes or intervention efforts. As a consequence, HIV incidence estimation has mostly been provided by mathematical

models.²⁻⁴ Indirect HIV incidence estimates have also been derived from prevalence surveys in young people (15 - 24 years) using prevalence data by single year of age and assuming that HIV prevalence differences between the age strata represent incident HIV infections.⁵ However, this method is not applicable in older age groups, in which AIDS-related mortality has a major impact on HIV prevalence levels.

The complexities and limitations of epidemiological approaches to measure HIV incidence argue strongly for a laboratory-based method that can distinguish recent from established long-term HIV infections, independent of the age of the source population. Several laboratory-based methods have been developed that are based on the events of early HIV-1 infection.⁶⁻⁸ The underlying principle is that the response of a person to HIV during the early infection stage can be timed by the presence or absence of markers in that person's blood (Fig. 1). These unique and specific host responses to HIV infection enable the estimation of HIV incidence based on laboratory assays using blood specimens from cross-sectional rather than longitudinal survey designs.

Over the past years, the Centers for Disease Control and Prevention (CDC) introduced the BED capture enzyme immunoassay (CEIA) assay to identify incident infection. The BED assay uses a multi-subtype synthetic peptide and measures the increasing proportion of HIV-IgG to total IgG after seroconversion (Fig. 1). The assay is designed to work well in populations with different HIV-1 subtypes and the testing algorithm has been successfully evaluated in populations in the USA and Thailand with B and E subtypes,

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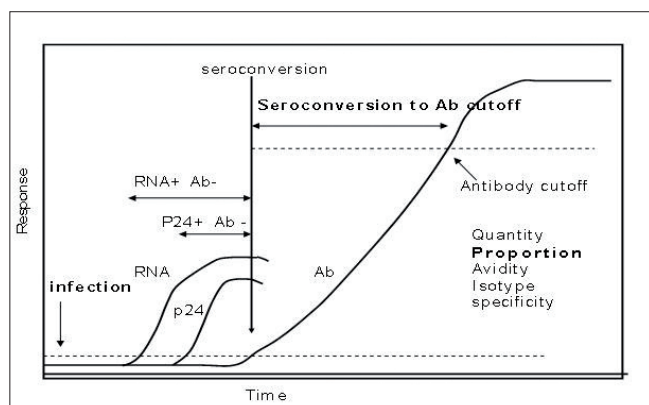


Fig. 1. Detection of early HIV infection (adapted from Parekh *et al.*⁷).

as well as in cohorts from the Netherlands, Kenya, Ethiopia, Zimbabwe and India which comprise A, B, C and D subtypes.⁷⁻¹⁰

In December 2005, the UNAIDS Reference Group on Estimates, Modeling and Projections issued a statement in response to preliminary data from population surveys and selected validation studies which demonstrated that the BED assay overestimated HIV-1 incidence by misclassifying a number of individuals with long-term infection as recent infection in cross-sectional settings.¹¹ In May 2006, the CDC's Surveillance and Survey and Laboratory working groups reviewed new study results and proposed adjustments to estimate HIV-1 incidence using the BED CEIA. Data were presented from China, Côte d'Ivoire, South Africa, Thailand, Uganda, the USA and Zimbabwe to address the concerns expressed by the UNAIDS Reference Group. On the basis of its review of the study results, the working groups developed guidelines with detailed adjustment procedures for the estimation of HIV-1 incidence in cross-sectional, population-based serosurveys.^{12,13}

The 2005 South African national household survey on HIV, Behaviour and Communication included HIV incidence testing in its survey protocol for the first time.¹⁴ Almost 16 000 blood specimens tested for HIV provided an unparalleled large sample to estimate HIV incidence on a national scale for South Africa. Using the adjusted BED HIV-1 incidence method, this paper presents national incidence estimates stratified by age, sex, race, province and locality type, compares the HIV incidence and HIV prevalence profiles for the male and female populations and examines the relationship between HIV prevalence, HIV incidence and associated risk factors.

Methods

Survey design and sampling

The survey targeted all persons over 2 years of age living in South Africa and residing in homes, i.e. excluding individuals living in educational institutions, old-age homes, hospitals

and uniformed service barracks but including those living in hostels. The survey applied a multi-stage stratified sampling approach based on a master sample consisting of 1 000 enumerator areas (EAs) used by Statistics South Africa for the national census in 2001. Three persons in each household were potentially eligible to be selected for the survey; however only one was selected from each of the age groups 2-14 years, 15-24 years, and 25 years and older. A total of 23 275 individuals aged 2 years and older participated in the 2005 survey and 15 851 respondents agreed to be tested for HIV. Linked anonymous HIV testing was performed using dried blood spot (DBS) specimens. Socio-demographic and behavioural information was collected with questionnaires administered by trained fieldworkers.¹⁴

HIV antibody testing

All samples were first tested with the Vironostika HIV-1 Uniform II Plus O enzyme immunoassay (BioMerieux). All HIV-positive samples were retested with a second EIA (Vitros ECI, Ortho Clinical Diagnostics). A second test was also conducted for 10% of cases where the first test was negative. Samples testing positive in enzyme immunoassay 1 and negative in enzyme immunoassay 2 (producing discordant results) were submitted to a third enzyme immunoassay (Biorad HIV 1 + 2) for final interpretation of discordant samples.

BED HIV incidence

The detection of recent infections was performed on confirmed HIV-positive samples, using the BED CEIA (Calypte HIV-1 BED Incidence EIA, Calypte Biomedical Corporation, Md, USA) optimised for DBS specimens. Adjustment procedures for BED HIV incidence calculation have been reviewed at a recent expert meeting at CDC/USA.¹² The method described by McDougal *et al.*¹⁵ uses an adjustment formula that corrects for both false long-term infections (sensitivity) and false recent infections (specificity) determined by the BED CEIA. Annualised BED HIV incidence calculation applied a window period of 180 days for HIV subtype C specimens.

Sensitivity/specificity adjusted BED HIV incidence formula:

$$I = \frac{(F) * (365/w) * R}{N + [(F) * (365/w) * (R/2)]} \times 100$$

BED HIV incidence is calculated as incidence percent per year (%/year). In order to provide national estimates, the HIV incidence calculation took into account the complex sampling design and used weighted numbers in the above formula (see section on data analysis below). The expression in the numerator of the formula was used to estimate the annual number of new HIV infections.



Calculation of the adjustment factor F:

$$F = \frac{(R/P) + \gamma - 1}{(R/P) (\alpha - \beta + 2\gamma - 1)}$$

Ninety-five per cent confidence bounds were calculated as follows:

$$I \pm 1.96 * Deft * \frac{1(2-1)}{2} * \sqrt{(1/R) + (1/N)}$$

Symbols:

I = incidence (number of new infections per year per 100 at risk)

F = adjustment factor for sensitivity/specificity adjustment

P = total testing HIV positive

N = total testing HIV negative

R = total testing recent in the BED-CEIA

Deft = design effect.

Imputed values:

w = 180 (window in days)

α = 0.7682 (sensitivity of BED test for detecting recent (< w) infection)

β = 0.7231 (specificity of the BED test over the period > w to < 2 w)

γ = 0.9443 (specificity of the BED test over the period > 2 w).

Data analysis

Taking into account the complex sampling design and adjusting for HIV testing non-response, a weighted analysis of HIV prevalence, HIV incidence and behavioural characteristics was carried out for the reporting domains sex, age group, race, province and type of residence. Individual sample weights were benchmarked to produce a final weighted sample that closely matched the socio-demographic characteristics of the 2005 mid-year population estimates provided by Statistics South Africa.¹⁶ Weighted data were analysed with STATA 8.0 software. STATA (*svy* methods) was also used to obtain HIV prevalence estimates with confidence intervals (95% CI) that took into account the survey design.

Results

Tables I and II present HIV incidence estimates for South Africa in both relative terms (% per year) and absolute terms (number of new infections per year). HIV incidence among persons aged 2 years and older is calculated at 1.4% per year (95% CI: 1.0 - 1.8), with 571 000 new HIV infections estimated for 2005 (Table I). The incidence of HIV in the child population aged 2 - 14 years is of concern; a relative incidence of 0.5% (95% CI: 0.0 - 1.2) translates to 69 000 estimated new infections in this age group. The HIV incidence for youth 15 - 24 years of age is higher than the incidence rate for people 25 years and older, 2.2% (95% CI: 1.3 - 3.1) and 1.7% (95% CI: 1.1 - 2.3) respectively. An HIV incidence of 2.4% (95% CI: 2.2 - 2.7) and 500 000 new infections were estimated for the age group 15 - 49 years.

Table II shows the calculated HIV incidence by race, province and locality type for the population 2 years and older. HIV incidence in the black race group is 9 times higher than the incidence found in the other race groups, with figures of 1.8% (95% CI: 1.3 - 2.3) and 0.2% (95% CI: 0.0 - 0.3) respectively. Mpumalanga (2.4%, 95% CI: 0.9 - 3.8), Free State (1.9%, 95% CI: 0.4 - 3.4), Gauteng (1.9%, 95% CI: 0.8 - 3.0), KwaZulu-Natal (1.7%, 95% CI: 0.7 - 2.7) and Limpopo (1.6%, 95% CI: 0.3 - 2.8) recorded the highest incidence, while North West (1.0%, 95% CI: 0.2 - 1.8), Western Cape (0.8%, 95% CI: 0.2 - 1.5), Eastern Cape (0.7%, 95% CI: 0.1 - 1.2) and Northern Cape (0.2%, 95% CI: 0.0 - 0.4) had incidence rates of 1% and lower. In absolute terms, however, most new HIV infections occurred in the populous provinces of Gauteng and KwaZulu-Natal, totalling an estimated 144 000 and 134 000 respectively.

Persons living in urban informal settlements have by far the highest incidence rates (5.1%, 95% CI: 3.2 - 7.0) compared with those living in rural formal areas (1.6%, 95% CI: 0.7 - 2.5), rural informal areas (1.4%, 95% CI: 0.1 - 2.8) and urban formal areas (0.8%, 95% CI: 0.3 - 1.2).

Fig. 2 compares the HIV incidence and HIV prevalence profile in the South African population by age and sex. The differences in HIV incidence between males and females are especially large in the younger age groups under 30 years of age. HIV incidence among females rises fast and peaks in the 20 - 29 age band at 5.6% (95% CI: 2.8 - 8.4), more than 6 times

Table I. HIV incidence and number of new infections* by age group, South Africa, 2005

Age group (yrs)	Weighted sample (N)	HIV incidence (%per year) (95% CI)	Estimated number of new infections per year (N)
> 2	44 513 000	1.4 (1.0 - 1.8)	571 000
2 - 14	13 253 000	0.5 (0.0 - 1.2)	69 000
15 - 24	9 616 000	2.2 (1.3 - 3.1)	192 000
> 25	21 645 000	1.7 (1.1 - 2.3)	310 000
15 - 49	24 572 000	2.4 (2.2 - 2.7)	500 000

*Numbers rounded off to the nearest thousand.



Table II. HIV incidence and number of new infections* by race, province and locality type (age ≥ 2 years), South Africa, 2005

Variable	Weighted sample (N)	HIV incidence (% per year) (95% CI)	Estimated number of new infections per year (N)
Race			
Black	35 113 000	1.8 (1.3 - 2.3)	557 000
Other	9 337 000	0.2 (0.0 - 0.3)	14 000
Province			
Mpumalanga	3 083 000	2.4 (0.9 - 3.8)	63 000
Free State	2 827 000	1.9 (0.4 - 3.4)	47 000
Gauteng	8 512 000	1.9 (0.8 - 3.0)	144 000
KwaZulu-Natal	9 213 000	1.7 (0.7 - 2.7)	134 000
Limpopo	5 207 000	1.6 (0.3 - 2.8)	76 000
North West	3 642 000	1.0 (0.2 - 1.8)	33 000
Western Cape	4 382 000	0.8 (0.2 - 1.5)	33 000
Eastern Cape	6 777 000	0.7 (0.1 - 1.2)	40 000
Northern Cape	871 000	0.2 (0.0 - 0.4)	1 000
Locality type			
Urban informal	3 878 000	5.1 (3.2 - 7.0)	166 000
Rural formal	3 577 000	1.6 (0.7 - 2.5)	52 000
Rural informal	16 495 000	1.4 (0.1 - 2.8)	211 000
Urban formal	20 563 000	0.8 (0.3 - 1.2)	142 000

*Numbers rounded off to the nearest thousand.

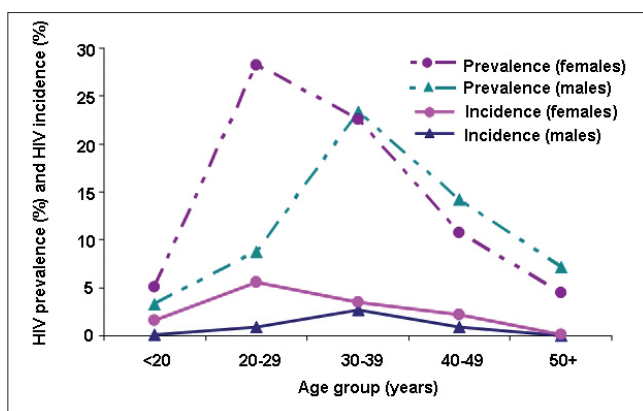


Fig. 2. HIV incidence and HIV prevalence by age and sex, South Africa, 2005.

the incidence found in males in this age group (0.9%, 95% CI: 0.0 - 1.9). The incidence of HIV among males increases much more slowly than in females and peaks at a lower level in the 30 - 39-year age group at 2.7% (95% CI: 0.0 - 5.7).

These differential HIV transmission dynamics between males and females are reflected in the HIV prevalence profiles. HIV prevalence increases dramatically among young females and peaks at 28.2% (95% CI: 24.5 - 32.1) in the 20 - 29-year age group. In males the increase in HIV prevalence is more progressive, and peaks at 23.3% (95% CI: 18.9-28.3) 10 years later in the age group 30 - 39 years.

Table III examines the relationship between HIV prevalence, HIV incidence and various socio-behavioural factors among 15 - 49-year-olds. Individuals who were single were more likely

to be HIV positive than those who were married, with a figure of 16.6% (95% CI: 14.9 - 18.5) versus 14.3% (95% CI: 12.3 - 16.6), and the incidence of HIV among single people was also higher at 3.0% (95% CI: 1.9 - 4.1) versus 1.3% (95% CI: 0.5 - 2.1). The prevalence of HIV among individuals who were widowed was considerably higher than for those who were either single or married, at 34.0% (95% CI: 25.5 - 43.7). Widowed individuals also had a considerably higher HIV incidence than individuals who were single or married, with a figure of 5.8% (95% CI: 0.0 - 13.8).

Individuals who were sexually active in the past 12 months recorded an HIV prevalence of 18.7% (95% CI: 17.0 - 20.6) and an HIV incidence of 2.4% (95% CI: 1.5 - 3.3). Interestingly, a substantial rate of recent HIV infections was also recorded in survey participants who reported that they never had sex (1.5%, 95% CI: 0.0 - 3.0) or no sex in the past 12 months (2.4%, 95% CI: 0.8 - 4.1), illustrating contradictions between biological test results and self-reported sexual behaviour. Currently pregnant women were found to have among the highest prevalence and incidence rates, 37.0% (95% CI: 24.9 - 51.0) and 5.2% (95% CI: 0.0 - 12.9), respectively. Individuals who reported only one sexual partner in the past year were less likely to be HIV positive in comparison with those who reported two or more partners, with a figure of 18.4% (95% CI: 16.7 - 20.4) versus 21.3% (95% CI: 15.9 - 28.0), and similarly had a lower HIV incidence, 2.1% (95% CI: 1.3 - 3.0) versus 3.1% (95% CI: 0.0 - 6.4).

Among young people aged 15 - 24 years, reported condom use at last sex is correlated with lower HIV prevalence, 14.2% (95% CI: 11.0 - 18.4) versus 20.8% (95% CI: 15.3 - 27.8), and



Table III. HIV prevalence and incidence by self-reported socio-behavioural factors (age group 15 - 49 years)

Variable	Survey sample (N)	HIV prevalence (%) (95% CI)	HIV incidence (% per year) (95% CI)
Marital status			
Single	5 306	16.6 (14.9 - 18.5)	3.0 (1.9 - 4.1)
Married	3 240	14.3 (12.3 - 16.6)	1.3 (0.5 - 2.1)
Widowed	227	34.0 (25.5 - 43.7)	5.8 (0.0 - 13.8)
Divorced	318	15.1 (9.5 - 23.0)	0.5 (0.0 - 1.6)
Sexual history			
Never had sex	1 747	4.3 (2.7 - 7.0)	1.5 (0.0 - 3.0)
No sex in the past 12 months	1 358	18.0 (14.9 - 21.5)	2.4 (0.8 - 4.1)
Sexually active in the past 12 months	5 803	18.7 (17.0 - 20.6)	2.4 (1.5 - 3.3)
Current pregnancy	215	37.0 (24.9 - 51.0)	5.2 (0.0 - 12.9)
Number of sexual partners			
One sex partner in the past 12 months	5 233	18.4 (16.7 - 20.4)	2.1 (1.3 - 3.0)
More than one sex partner in the past 12 months	468	21.3 (15.9 - 28.0)	3.1 (0.0 - 6.4)
Condom use at last sex			
15 - 24 years			
Yes	1 011	14.3 [(11.0 - 18.4)	2.9 (0.5 - 5.2)
No	392	20.8 (15.3 - 27.8)	6.1 (0.0 - 12.9)
25 - 49 years			
Yes	1 049	24.9 (21.1 - 29.1)	2.2 (0.4 - 4.0)
No	1 068	16.0 (12.3 - 20.6)	1.9 (0.0 - 3.7)

lower HIV incidence, 2.9% (95% CI: 0.5 - 5.2) versus 6.1% (95% CI: 0.0 - 12.9). This is in contrast to the findings in respondents aged 25 - 49, where HIV prevalence was significantly ($p < 0.001$) higher among condom users (24.9%, 95% CI: 21.1 - 29.1) than in non-condom users (16.0%, 95% CI: 12.3 - 20.6) while HIV incidence was similar in these groups, 2.2% (95% CI: 0.4 - 4.0) and 1.9% (95% CI: 0.0 - 3.7) respectively.

Discussion

The HIV incidence estimates reflect the underlying transmission dynamics that are currently at work in South Africa. It is important to keep in mind that HIV incidence is a point estimate of recent HIV infections, while HIV prevalence is the result of cumulative new infections over time minus the cumulative deaths among HIV-infected persons.

Our analysis indicates that 571 000 new HIV infections occurred in the population 2 years and older during the year 2005 in South Africa. Of all new HIV infections, 34% occurred in young people aged 15 - 24 years. The incidence rates among young females in their prime childbearing age are especially alarming. The HIV incidence among females in the 20 - 29 age group was 5.6%, more than 6 times that in males of the same age (0.9%). Among youth aged 15 - 24 years, females account for 90% of recent HIV infections.

The incidence data show that new non-vertical infections have occurred among children in South Africa, confirming the findings of the 2002 Nelson Mandela/HSRC study of HIV/

AIDS.¹⁷ These infections in children between 2 and 14 years are probably not linked to mother-to-child transmission, and infection would therefore have occurred through other modes of transmission, potentially including child sexual abuse, scarification practices and health care services – a research topic that needs urgent attention.

Place of residence is an important epidemiological variable because it embodies socio-economic contexts that influence risk of HIV infection. In South Africa, some black people live in contexts that increase vulnerability to many illnesses – and HIV is no exception. Although only 8.7% of the total South African population aged 2 years and above lives in urban informal settlements, 29.1% (166 000/571 000) of the total estimated number of new HIV infections in South Africa are found in this residence geotype.

The analysis of condom use at last sex by age group illustrates that HIV incidence rather than HIV prevalence is the more appropriate measure to interpret the effects of recent behaviours on HIV infection. While more complex contextual measures of condom use are necessary for elaborating on the findings in the older age group, it is important to note that reported condom use at last sex in the younger age group is associated with lower HIV incidence.

The incidence analysis also found contradictions between the biological data and self-reported sexual behaviour, indicating some reticence in providing detailed information about sexual behaviour in a cross-sectional survey. For example, new



HIV infections were found in individuals who reported that they had had no sex in the past 12 months. Further analysis revealed that some of these individuals also reported that they had a recent sexually transmitted infection (2.5% of males, 3.1% of females). A surprising finding was the observed high incidence among some older sub-populations. Widowed individuals (median age 43 years, 79.6% females) had a remarkably high HIV incidence of 5.8%, pointing to a lack of perceived risk of HIV infection among older people in South Africa. Our analysis also supports recent findings from Uganda by Gray *et al.*¹⁸ that suggest an increased risk of HIV acquisition during pregnancy. Females aged 15 - 49 years who reported a current pregnancy in the survey were found to have an HIV incidence of 5.2%, compared with 3.8% in the non-pregnant female population 15 - 49 years of age.

HIV incidence estimates derived with the BED methodology are the subject of ongoing validation research. Our HIV incidence analysis is based on the recommended adjustment for BED HIV incidence calculation that has been validated for subtype C specimens, the predominant HIV subtype in South Africa.^{12,13} The potential errors and biases associated with the BED assay methodology are expected to remain stable over time.¹ This is important because the main purpose of incidence estimation is to measure trends in HIV incidence and relative differences in incidence in the same population or between subpopulations of the same population over time.

Conclusion

The relationship between HIV incidence and prevalence grows increasingly complex as the epidemic matures and prevention and care efforts try to mitigate it at the same time. Incidence data provide critical new insights into the dynamics of the HIV epidemic and is a more appropriate measure to correlate biological data with recent behaviours or recent behavioural changes. The availability of laboratory-based tests for recent HIV infection also provides insights into the limits of self-reported sexual behaviour in cross-sectional surveys. The 2005 national HIV incidence estimates presented in this study will serve as benchmark figures for future assessments of the dynamics and trends of the South African HIV epidemic, and provide a mechanism for tracking the impacts of prevention interventions.

A number of areas require urgent further investigation, including evidence of new HIV infections among children aged 2 - 14, and high HIV incidence among widowed persons. High incidence rates among females, among pregnant females, and among people living in informal settlements illustrate high levels of disproportionate risk. The highly resourced plethora

of prevention programmes in South Africa has failed to address HIV incidence in these high-risk categories sufficiently, and more efficient and targeted interventions are clearly urgently required.

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