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HIV testing rates and outcomes in a South African community, 2001–2006: implications for expanded screening policies

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Abstract

Background—Revised World Health Organization recommendations seek to increase HIV testing. We assessed the need for expanded testing in South Africa by examining current testing and treatment trends among a high-prevalence population.

Methods—We determined the numbers of adults receiving HIV testing and antiretroviral treatment (ART) during 2001–2006 using testing registers linked to patient records from two healthcare facilities believed responsible for virtually all HIV services available to the population. We evaluated annual population testing rates using census population counts; proportions of clients testing seropositive (yield); CD4 counts and WHO stage at diagnosis; and ART initiation rates.

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Results—HIV testing rates rose from 4% in 2001 to 20% in 2006 ($p<0.001$) and were highest among pregnant females receiving provider-initiated testing. Yield for first-time testers decreased from 47% in 2001 to 28% in 2006. Median CD4 counts and WHO stage distributions for newly-diagnosed clients remained stable. HIV-infected clients receiving ART within six months of eligibility increased from 0% in 2001 to 68% in 2006 ($p<0.001$).

Conclusions—Population testing and ART initiation rates rose dramatically during 2001–2006. Yet, yield remained high and HIV-infected persons continued to receive late diagnoses. These findings highlight the continuing need for expanded testing and linkage to care.

Introduction

In May 2007, the World Health Organization (WHO) released guidelines supporting expanded human immunodeficiency virus (HIV) testing worldwide.¹ The guidelines recommend that providers offer testing routinely to all adults accessing healthcare facilities in high-prevalence settings (antenatal prevalence $>1\%$), and that all clients be tested for HIV unless they explicitly opt out. The guidelines further advocate retesting seronegative adults at high risk for infection every 6–12 months. These recommendations, together with other calls for expanded HIV testing,² signal a marked departure from prior testing practices: provider-initiated, opt-in testing for select groups deemed to be at high risk (e.g., pregnant females and tuberculosis patients) and client-initiated, opt-in testing for other individuals.³

Expanded HIV testing policies deserve special consideration in South Africa, the country with the largest number of HIV infections in the world⁴ and an estimated adult HIV prevalence of 16%.⁵ As life-saving antiretroviral treatment (ART) becomes increasingly available, the need for expanded testing will hinge upon its ability to increase case detection, identify cases at earlier stages of infection, and link newly-identified HIV-infected persons to effective treatment and care. This capacity in turn depends upon the extent to which these outcomes are already being achieved by current HIV testing practices in the absence of expanded screening.

Previous studies have measured testing and linkage-to-care rates among various groups accessing healthcare facilities in sub-Saharan Africa.^{6–9} However, these studies did not measure testing rates and outcomes at a population level. Our objective was to examine trends in testing rates and outcomes in a South African community during 2001–2006.

Methods

Setting

The study was conducted in a peri-urban African community located near Cape Town (<20 km). The settlement has well-demarcated borders facilitating definition of its population. A 2006 census found 13,180 individuals living in 2,099 households – predominantly informal dwellings such as shacks – with unemployment exceeding 50%.¹⁰ A 2005 study estimated 23% HIV prevalence among the adult population.¹¹ A government-run primary healthcare facility within the community provides basic outpatient care free of charge to all patients. A nearby hospital (<5 km) provides all secondary care for the population, including inpatient and antenatal services.

Client-initiated voluntary counseling and testing (VCT) services (i.e., HIV testing which must be actively requested by patients) were available to all individuals accessing either the local clinic or the hospital during 2001–2006. In addition, provider-initiated testing (i.e., testing automatically offered to patients by healthcare providers) was routinely provided throughout the study period to any patient accessing TB services whose HIV status was

unknown. Starting in 2002, all pregnant females accessing the hospital or clinic were similarly offered provider-initiated antenatal testing. All testing was 'opt in', requiring signed consent. Given the closed nature of the community and high levels of poverty precluding travel, virtually all of the population's testing was believed to occur at these two healthcare facilities.

The standard of HIV-related care in the community evolved substantially over the study period. Since 2001, HIV-related care consisted of a "positive living" clinic meeting weekly to provide education on HIV-related and general health issues, specifically including nutritional and reproductive health,¹² and prescription of cotrimoxazole prophylaxis for eligible clients ($CD4 < 200$ cells/mm³ or WHO stage 3/4).¹³ Pregnant females started receiving single-dose nevirapine in 2002 and dual therapy (nevirapine and zidovudine) in 2006 for prevention of mother-to-child transmission (PMTCT). Three-drug combination ART became available for eligible clients ($CD4 < 200$ cells/mm³ or WHO stage 4) in 2003.¹⁴

Data collection

We collected data from three sources. First, community censuses administered by Desmond Tutu HIV Foundation¹⁵ employees in 2002, 2004, and 2006 provided data solicited from one member of every community dwelling on the number, age, and sex of the inhabitants of each household. These data were used to generate adult (>14 years) population counts for each year and were not linked to the other two data sources. Numbers of adults belonging to age- and sex-specific categories in 2001 were estimated using linear extrapolation, while those for 2003 and 2005 were estimated using linear interpolation. Annual pregnancy rates within each age stratum were estimated using the baseline projections of the Actuarial Society of South Africa (ASSA) 2003 model¹⁶

Second, the healthcare clinic and hospital HIV testing registers provided all data on the number of test encounters experienced by adult community residents during 2001–2006. For each test encounter recorded in the registers, we retrieved data on client identification variables (first name, surname, date of birth, and medical record number); place of residence; sex; test acceptance; test result; and testing site (clinic or hospital). We also recorded the service (VCT, antenatal care, or TB care) through which each encounter occurred; as outlined above, all tests offered through VCT any year or antenatal care in 2001 were classified as client-initiated whereas all other tests were provider-initiated. Repeat test encounters by single individuals were linked retrospectively by matching observations in which at least three of the four identification variables were identical.

Third, the medical records of seropositive adults provided data on WHO stage at diagnosis;¹⁷ dates and results of all CD4 counts and HIV viral load measurements; dates of death; and dates of eligibility for and initiation of cotrimoxazole and ART. All of these data were linked to the register data described above. Data collection was approved by the University of Cape Town Ethics Committee and Partners Human Subjects Institutional Review Board.

Statistical analysis

All analyses excluded observations of testing by individuals with known prior HIV-positive diagnoses ($n=604$), unknown age ($n=233$), or unknown place of residence ($n=1,308$). We performed analyses on four groups.

First, we calculated HIV testing rates for the community's entire adult population. Numbers of HIV tests among eligible community members each year were divided by annual population size estimates, stratified by males, non-pregnant females, and pregnant females. Missing census data for age and sex were found to be missing completely at random¹⁸ and

therefore imputed based on the distribution of non-missing data to preserve denominator size. These population counts were further adjusted to account for testing eligibility. Specifically, the numbers of community residents receiving HIV-positive diagnoses each year were subtracted from the population counts used in subsequent years to ensure the testing rates reflected the cumulative effect of case detection.

The second analysis examined individuals who had one or more additional HIV tests following a negative first-time test result during the study period, excluding females tested through antenatal services. We used this group to compare retest frequencies between males and non-pregnant females and estimate incidence of seroconversion.

The third analysis encompassed all individuals who received HIV testing during 2001–2006. Restricting our analysis to these individuals' first-time test encounters for the study period, we tested for linear trend over time the annual probabilities of test encounters yielding positive results.

The fourth group comprised all clients receiving HIV-positive diagnoses, excluding females diagnosed through antenatal testing. We tested for linear trend over time the annual median CD4 counts and WHO stage distributions for this group of clients at diagnosis. We further determined annual rates of post-test counseling, referral, and treatment for this group. For these rate calculations, referral was defined as receipt of a CD4 count or total lymphocyte count within six months of diagnosis. Eligibility for cotrimoxazole prophylaxis or ART was defined using the afore-mentioned criteria with the additional requirement that clients receive referral as defined above prior to treatment. Finally, treatment with ART or cotrimoxazole was defined as receipt of first drugs within six months of CD4- or WHO stage-based eligibility.

Statistical tests for trend were conducted using Chi-square tests for categorical outcomes and analyses of variance or linear regression models for continuous outcomes. Survival analysis techniques were used to estimate time to retesting and time to positive retest, and the log-rank test used to compare time to retesting between males and non-pregnant females. All analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC).

Results

Population characteristics

The community's adult population increased steadily during the study period, from 7,718 in 2002 to 10,165 by 2006. Age and sex distributions of the adult population remained stable; in 2006, the adult population's mean age was 30 years and 52% were male.

HIV test encounters

During the study period, 5,006 adult community residents not previously diagnosed with HIV infection had 6,322 test encounters, 1,890 (30%) of which were provider-initiated. Acceptance rates averaged 94% and were similarly high across all sexes, age groups, test services, test venues, and years (data not shown). Specifically, 4,679 of the 5,006 first-time test encounters were accepted (Table 1). Most first-time testers were young adults: 2,521 (54%) were aged 20–29 years. Females consistently received a higher proportion (41% vs. 29%) of first-time tests than males, excluding antenatal testers. These distributions remained stable during the study period.

Among first-time testers, 3,125 (67%) initiated VCT encounters, 162 (3%) were TB patients, and 1,385 (30%) were antenatal care users (Table 1). The proportion of first-time tests administered to antenatal care users rose from 7% in 2001 to 40% in 2002 when testing

of pregnant females became provider-initiated. After 2002, this proportion declined while that of first-time tests initiated by clients through VCT services rose from 55% in 2002 to 74% by 2006.

Population HIV testing rates

Annual population HIV testing rates increased from 4% in 2001 to 20% in 2006. Rates among pregnant females were substantially higher than those for non-pregnant females and males from 2002 onward (Figure 1). The rise in rates among males and non-pregnant females increased after 2003, the year ART first became available. Males consistently tested at lower rates than non-pregnant females ($p<0.001$ for all years). There were no substantial differences in testing rates by age stratum (data not shown).

Retesting

Of 5,932 accepted tests, 1,171 (20%) were retests; this proportion increased from 3% in 2001 to 28% in 2006 ($P<0.001$). Of 2,214 adults who received negative results following first-time testing – excluding females tested through antenatal services – 16% retested within one year, 30% within two years, and 53% within five years. Time to retesting was shorter among non-pregnant females than males (61% vs. 44% retested within 5 years, $p<0.001$). The incidence of seroconversion among these retesters was observed to be 1.9% within one year of initial testing, 3.6% within two years, and 12.6% within five years (data not shown).

Trends in yield

Proportion of first-time testers receiving positive diagnoses (yield) decreased over time but remained high, dropping from 47% in 2001 to 28% in 2006 (Table 2). Yield among clients aged >19 years was consistently nearly double that for clients aged 15–19. Yield for females not tested through antenatal services (40%) exceeded that for males (32%), $p<0.001$. The yield for TB care testing was the highest of the three services (51%) while that for antenatal testing was the lowest (26%).

Clinical characteristics and linkage to care for HIV-positive clients

We retrieved medical records for 1,123 (84%) of the 1,340 seropositive clients diagnosed during the study period, excluding females diagnosed through antenatal services. Clinical characteristics for these clients did not change over time (Table 3). The proportion receiving a CD4 within six months of diagnosis increased in later years although we did not find significant linear trends in the medians of first CD4 counts ($p=0.15$). Of these first CD4 counts, 36% were <200 cells/mm³. The proportion of clients determined at diagnosis to be asymptomatic (WHO stages 1–2) was approximately twice (57% vs. 26%) that of patients with HIV-related symptoms (WHO stages 3–4).

Among those clients whose records were retrieved, post-test counseling rates exceeded 96% each year (Figure 2). Referral rates increased from 29% of seropositive clients in 2001 to 67% in 2006 ($p<0.001$). The proportion of seropositive clients diagnosed each year and determined to be eligible for ART before the end of the study period remained stable. The proportion immediately eligible for ART upon diagnosis (20%) similarly remained stable (data not shown). Finally, rates of ART initiation within six months of determination of eligibility increased dramatically, from 0% of all seropositive clients in 2001 to 16% in 2006 (corresponding to 0% of eligible clients in 2001 to 68% in 2006, $p<0.001$, data not shown).

Discussion

We examined trends in HIV testing rates and outcomes during 2001–2006 in a small African community with an estimated HIV prevalence of 23%.¹¹ Testing rates increased substantially and were highest among pregnant females from 2002 onwards when antenatal testing became provider-initiated. Retesting accounted for much of the population's testing, but growth in the proportion of seronegative first-time testers retesting leveled off as a function of time elapsed from first-time testing. HIV-positive yield of testing decreased, but nevertheless exceeded 28% in all years. Retesting yield similarly remained high with 12.6% of seronegative first-time testers diagnosed with HIV within five years of first-time testing. The median of CD4 counts at diagnosis (276 cells/mm³ for the entire study period) did not change significantly. Finally, client throughput for the two principal rate-limiting steps in the linkage-to-care process, referral for CD4 count and ART initiation, increased markedly during the study period as the availability of these services expanded.

The testing rate among adults not previously diagnosed HIV-positive increased from 4% in 2001 to 8% in 2003 and then experienced even more dramatic growth, eventually reaching 20% by 2006. This increased growth after 2003, when the ART rollout began in the community, suggests that HIV treatment availability encouraged testing. Given that ART is only now becoming widely available elsewhere in South Africa,¹⁹ the 2003 testing rate may be more indicative of current national testing rates, although this study clearly demonstrates that these rates are dynamic. These findings suggest that ongoing efforts to increase and advertise ART availability could contribute to further expansion of testing.²⁰

The substantially higher testing rates among pregnant females demonstrate the potential effectiveness of provider-initiated testing. Pregnant females may have tested at higher rates in part because they comprise a unique group likely to receive provider-initiated test offers through antenatal care^{21–23} and to accept such offers out of concern for their unborn babies.²⁴ Yet, testing rates among pregnant females were comparable to those for all other groups until 2002 when antenatal testing became routine. Thus, we expect that provider-initiated testing may effectively elevate testing rates among groups regularly accessing healthcare facilities.

Of course, provider-initiated testing will be less effective for increasing testing among groups not regularly accessing healthcare facilities. For such groups, detection of later-stage infections through TB testing will continue to contribute to a large proportion of case detection. Because we were unable to quantify either the total number of tests of TB-infected residents (the VCT data did not indicate clients' presenting illnesses) or the numbers of residents infected with TB, we could not estimate rates of provider-initiated testing among the TB patients in this population. Nevertheless, we presume they were significantly higher than the rates of client-initiated testing among the general community population. Future research should continue to consider strategies (e.g., home-based testing²⁵) beyond TB testing for achieving earlier diagnoses of HIV infections among groups with irregular access to healthcare facilities.

HIV testing yield decreased as testing rates increased. This is an indication of testing program success in increasing case detection at the population level: as undiagnosed HIV prevalence falls, more tests are required for each new case identified. Nevertheless, annual yield never fell below 28% for first-time testers. Yield remained high even among antenatal care users and TB patients already receiving provider-initiated testing. These figures indicate the need for expanding testing further among the general population while continuing aggressive case detection for pregnant females and TB patients. Furthermore, the observed incidence rate of 1.9% over one year among retesters (excluding antenatal testers)

highlights the importance of sustaining any expanded testing to achieve regular retesting to identify new infections.

Further evidence of the need for retesting comes from the lack of substantial change in the clinical characteristics of newly-diagnosed HIV-infected patients. Neither median CD4 counts nor distributions by WHO stage at diagnosis changed markedly. Thus, clients did not appear to be testing any earlier in the course of infection despite the rising population testing rates.

Linkage to effective HIV treatment will be necessary for seropositive clients to realize the benefits of expanded testing. The dramatic rise in referral and treatment rates observed in this study are encouraging signs of the capacity of South Africa's healthcare sector to absorb the increased caseload that will be identified through expanded testing. Also important will be ensuring linkage of HIV-infected patients not yet eligible for treatment to social support, positive living messages, monitoring and other pre-ART care. Scaling up nutritional, educational, and psychosocial interventions for HIV-infected persons will be an important component to any effort to increase HIV testing in South Africa.

Indeed, a substantial proportion newly-diagnosed HIV-infected patients were not yet eligible for treatment upon diagnosis under current treatment guidelines.^{13, 14} This proportion will presumably increase further if testing expands sufficiently as HIV-infected persons are identified at earlier stages of infection. Any expanded testing program will need to be accompanied by initiatives to track these individuals, educate them regarding prevention, and provide them ongoing clinical and laboratory monitoring. As growing numbers of HIV-infected individuals not yet eligible for treatment are identified, it may also become increasingly relevant to consider revising treatment guidelines to begin ART earlier,²⁶ though this raises further issues of treatment capacity.²⁷

This study illuminates HIV testing rates and outcomes at the population level. Several studies in South Africa²⁸ and elsewhere in sub-Saharan Africa¹⁹ have attempted to estimate the effects of baseline population testing through cross-sectional surveys, determining proportions of individuals who have already received HIV testing. However, these surveys sampled only small portions of the populations of interest, may have experienced substantial self-selection biases, and did not provide longitudinal data. One study estimated testing rates for Botswana's national population by using aggregate statistics from healthcare facility reports. However, low levels of reporting and the lack of patient-specific data precluded calculation of the annual rates at which unique individuals received testing and linkage to care.²⁹

This study has several limitations. Although we compared testing rates by age, small sample sizes for the older categories (e.g., >49) made it impossible for us to examine whether specific age groups should receive priority for HIV testing in South Africa. Moreover, the community's small size and access to ART and other HIV-related services since 2003 may limit the generalizability of these findings to other African settings. Yet, the community's small size made possible the measurement of population-level testing rates. Similarly, while this study's retrospective design entailed use of incomplete data from testing registers and clinical records, it was required for analyzing the entire population, given that prospectively following every population member would have been impractical. Since each member of the study population was not followed prospectively, we also cannot account for immigration or emigration. However, the 2006 census found that only 1.0% of residents had immigrated and 0.4% planned to emigrate during that year, indicating that the population was relatively closed during the latter years of the study period.

We found a dramatic increase in population HIV testing rates over the last six years in a small South African community. Yet, in spite of these increases, testing yield remained high and patients were not diagnosed any earlier in the course of HIV disease. Thus, further expansion of testing – combined with effective programs for linking seropositive clients to care, monitoring, and treatment once eligible – remains an important public health goal. The move to provider-initiated testing increased testing rates among pregnant females in this setting. Provider-initiated testing for all non-pregnant females and males accessing healthcare facilities – as recommended by the WHO¹ – coupled with careful linkage to care for seropositive clients, should be considered a critical component of the response to the HIV epidemic in South Africa.

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Figure 1.

Annual rates of HIV testing among adult study community residents not previously diagnosed with HIV, 2001–2006, stratified by sex and pregnancy status. Pregnant females received client-initiated testing in 2001 and provider-initiated testing from 2002 onward. Throughout the study period, males and non-pregnant females received a combination of provider-initiated testing through tuberculosis services and client-initiated voluntary counseling and testing. Pregnant females (bold line) tested at much higher rates than all others from 2002 onward. Males (dashed line) tested at lower rates than non-pregnant females (solid line) for the study period entirety. Testing rates among males, pregnant females, and non-pregnant females all increased throughout the study period.

Figure 2.

Annual linkage-to-care rates for adult community residents testing HIV-positive during 2001–2006, excluding females tested through antenatal services. Post-test counseling rates (solid line) remained uniformly high during the study period, while referral rates (dashed line), defined as receipt of a CD4 or total lymphocyte count within six months of diagnosis, increased from 31% of counseled clients in 2001 to 69% in 2006. The rates at which referred HIV-positive clients were determined to be eligible for ART (solid bold line), defined as CD4 <200 cells/mm³ or diagnosis with a WHO stage 4 illness following referral, remained stable. Finally, rates of receipt of ART within six months of eligibility (bold dashed line) increased dramatically from 0% of seropositive clients in 2001 to 16% in 2006, or from 0% of eligible clients to 68%.

Table 1

Characteristics of clients accepting first-time test encounters during 2001–2006, stratified by sex, age, and test service.

	2001	2002	2003	2004	2005	2006	All
No. tests	280	483	603	970	952	1,391	4,679
% tests, by sex [†]							
Male	35	22	24	28	29	32	29
Non-pregnant female	58	38	38	42	37	43	41
% tests, by age [*]							
15–19	15	11	12	16	13	15	14
20–29	54	55	53	52	56	54	54
30–39	21	23	25	22	22	23	23
40–49	8	7	8	7	7	6	7
>49	2	5	2	4	3	3	3
% tests, by service [*]							
VCT [‡]	86	55	60	68	60	74	67
Tuberculosis care [§]	6	5	2	2	6	2	3
Antenatal care [¶]	7	40	37	30	34	24	30

* Reported percentages within each year may not add to unity due to missing values and rounding

[†] For percent tests for pregnant females, see those reported for recipients of tests offered through antenatal care

[‡] All voluntary counseling and testing (VCT) for HIV was client-initiated and includes client-initiated testing by TB patients

[§] HIV testing offered through tuberculosis (TB) care was provider-initiated for patients initiating TB treatment and without a known HIV status

[¶] Antenatal HIV testing includes all screening by females known to be pregnant at the time of testing and was client-initiated in 2001 and provider-initiated from 2002 onward

Trends in proportions of clients testing HIV-positive for accepted first-time test encounters during 2001–2006, stratified by sex, age, and test service.

Table 2

	2001	2002	2003	2004	2005	2006	All	p
% seropositive, all	47	46	40	32	30	28	34	<0.001
% seropositive, by sex*								
Male	38	44	47	32	26	26	32	<0.001
Non-pregnant female	48	52	54	38	37	33	40	<0.001
% seropositive, by age								
15–19	43	29	30	12	11	16	18	<0.001
20–29	47	46	42	33	31	28	35	<0.001
30–39	53	53	40	40	38	35	40	<0.001
40–49	45	47	47	37	27	35	38	0.04
>49	0	36	36	41	24	19	29	0.34
% seropositive, by service								
VCT†	43	48	50	36	32	29	36	<0.001
Tuberculosis care‡	61	60	79	53	34	55	51	0.04
Antenatal care§	75	40	23	22	25	21	26	<0.001

* For HIV-positive yield for pregnant females, see those reported for recipients of tests offered through antenatal care

† All voluntary counseling and testing (VCT) for HIV was client-initiated and includes client-initiated testing by TB patients

‡ HIV testing offered through tuberculosis (TB) care was provider-initiated for patients initiating TB treatment and without a known HIV status

§ Antenatal HIV testing includes all screening by females known to be pregnant at the time of testing and was client-initiated in 2001 and provider-initiated from 2002 onward

Table 3

Clinical indicators of adult community residents testing seropositive, 2001–2006, by year of diagnosis (excluding females tested through antenatal services).

	2001	2002	2003	2004	2005	2006	All	p
No. seropositives	117	147	203	272	226	375	1340	
CD4 counts*								
% cases w/ CD4	3	11	30	40	51	62	40	<0.001
Median, cells/mm ³	265	205	267	297	221	288	276	0.15
% <200 cells/mm ³	33	44	37	33	45	31	36	0.38
WHO stage†								
% cases w/ stage	85	65	74	85	84	92	83	<0.001
% stages 1–2‡	76	61	67	72	57	74	69	<0.001
% stages 3–4‡	24	39	33	28	43	26	31	0.20

* Only CD4 counts received within six months of diagnosis included

† WHO: World Health Organization

‡ Values are percentages of patients on whom WHO stage data was available classified as WHO stage 1–2 or 3–4 due to rounding