Swaziland HIV Incidence Measurement Survey (SHIMS)

Results Update, October 2014

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Acknowledgements

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CD4 Count Distribution and ART Use in a Nationally Representative Sample of HIV-infected Adults: Swaziland HIV Incidence Measurement Survey (SHIMS)

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Background

CD4 enumeration measures the severity of HIV infection in individuals and helps determine eligibility for ART. The distribution of CD4 counts among HIV-infected individuals in a population, and therefore the true level of ART 'coverage' in a region, is unknown. We describe the first direct assessment of national distribution of CD4 cell counts and of ART coverage at a population level, conducted in Swaziland in 2012.

Methods

In the Swaziland HIV Incidence Measurement Survey, a nationally representative sample of 18,169 men and women, age 18-49, underwent household-based counselling and rapid HIV testing and provided clinical/demographic information. Among 5802 HIV-infected individuals identified during the survey, 1000 were randomly selected to participate in a follow-up visit, with collection of blood for CD4 enumeration via automated flow cytometry, a questionnaire to assess use of HIV care services and review of each participant's personal medication booklet.

Results

Of the 945 HIV-infected individuals who were located and consented to participate, 66% were women; 67% resided in a rural setting; 59% reported being married/co-habitating; 44% were employed. Median CD4 count was 480 cells/mm3; 284 (30%) had a CD4 count <350 and of these, 101 individuals (11% of total) had a CD4 count of <200. Among men and women, 41% and 25%, respectively had a CD4 count <350 (Figure 1). While education was associated with CD4 count (32% of those with less than secondary education had CD4 count <350 vs. 20% of those with tertiary education, $\chi 2 = 3.8$, p .05), urban versus rural residence, age group, employment and marital status did not show an association with CD4 count category.

Six hundred individuals reported having been told by a clinician to take ART; of these, 482 (80%) reported initiating ART and 463 (77%) reported current ART use. These 463 represent 75% of 619

participants who were eligible for ART based on CD4 count <350 cells/mm3 (Figure 2). No prior enrollment in HIV care was reported by 19% of all and by 25% of those with CD4 <350.

Figure 1. CD4 count (cells/mm^3) distribution by

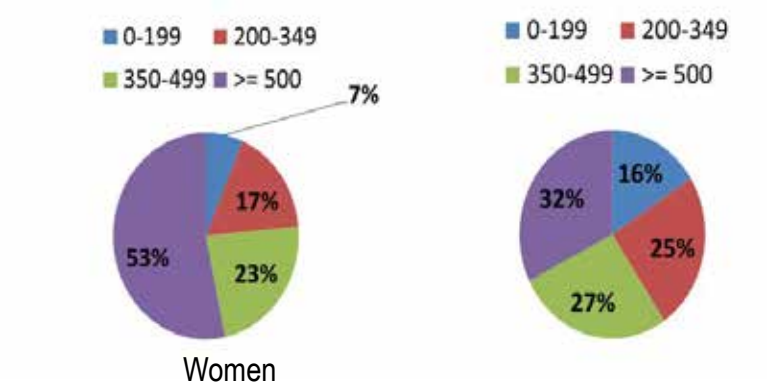
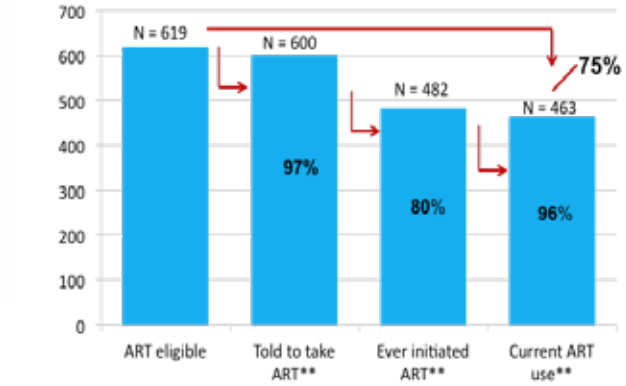


Figure 2. Enrollment and retention on ART



Conclusions

Over half of HIV-infected individuals in Swaziland have a CD4 count over 480. A quarter of ART eligible adults reported no prior HIV-care enrollment and 23% of those advised to take ART were not currently taking it. However, this population-level assessment of Swaziland's treatment program expansion shows high ART coverage of eligible HIV-infected persons and high retention among those who start ART.

Population HIV Viral Load Estimate in Swaziland: Assessing ART Program Effectiveness and Transmission Potential

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Background

Community viral load (CVL) describes the viral load of persons with known HIV infection, but does not include those with undiagnosed HIV, and thus does not accurately reflect transmission potential in the community. True population viral load (PVL) includes data from both diagnosed and undiagnosed HIV+ individuals, accurately reflecting the status of HIV epidemics and the effectiveness of ART programs. We describe the first national estimate of PVL, conducted in Swaziland in 2011.

Methods

In the Swaziland HIV Incidence Measurement Survey, a nationally representative sample of 18,169 men and women, age 18-49, underwent household-based counseling and rapid HIV testing and provided clinical/demographic information. All HIV+ sera were analyzed for viral load (VL) [Cobas AmpliPrep/Taqman HIV-1 test, v2.0]. PVL is described as survey-weighted mean and median VL, and proportion with low (<1,000 c/ml) and high (>50,000 c/ml) VL. Two separate logistic regression models identified predictors of low and high VL, adjusted for knowledge of HIV+ status, age, gender, marital status, ART use, and region.

Table 1. Viral load measurements (c/ml) among HIV+ SHIMS participants (weighted)

Population	N	Mean PVL (SD)	Median PVL[1] (IQR)	VL <1,000 (%)	VL >50,000 (%)
Total HIV+ cohort	5,828[2] (100%)	94,644 (4,246)	14,471 (11-85,939)	2,031 (35%)[3]	2,012 (35%)
Unaware of status	1,925 (33%)	126,916 (8,850)	53,684 (12,054 - 131,918)	165 (9%)	995 (52%)
Aware of status	3,903 (67%)	78,756 (4,349)	2,093 (0 - 56,638)	1,865 (48%)	1,018 (26%)
Current ART use	1,895 (50%)	23,025 (4,981)	0 (0 - 62)	1,605 (85%)	122 (6.4%)
No current ART use	1,902 (50%)	132,476 (7,078)	40,405 (6,948 - 119,249)	233 (12%)	851 (45%)

1: Viral load "<20" and "Target not detected" are treated as 0.
2: Viral load data available on 5,789 individuals (unweighted) and 5,828 (weighted).
3: Most individuals (71%) in "Total HIV+ cohort" with VL<1000 c/ml had VL<20.

Results

Of 5,802 HIV+ adults identified, VL data were available on 5,789. In the HIV+ adult population, 67% knew of their HIV infection, and of those 50% reported current ART use (33% men, 67% women). PVL differed from CVL: mean 94,644 vs 78,756 c/ml and median 14,471 vs 2,093 c/ml (Table 1). Low VL was found in 35% of total HIV+ population, 9% of undiagnosed HIV+'s, and 85% of those reporting ART use; high PVL was found in 35% of the total population. Men were less likely than women to have low VL [aOR 0.74, 95% CI 0.62, 0.88] and more likely to have a high VL [aOR 1.93, 95% CI 1.70, 2.19]. Younger HIV+s were less likely to have low PVL (Table 2).

Table 2. Multivariable models of correlates of low and of high viral load among HIV+ SHIMS participants (weighted)[1]

	Low viral load (VL<1000)		High viral load (VL>50,000)	
Effect	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Knowledge of HIV+ status				
Unaware of HIV status	0.02 (0.02, 0.02)	<0.0001	14.7 (12.1, 17.90)	<.0001
Aware of HIV status - no current ART use	0.03 (0.02, 0.03)	<0.0001	13.1 (10.8, 16.01)	<.0001
Aware of HIV status - current ART use	1.0		1.0	
Gender				
Female	1.0		1.0	
Male	0.74 (0.62, 0.88)	0.0005	1.93 (1.70, 2.19)	<.0001
Age (y)				
18-29	0.48 (0.04, 0.59)	<0.0001	1.07 (0.91, 1.27)	0.39
30-39	0.86 (0.72, 1.02)	0.0855	1.01 (0.86, 1.19)	0.93
40-49	1.0		1.0	

1: Adjusted for region and marital status

Conclusions

Findings from the first national PVL estimate demonstrate important differences between true PVL and CVL, the latter more commonly reported. PVL provides better estimates of ART program effectiveness and transmission risk in a population. Men were more likely to have a high VL, corresponding to the recently reported finding that national HIV incidence is twice as high among women as men. The success of Swaziland's ART program, with low PVL in 85% of those reporting ART use, compares favorably with US data.

Potential Impact of Viral Load on ART Eligibility Criteria in Swaziland

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Presented at the 21st Conference on Retroviruses and Opportunistic Infections, March 3-6, 2014, Boston, Massachusetts, United States

Background

Antiretroviral therapy (ART) programs implementing "treatment as prevention" need to target not only those who need ART for their own health but also those likely to transmit HIV. Observational studies suggest that HIV transmission risk differs depending on whether the viral load (VL) is above or below 10, 000 copies/ml. We describe an assessment of the additional persons who would need ART if VL criteria were added to current CD4 count eligibility criteria in Swaziland.

Methods

In the Swaziland HIV Incidence Measurement Survey, a nationally representative sample of 18,172 men and women, age 18-49, underwent household-based counselling and rapid HIV testing and provided clinical/demographic information in 2010-11. Among 5802 HIV+ individuals identified during the survey, 1000 were randomly selected to participate in a follow-up visit, with collection of blood for CD4 enumeration via automated flow cytometry and viral load using Roche CAPTAQ HIV-1 Test, V2.0.

Results

Among 949 HIV+ individuals who participated in this sub-study, complete CD4 and VL data were available on 927; in unweighted analysis, 456 of these (49%, 95% CI: 46-52%) did not report ART use. Based on current Swaziland guidelines of ART initiation at CD4 threshold of < 350 cells/ml3, 148 of the 456 (32%, 95% CI: 28-37%) were eligible for ART and 308 (68%, 95% CI 63-72%) were not. If VL>10,000 copies/ ml were added as a separate ART initiation criterion, the number eligible for ART at CD4<350 would increase by 193 (63%, 95% CI: 57-68%) of the 308 currently ineligible individuals not on ART, an additional 42% (95% CI: 38-47%) of the 456 of the untreated HIV+ sample, and 21% (95% CI: 18-24%) of the entire HIV+ sample.

Table 1. Viral load distribution by CD4+ T-cell count among HIV-infected adults reporting no ART use (unweighted)					
	CD4 cells/ml^3				
	0-199	200-349	350-499	≥500	Total
HIV viral load copies/ml					
<1000	3	6	5	28	42
1,000-9,999	1	7	19	63	90
10,000-99,999	33	38	66	89	226
≥100,000	26	34	20	18	98
Total	63	85	110	198	456

Conclusions

We provide an estimate of the proportion of additional HIV+ adults who would be ART eligible if a VL threshold were added to CD4 eligibility criteria. Almost one-third of untreated HIV+ persons in our sample are already eligible for ART based on current national CD4 count criteria; effective linkage to ART for them is a program priority. The addition of VL > 10,000 copies/ ml to the initiation criteria would increase the ART-eligible proportion of untreated HIV+ adults in our sample by 42%, to almost 75%. These results indicate that the addition of VL to eligibility criteria could modestly increase demand on Swaziland's ART program. These targeted increases in coverage would be expected to lead to notable reductions in transmission.

Changes in Viral Load after Home-based HIV Testing and Counselling Swaziland

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Presented at International AIDS Society (IAS) Conference, July 20-25, 2014, Melbourne, Australia

Background

Home-based HIV testing and counselling (HBHTC) increases uptake of testing among persons who have not previously sought or received testing. We assessed viral load (VL) change for individuals identified as HIV-positive during HBHTC.

Methods

As part of the Swaziland HIV Incidence Measurement Survey (SHIMS), 18,172 adults age 18-49 received HBHTC and counselling about linkage to HIV care and treatment in 2010-11. Of the identified 5803 HIV-positive individuals, 1067 were randomly selected to participate in VL measurement and a follow-up survey 8-12 months later.

Results

Among the 922 HIV-positive individuals with measured baseline and follow-up VL, 71% were aware of their HIV-positive status prior to HBHTC. Of these HIV-aware individuals, 57% reported current ART use. At baseline, 41% of all HIV-positive individuals and 86% of the sub-group on ART were virally suppressed (VL< 1000 copies/mL). The increase in the proportion of those with viral suppression was 7.0% overall. The largest changes in viral load suppression were seen for the 99 individuals who initiated ART between baseline and follow-up; 78% and 67% of the HIV-aware individuals and the newly-identified individuals at baseline achieved viral suppression by follow-up. Effect sizes were similar across gender; at follow-up, 50% of females and 45% of males were virally suppressed.

Table 1. Change in proportion with viral load suppression by HIV awareness and by ART use at baseline and follow-up of 922 adults				
	Total (N)	VL <1000 at baseline	VL <1000 at follow-up	Change
HIV aware at baseline	654	54%	60%	6%
ART use at baseline	372	86%	85%	-1%
Initiated ART between baseline and FU	60	18%	78%	60%
No reported ART use	223	9%	12%	3%
Unaware at baseline (newly diagnosed)	268	7%	15%	8%
Initiated ART between baseline and FU	39	10%	67%	57%
No reported ART use	229	7%	6%	-1%
Total	922	41%	47%	7%

Conclusions

Viral load suppression at baseline was high among those reporting ART use. After HBHTC conducted as part of SHIMS, there was a slight overall increase in the proportion of those with viral suppression, largely driven by those individuals initiating ART between baseline and follow-up measurements. HBHTC combined with improved linkage to care and more widespread initiation of ART has the potential to increase viral suppression in the population, thereby improving clinical outcomes and reducing transmission.

Potential Impact of Targeting Prevention Strategies to HIV-Discordant Households

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Presented at the 21st Conference on Retroviruses and Opportunistic Infections, March 3-6, 2014, Boston, Massachusetts, United States

Background

While HIV prevention trials have identified promising interventions, it remains unclear how to maximize population-level impact and efficiency. Swaziland HIV Measurement Survey (SHIMS) data allow exploration of the potential public health gains achieved through targeting prevention to HIV-negative individuals living in HIV-discordant households.

Methods

SHIMS estimated HIV incidence in Swaziland using prospectively observed seroconversions in a population-based longitudinal cohort. From a representative sample of 14,891 households, 18,172 adults (age 18-49) provided baseline clinical and demographic information and underwent HIV counseling and testing; 11,227 HIV-uninfected participants (6,225 women, 5,002 men) were retested 6 months later. Using logistic regression models, we examined whether HIV-negative individuals living in households with HIV-positive members, i.e., in HIV-discordant households, were at heightened risk of seroconversion. We compared the number needed to treat (NNT) to prevent one seroconversion per year under a hypothetical roll-out of pre-exposure prophylaxis (PrEP), applying the highest observed PrEP efficacy of 73%.

Table 1. Household Composition from Baseline Survey Participants

	N (%)
All households with baseline survey participants	9,944
Households with only HIV-negative members	5,383 (54.1%)
Households with only HIV-positive members	2,471 (24.9%)
Serodiscordant households	2,090 (21.0%)
Households with a male HIV+ member	630 (6.33%)
Households with a female HIV+ member	1,693 (17.0%)

Results

Baseline HIV prevalence in 2011 was 32% (women: 38%, men: 22%). A total of 2,090 households (21%) were HIV-discordant per baseline testing (Table 1). There were 145 seroconversions corresponding to an annualized incidence of 2.4% (women: 3.1%, men: 1.7%), and 39% of seroconversions occurred in HIV-discordant households. Having an HIV-positive household member of either sex predicted seroconversion for women (OR: 1.48, 95% CI: 0.97-2.3) and men (OR: 1.78, 95% CI: 1.0-3.2) (Table 2).

Table 2. Measures of Association and Impact

	Women			Men		
	OR (95% CI)	% of Seroconverters	PrEP NNT	OR (95% CI)	% of Seroconverters	PrEP NNT
All HIV-negative adults	--	63.70%	43	--	36.30%	79
Household Discordancy						
Living with only HIV-negative adults	--	40.20%	48	--	20.90%	97
Living with HIV+ household member	1.48 (0.97, 2.3)	23.40%	33	1.78 (1.0, 3.2)	15.40%	55
Living with HIV+ man	3.31 (2.1, 5.3)	14.30%	16	1.33 (0.6, 3.1)	4.40%	62
Living with HIV+ woman	0.98 (0.6, 1.6)	14.60%	43	1.57 (0.8,2.9)	12.10%	57
Age						
Age < 25	--	36.10%	32	--	13.70%	97
Age > 25	0.58 (0.4, 0.9)	27.60%	56	1.4 (0.78, 2.6)	22.60%	68
Marital status						
Married	--	23.20%	59	--	9.40%	91
Unmarried	1.74 (1.1, 2.7)	40.40%	33	1.20 (0.6, 2.3)	26.90%	75
Number sexual partners (last 6 months)						
0	--	8.10%	65	--	4.30%	212
1	1.58 (0.9, 2.8)	50.60%	41	3.08 (1.2, 7.7)	20.60%	69
2+	3.32 (1.3, 8.7)	4.30%	18	4.60 (1.7, 12.4)	10.60%	46

For women, having an HIV-positive man in the household was associated with seroconversion (OR: 3.4, 95% CI: 2.1-5.5); however, for men, having an HIV-positive woman in the household was not (OR: 1.6, 95% CI: 0.8-2.9). The NNT with PrEP in order to prevent one seroconversion per year would be 41 among individuals of either sex living in HIV-discordant households. Defining target populations by both household and individual demographic, the PrEP NNT for unmarried women living with HIV+ men is 11, and this population accounts for 10% of the population incidence.

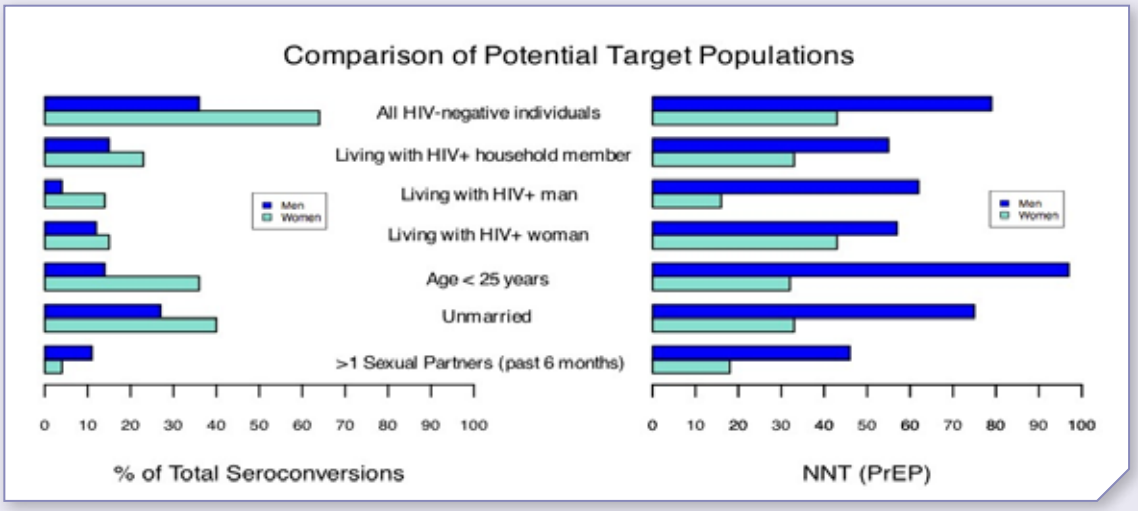

Figure 1.
Left: Comparison of the percentage of total seroconversions that occurred within each target population.
Right: The number of individuals in the target population that would need to be treated with 75% efficacious PrEP in order to prevent one seroconversion/year.

Conclusions

In Swaziland, a large fraction of seroconversions occur in HIV-discordant households. Identification of women in HIV-discordant households may allow more efficient targeting of prevention for women, while targeting prevention for men may require other approaches. Further work is needed to distinguish whether the observed association between household HIV-discordancy and seroconversion is due to within-household transmission or shared household risk factors.

National Prevalence of Transmitted HIV Drug Resistance in Swaziland in 2011

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Presented at International AIDS Society (IAS) Conference, July 20-25, 2014, Melbourne, Australia

Background

In Swaziland, 32% of adults are living with HIV. As access to ART in Swaziland increases, emergence and transmission of HIV drug resistance (HIVDR) may also increase. To assess the national level of transmitted DR (TDR), we analyzed samples collected from seroconverters and acutely HIV-infected persons enrolled in the Swaziland HIV Incidence Measurement Survey (SHIMS).

Methods

A nationally representative sample of 18,169 adults in Swaziland completed household-based counseling and rapid HIV testing in 2011. Among these, 13 had evidence of acute infection and of 11,155 HIV-negative individuals who had repeat HIV testing six months later, 146 seroconverted. Of the 159 HIV-positive samples, 151 were available for HIVDR analysis. Viral load (VL) was determined by using the Abbott RealTime HIV-1 assay. Genotyping was performed with three assays: CDC in-house sequencing-based, Multiplex Allele-Specific (MAS), and Allele-Specific Real-Time PCR (AS-PCR). These assays have a lower detection limit of minor mutations at 20%, 1.6-12.5%, and 0.2-1.7% respectively. TDR mutations were determined by Calibrated Population Resistance tool using the 2009 WHO DR mutation list.

Results

The median VL was 4.42 log10 cp/mL (IQR: 3.89 to 5.02). Of the 140 samples tested by both in-house and MAS assays, 139 had results in both assays and three had evidence of NNRTI mutations, yielding an estimated prevalence of NNRTI TDR of 2.16% (3/139, 95% CI: 0.74-6.16) (Table 1). A protease inhibitor mutation, M46I, was detected in one sample by the in-house assay but was not analyzed by the MAS. Of the 151 samples tested by AS-PCR for five DR mutations in the reverse transcriptase region (K103N, V106M, Y181C, M184V, G190A), 142 samples had results and 15 additional NNRTI mutations were detected in 12 samples, yielding an estimated TDR prevalence of 8.45% (12/142, 95% CI: 4.90-14.19). We did not detect any NRTI mutations.

Table 1. HIV-1 transmitted drug resistance mutations detected by sequence-based in-house assay, multiplex allele-specific drug resistance (MAS-DR) assay or allele-specific Real-time PCR assay (AS-PCR).

Specimen ID^ (N=13)	Infection Status	HIV-1 subtype	Transmitted Drug Resistance Mutations Detected								
			Sequenced-based assay			MAS-DR+			AS-PCR+		
			Antiretroviral drug classes								
			PI	NNRTI	NRTI	PI	NNRTI	NRTI	PI	NNRTI	NRTI
20*	SC	C								K103N	
21	SC	C		*V106A*			*V106AV*				
31	SC	C								Y181C	
33	SC	C								Y181C	
48	SC	C	M46I+								
72	SC	C								V106M	
80	SC	C								V106M, Y181C	
85	SC	C								Y181C	
101	SC	C								V106M	
103	SC	C								V106M, Y181C	
122	SC	C		Y181C			Y181C			Y181C	
140	SC	C								Y181C	
148	Acute	C		K103N			K103N			K103N, Y181C	
151	Acute	C								Y181C	
Total			1	3	0	0	3	0	0	13	0
Transmitted DR Prevalence			3/139 (2.16%)			3/139 (2.16%)			12/142 (8.45%)		
			95% CI: 0.74-6.16			95% CI: 0.74-6.16			95% CI: 4.90-14.19		

Conclusions

These findings from Swaziland provide the first estimate of national prevalence of TDR, using samples from a nationally representative cohort of HIV seroconverters and acutely HIV-infected individuals. Per WHO definitions, TDR level in Swaziland is low (<5%) based on the sequencingbased in-house or more sensitive MAS assay, but moderate (between 5-15%) based on the ultrasensitive AS real-time PCR.

Performance of Determine™ HIV-1/2 Ag/Ab Combo Test to Detect Acute Infections in a High Prevalence Cross-Sectional Population in Swaziland[a]

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Presented at the 20th Conference on Retroviruses and Opportunistic Infections, March 3-6, 2013, Atlanta, Georgia, United States

Background

Fourth generation HIV rapid tests (RTs) incorporate p24 antigen detection for early identification of acute infections. Identification of acute HIV infections may be an important approach in preventing HIV transmission.

Methods

As a part of the Swaziland HIV Incidence Measurement Survey (SHIMS), 18,154 individuals were household tested for HIV infection using a two RT serial algorithm; Determine™ HIV-1/2 Ag/Ab Combo followed by UniGold™ as the confirmatory RT. Discordant samples were resolved by tiebreaker EIAs. Determine Ag+ only samples were further tested for viral load using Roche CAPTAQ HIV-1 Test, V2.0. All RT non-reactive samples had nucleic acid amplification testing (NAAT) performed in plasma pools of 10 to identify true acute infections. Determine™ Combo Ag+/Ab- and NAAT-positive acute cases had follow-up testing to confirm seroconversion.

[a] This manuscript has been published in a peer-reviewed journal with the following citation:
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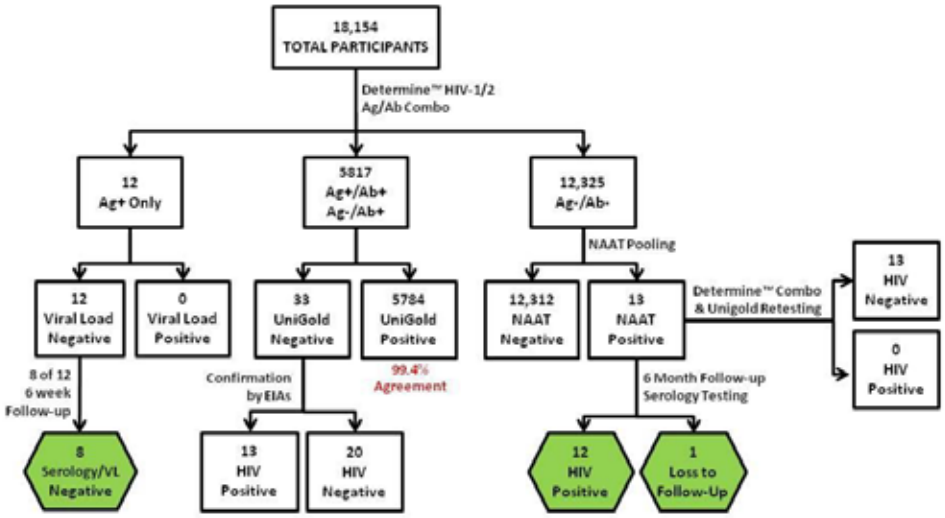
Figure 1. HIV Testing Algorithm



Results

Of 18,154 whole blood specimens tested, 5817 specimens were Ab+ by Determine™ Combo and of those, 5784 were confirmed reactive by Unigold (99.4% agreement, Figure 1). While Determine™ Combo identified 12 Ag+/Ab- samples, all were viral load negative and therefore not confirmed acute infections. Of these, 8 had a 6-week follow-up visit and were found to be HIV negative.

Plasma pooling on the 12,325 Ag-/Ab- non-reactive Determine™ Combo specimens revealed 13 NAAT-positive specimens with HIV RNA values ranging from 300 to >10,000,000 copies/mL. Repeat HIV serology on these 13 NAAT-positive specimens confirmed all were Ag and Ab non-reactive. Follow-up testing of 12 of the 13 NAAT-positive individuals at 6 months demonstrated 12 seroconversions (1 case was lost to follow-up). Therefore, Determine™ Combo had a sensitivity of 0% (95% CI 0%-25%) and positive predictive value of 0% for detection of acute infections.

Conclusions

The ability of the 4th-generation Determine™ Combo to detect antigen was very poor in Swaziland. Thus, the Determine™ Combo test does not add any value to the current testing algorithm; rather, it adds additional costs and complexity to HIV diagnosis. The detection of acute HIV infections may need to rely on other testing strategies.

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