Antiretroviral drug use in a cross-sectional population survey in Africa: HPTN 043

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BACKGROUND

The NIMH Project Accept trial (HIV Prevention Trials Network [HPTN] 043) was a phase 3, community-randomized trial in Africa and Thailand that assessed the impact of behavioral interventions on HIV incidence.

Interventions (enhanced community-based voluntary counseling and testing) were delivered over 3 years. HIV incidence was then assessed in a cross-sectional survey of >50,000 randomly-sampled adults (survey period: 2009-2011). At the African sites (Zimbabwe, Tanzania, KwaZulu-Natal and Soweto, South Africa), HIV incidence was 1.52% and 1.81% in intervention and control communities, respectively (P=0.082) [1].

We evaluated antiretroviral (ARV) drug use among HIV-infected adults at these sites using a qualitative, multi-drug ARV assay.

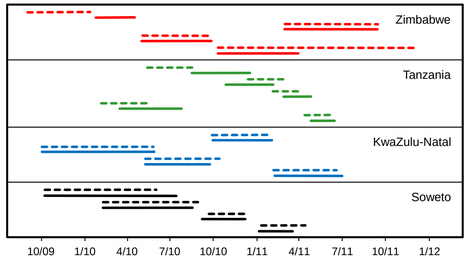
METHODS

Blood samples were collected from adults (18-32 years of age) during the post-intervention survey (Figure 1). Plasma samples from 7,354 HIV-infected adults were retrospectively tested for the presence of 20 ARV drugs using a qualitative assay, including:

- 9 protease inhibitors (PIs)
- 6 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)
- 3 non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- 1 integrase inhibitor (raltegravir)
- 1 CCR5 receptor antagonist (maraviroc)

The lower limit of detection was 10 ng/mL for all drugs. ARV drug use was defined as detection of ≥ 1 ARV drug.

FIGURE 1. Post-intervention survey periods for the African HPTN 043 sites.



The lines indicate survey periods for control communities (dashed) and intervention communities (solid).

RESULTS

Results were obtained from 7,347 (99.9%) of the 7,354 samples tested. ARV drugs were detected in 2,011 (27.4%) of the samples (Table 1); 88.1% had 1 NNRTI +/- 1-2 NRTIs. The most commonly detected drugs were efavirenz and lamivudine (detected in 62.3% and 57.3% of the samples, respectively).

Table 1. ARV drugs detected in study samples.

	Zimbabwe N=1,529	Tanzania N=531	KwaZulu-Natal N=3,640	Soweto N=1,647	All sites N=7,347
Samples with ≥1 ARV drug detected, N (%)	326 (21.3)	114 (21.5)	1,154 (31.7)	417 (25.3)	2,011 (27.4)
NNRTI, N (%)	305 (19.9)	85 (16.0)	1,064 (29.2)	371 (22.5)	1,825 (24.8)
NRTI, N (%)	203 (13.3)	85 (16.0)	788 (21.6)	246 (14.9)	1,322 (18.0)
PI, N (%)	7 (0.5)	1 (0.2)	29 (0.8)	20 (1.2)	57 (0.8)
Raltegravir, N (%)	1 (0.1)	0 (0.0)	3 (0.1)	0 (0.0)	4 (0.1)
Maraviroc, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

ARV detection was strongly associated with female sex, pregnancy, age (>24 years), and study site (KwaZulu-Natal > Soweto > Tanzania and Zimbabwe). ARV detection was also more frequent in widowed compared to married or single adults and in unemployed compared to employed adults (Table 2).

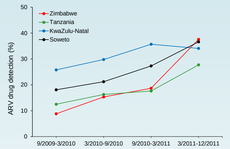
Table 2. Factors associated with ARV drug use.

Variable		N (%)	Adjusted OR (95% CI)	P-value
Sex	Men Non-pregnant women	1867 (25.8) 4996 (69.1)	1.00 (ref.) 1.44 (1.26-1.64)	<0.0001
Pregnancy	Non-pregnant women Pregnant women	4996 (69.1) 362 (5.0)	1.00 (ref.) 2.03 (1.60-2.56)	<0.0001
Age	18-24 years 25-32 years	2213 (30.6) 5012 (69.4)	1.00 (ref.) 1.93 (1.70-2.19)	<0.0001
Marital status	Single Married Separated Widowed	5182 (71.7) 1547 (21.4) 329 (4.6) 167 (2.3)	1.00 (ref.) 1.00 (0.80-1.24) 0.85 (0.60-1.20) 2.03 (1.33-3.08)	0.002
Employment status	Employed Unemployed	3900 (54.0) 3325 (46.0)	1.00 (ref.) 1.14 (1.02-1.28)	0.02
Site	Zimbabwe Tanzania KwaZulu-Natal Soweto	1522 (21.0) 531 (7.3) 3556 (49.2) 1616 (22.4)	1.00 (ref.) 0.99 (0.72-1.33) 2.29 (1.79-2.96) 1.54 (1.19-1.99)	<0.0001
Study arm (Period <6 mo)	Control Intervention	3662 (50.7) 3563 (49.3)	1.00 (ref.) 1.58 (1.06-2.35)	0.01
Survey period (Control)	Period <6 mo Period >6 mo	703 (19.2) 2959 (80.8)	1.00 (ref.) 1.59 (1.16-2.17)	0.004
Survey period (Intervention)	Period <6 mo Period >6 mo	546 (15.3) 3017 (84.7)	1.00 (ref.) 0.91 (0.66-1.24)	0.54

RESULTS

ARV drug use increased 1.8-fold during the 28-month post-intervention survey period; the increase was highest in Zimbabwe (4.3-fold) and lowest in KwaZulu-Natal (1.3-fold, Figure 2).

FIGURE 2. Detection of ARV drugs over time.



There was no association between ARV drug use and HIV incidence at three of the four study sites (Zimbabwe, Tanzania, and Soweto). In KwaZulu-Natal (the site with the highest HIV incidence and highest prevalence of ARV drug use), a 1% increase in ARV drug use was associated with a 0.14% absolute decrease in HIV incidence (P=0.018, Figure 3).

FIGURE 3. Association of HIV incidence and ARV drug use.

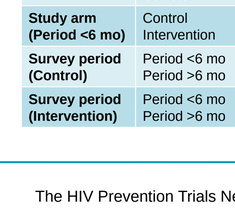


Table 3. ARV drug use in the control and intervention arms of HPTN 043.

Site	# with ARV test results		# with ARV drugs detected (%)		Effect	Analytic weight
	Control	Intervention	Control	Intervention		
Zimbabwe	751	776	133 (17.7)	192 (24.7)	7.08	20.9
Tanzania	250	281	59 (23.6)	55 (19.6)	-5.03	7.2
KwaZulu-Natal	1,777	1,834	572 (32.2)	571 (31.1)	-0.90	49.8
Soweto	932	712	242 (26.0)	175 (24.6)	-0.75	22.0
All	3,710	3,603	1,006 (27.1)	993 (27.6)	0.51	100.0

ARV drugs were detected more frequently in the intervention communities compared to the control communities during the first 6 months of the survey (9/2009-3/2010, P=0.01, Table 2). However, there was no difference between ARV drug use in control vs. intervention communities over the entire period (P=0.77, Table 3).

CONCLUSIONS

The availability of a low-cost, high-throughput multi-drug assay allowed a population-level assessment of ARV use in this large clinical trial.

We identified demographic factors associated with ARV drug use and changes in ARV drug use over time. We also demonstrated an association of reduced HIV incidence with higher prevalence of ARV drug use at one of four study sites.

This objective testing approach may provide more accurate assessments of ARV drug use than other methodologies.

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References: [1] Coates T, et al. Lancet Glob Health, **2014**; 2: e267-77.

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