

Undiagnosed HIV Infection and Couple HIV Discordance Among Household Members of HIV-Infected People Receiving Antiretroviral Therapy in Uganda

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Introduction: Systematic efforts to identify HIV-infected members and HIV-discordant couples in households of individuals taking antiretroviral therapy (ART) could theoretically reduce HIV transmission and improve ART adherence.

Methods: We enrolled HIV-infected clients of an AIDS support organization in a randomized evaluation of different ART monitoring regimens that offered home-based ART care to them and their clinically eligible household members. At baseline, counselors visited participants' homes and offered voluntary counseling and testing (VCT) to all household members. We assessed uptake, HIV prevalence, HIV discordance, and rate of ART eligibility.

Results: Of the 2373 household members, 2348 (99%) accepted VCT. HIV prevalence among household members was 7.5% and varied by age with 9.5% among children aged 0 to 5 years, 2.9% among persons aged 6 to 24 years, and 37.1% among adults aged 25 to 44 years. Of the household members with HIV, 74% had never been previously tested, and 39% of these were clinically eligible for ART. Of the 120 spouses of ART patients that were tested for HIV, 52 (43%) were HIV negative, and of these, 99% had not been previously tested.

Conclusions: Provision of home-based VCT to household members of people initiating ART was well accepted and resulted in the

detection of a large number of previously undiagnosed HIV infections and HIV-discordant relationships.

Key Words: HIV, prevalence, family members, voluntary counseling and testing, antiretroviral therapy, Uganda

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Both HIV/AIDS care and antiretroviral therapy (ART) are rapidly expanding in Africa and other resource-limited settings.¹ Most care and treatment programs are clinic-based and utilize an individual approach to HIV care and treatment. However, the burden of HIV infection in households of people living with HIV may be high.^{2–4} In addition, HIV discordance is common within couples in Africa, ranging from 3% to 20% in the general population^{5–7} and 30% to 51% within couples in which one partner seeks HIV care services.^{2,8} However, knowledge of partner's HIV status is extremely low.⁹ Systematic efforts to identify HIV-infected members and HIV-discordant couples in households of individuals taking ART could theoretically reduce HIV transmission and drug sharing pressures, improve ART adherence, and prolong survival for people with previously unrecognized HIV infection.

In a study in rural Uganda, we offered home-based HIV voluntary counseling and testing (VCT) to household members of people initiating ART. We assessed acceptance of home-based VCT, HIV prevalence, the proportion of household members with unrecognized HIV infection, the proportion of ART-eligible household members, and the proportion of HIV discordant couples.

METHODS

Between May 2003 and December 2004, we enrolled HIV-infected adults aged 18 years and older (index participants) in the Home-Based AIDS Care project, a randomized evaluation of different ART monitoring regimens for persons receiving home-based ART care. Participants were recruited from The AIDS Support Organization, a nongovernmental organization in Tororo and Busia Districts, Uganda. After written informed consent was provided by the participants, a venous blood sample was collected for confirmation of HIV infection and CD4 cell count enumeration, and a physical examination and medical history were conducted for clinical

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Conflict of interest statement: None of the authors had any conflicts of interest. Reprints: Willy A. Were, MBChB, MPH, CDC-Uganda, Uganda Virus Research Institute, P.O. Box 49, Entebbe, Uganda (e-mail: wgw7@ug.cdc.gov).

staging. If found eligible for ART, the index participants provided written informed consent for study staff to visit their homes to request for the consent of their household members for VCT. A household was defined as persons who shared food cooked at a common hearth and slept in the same house or cluster of houses for at least 5 days in a week for the preceding 3 months. Consenting household members provided a finger stick sample of blood on filter paper for HIV testing. Results were returned after 2 weeks to individuals or couples at home or at the study clinic, depending on participants' preference. All participants could request for follow-up counseling and support, including counselor-assisted disclosure if desired.

For participants aged 10 to 17 years, VCT counseling included both the child and parent or legal guardian; consent was required from the parent or guardian, and assent was required from the child. For children aged 0 to 9 years, only the parent or legal guardian provided consent. Neither consent for HIV testing nor receiving test results was required for household members to receive free clinical care that was part of the study. The VCT was voluntary and confidential. We collected standardized information about testing history and, for first-time testers, previous barriers to testing. HIV-infected household members were offered cotrimoxazole prophylaxis (unless medically contraindicated), sexual risk reduction counseling for adults, and access to care at the study clinic; those found to be eligible by CD4 of 250 cells/ μ L or less or symptomatic AIDS were offered standard ART, most often consisting of lamivudine, stavudine, and either nevirapine or efavirenz.

Counselors encouraged couples to receive results together and, where HIV discordance was recognized, offered enhanced couple counseling, focusing on understanding discordance, making personalized couple risk reduction plans, and coping with challenges and social pressures around childbearing.

Plasma was screened for HIV infection using 2 enzyme-linked immunoassays (EIA) in parallel (Recombigen HIV-1/HIV-2; Trinity Biotech, Dublin, Ireland and Murex HIV 120; Abbot Diagnostics, Chicago, IL). Specimens negative on both EIA screening tests were considered negative; specimens positive on both assays were considered positive. Specimens with discordant results were retested by Western Blot (LAV Blot; Biorad, Richmond, CA). HIV testing of dried blood spots consisted of a screening EIA (Virinostika HIV; BioMerieux, Durham, NC) and a confirmation of reactive specimens by Western Blot. HIV-reactive specimens from children younger than 24 months were tested for HIV using the Roche Cobas r1.5 (Roche, Raritan, NJ) assay.

Although all household members were offered the opportunity to have an HIV test, only household members who had not received home-based VCT in a previous study¹⁰ were included in this analysis. Index participants were categorized as married if they were legally married or cohabiting with a partner at the time of enrollment in the study. If they had never married or cohabited or had divorced or were widowed, they were classified as unmarried. Children were categorized in the age groups of 0 to 5, 6 to 10, and 11 to 17 years. Data were double-entered in Epi-Info 2000 (CDC, Atlanta, GA) and analyzed using SAS version 9.1 (SAS

Institute, Cary, NC). Frequency distributions were used to compute the proportion of clients who accepted testing, HIV prevalence, and the proportion eligible for ART.

The study was approved by the Science and Ethics Committee of the Uganda Virus Research Institute, the Uganda National Council of Science and Technology, the Institutional Review Boards of the Centers for Disease Control and Prevention, and the University of California, San Francisco.

RESULTS

We offered VCT to 2373 household members of 730 index clients. The median age of household members was 12 years (interquartile range, 7–17 years), and 52% were female. Overall, 2348 (99%) accepted VCT; 99% of them were tested in their home. HIV prevalence was 7.5% among all household members and varied by age. Among children aged 0 to 5 years, 9.5% were infected; among persons aged 6 to 24 years, 2.9% were infected. Among adults aged 25 to 44 years, 37.1% were infected (Table 1). HIV prevalence among people living in households did not vary by sex of the index participants (Table 2). Among children whose mothers had died or were HIV positive, HIV prevalence was 17.7% for those aged 0 to 5 years, 5.2% for those aged 6 to 10 years, and 1.7% for those aged 11 to 17 years (Table 3). Of the 238 whose mothers were HIV negative, only 1 child was HIV infected. Overall, 95% of the household members had never been previously tested for HIV. Only 1 of the 1575 children aged 14 years and younger had been previously tested. Previous barriers to testing among 657 (85%) of the 773 household members older than 15 years who had never been tested included no perceived risk of infection (52%), distance from testing sites (8%), and fear of knowing one's HIV status (17%). Less than 1% listed lack of access to antiretroviral (ARV) care as a barrier to HIV testing.

Of the 176 (7.5%) household members diagnosed with HIV infection, 130 (74%) had never been previously tested for HIV. None of the 76 children with HIV infection had been previously tested. All household members who tested HIV positive and all 52 HIV-infected household members (30%) who were clinically eligible for ART-initiated treatment received cotrimoxazole prophylaxis. Of the 397 spouses living in the households, 268 (68%) had never been tested for HIV. Of the 120 spouses of patients on ART tested, 52 (43%) were HIV negative (Table 2), and of these, 99% had not been previously tested.

DISCUSSION

Ninety-nine percent of the household members of people with HIV taking ART accepted VCT, and almost all were tested in their homes. The prevalence of previously undiagnosed HIV infection was high, particularly among adults and young children. Over 70% of HIV infections among household members were diagnosed for the first time through home-based provision of HIV counseling and testing. HIV discordance within couples

TABLE 1. Voluntary Counseling and Testing, HIV Prevalence, and ARV Eligibility Among Household Members in Tororo and Busia Districts, Uganda (2004)

Age in Years	VCT Acceptance, % (n/Total Offered Testing)	Overall HIV Prevalence Among VCT Acceptors, % (95% CI)	HIV Prevalence Among First-time Testers, n/Total = % (95% CI)	ARV Eligibility Among First-time Testers, % (n/Total)	Overall ARV Eligibility, % (n/Total)
0–5					
F	98.8 (248/251)	9.7 (6.0–13.4)	24/248 = 9.7 (6.0–13.4)	30.4 (7/23)	30.4 (7/23)
M	99.1 (215/217)	9.3 (5.4–13.2)	20/215 = 9.3 (5.4–13.3)	55.0 (11/20)	55.0 (11/20)
6–10					
F	99.7 (287/288)	3.5 (1.4–5.6)	10/287 = 3.5 (1.4–5.6)	44.4 (4/9)	44.4 (4/9)
M	99.7 (315/316)	4.1 (1.9–6.3)	13/315 = 4.1 (1.9–6.3)	53.9 (7/13)	53.9 (7/13)
11–17					
F	99.7 (356/357)	1.7 (0.4–3.0)	6/356 = 1.7 (0.4–3.0)	66.7 (4/6)	66.7 (4/6)
M	99.5 (378/380)	1.6 (0.3–2.9)	6/378 = 1.6 (0.3–2.9)	33.3 (2/6)	33.3 (2/6)
<17					
F	99.4 (891/896)	4.5 (3.1–5.9)	40/891 = 4.5 (3.1–5.9)	39.5 (15/38)	39.5 (15/38)
M	99.5 (908/913)	4.3 (3.0–5.6)	39/908 = 4.3 (3.0–5.6)	51.3 (20/39)	51.3 (20/39)
Overall children	99.5 (1799/1809)	4.4 (3.4–5.3)	79/1799 = 4.4 (3.4–5.3)	45.5 (35/77)	45.5 (35/77)
18–24					
F	95.7 (67/70)	9.0 (2.1–15.8)	4/60 = 6.7 (0.4–13.0)	25.0 (1/4)	16.7 (1/6)
M	98.9 (93/94)	2.2 (0.0–5.1)	2/87 = 2.3 (0.0–5.4)	50.0 (1/2)	50.0 (1/2)
25–34					
F	93.9 (61/65)	29.5 (18.1–41.0)	7/35 = 20 (6.8–33.3)	28.6 (2/7)	33.3 (6/18)
M	100.0 (40/40)	33.3 (18.5–48.1)	7/26 = 26.9 (9.9–44.0)	42.9 (3/7)	50.0 (6/12)
35–44					
F	95.8 (69/72)	37.7 (26.3–49.1)	14/44 = 31.8 (18.1–45.6)	14.3 (2/14)	26.9 (7/26)
M	92.6 (25/27)	60.0 (40.8–79.2)	7/11 = 63.4 (35.2–92.6)	28.6 (2/7)	33.3 (5/15)
45+					
F	99.2 (130/131)	3.1 (0.1–6.1)	3/118 = 2.5 (0.0–5.4)	66.7 (2/3)	50.0 (2/4)
M	98.5 (64/65)	20.3 (10.5–30.2)	7/52 = 13.5 (4.2–22.7)	57.1 (4/7)	46.2 (6/13)
Overall adults					
F	98.7 (1218/1234)	7.7 (6.2–9.2)	68/1148 = 5.9 (4.6–7.3)	33.3 (22/66)	33.7 (31/92)
M	99.2 (1130/1139)	7.3 (5.8–8.8)	62/1083 = 5.7 (4.3–7.1)	48.4 (30/62)	46.9 (38/81)

CI indicates confidence interval.

was high: 43% of spouses of HIV-infected index participants were HIV negative.

HIV prevalence among adults aged 15 to 44 years within households of HIV-infected patients was more than 3 times that found in a recent national HIV prevalence survey in Uganda,¹¹ highlighting the importance of

targeting family members of HIV-infected people for VCT even in a country with high prevalence of HIV in the general population. Theoretically, VCT can be provided within clinics or at home, although uptake seems to be much higher during home visits. For example, experience in facility-based Prevention of Mother-to-Child Transmission

TABLE 2. HIV Prevalence Among Adults and Children in Households of People With HIV Receiving ART in Tororo and Busia Districts, Uganda (2004)

Household Members	Women Index Participants in Household			Men Index Participants in Household			Overall Total
	Unmarried	Married	Overall Women	Unmarried	Married	Overall Men	
Adults							
Spouses of index participants		61.8 (21/34)			54.7 (47/86)		56.7 (68/120)
Other adults	7.2 (16/221)	2.1 (1/47)	6.3 (17/268)	1.7 (1/59)	11.9 (7/59)	6.7 (8/119)	6.5 (25/386)
Children, y							
≤5	8.6 (17/198)	12.9 (11/85)	9.9 (28/283)	5.7 (2/35)	11.8 (14/119)	10.1 (16/159)	9.9 (44/442)
6–10	3.6 (9/253)	5.5 (6/110)	4.1 (15/363)	0.0 (0/5)	4.6 (7/153)	3.4 (7/204)	3.9 (22/566)
11–17	2.4 (9/382)	0.9 (1/114)	2.0 (10/496)	2.0 (1/49)	0.7 (1/137)	1.1 (2/188)	1.8 (12/682)
<18	4.2 (35/833)	5.8 (18/309)	4.6 (53/1142)	2.2 (3/134)	5.4 (22/407)	4.5 (25/551)	4.6 (78/1685)

TABLE 3. HIV Prevalence Among Children with HIV-Infected, HIV-Negative, or Deceased Mothers in Tororo and Busia Districts, Uganda (2004)

Age Groups of Children, y	HIV Prevalence Among Children of Deceased Mothers, % (n/Total)	HIV Prevalence Among Children of HIV-Infected Mothers, % (n/Total)	HIV Prevalence Among Children of HIV-Negative Mothers, % (n/Total)
≤5	5.9 (1/17)	19.6 (21/107)	1.0 (1/100)
6–10	7.7 (3/39)	4.7 (9/191)	0.0 (0/66)
11–17	6.3 (3/48)	2.1 (2/244)	0.0 (0/72)
<18	6.7 (7/104)	6.5 (35/542)	0.4 (1/238)

programs has shown that only between 3% and 15% of the partners received testing.¹² Two general population studies in Uganda showed 2- to 4-fold increases in receipt of HIV test results when provided to participants in their homes rather than through a nearby clinic.^{13–16} The high rate of acceptance of VCT among family members of people with HIV in the present study does not seem to be caused by the availability of ART. Uptake of VCT was more than 97% in a previous study of more than 3000 household members of people with HIV in which no ART was offered to participants in the same area.¹³

In Uganda, like elsewhere in sub-Saharan Africa, most HIV care programs include mainly adult clients. Yet, approximately 2.5 million children in Africa have HIV,¹⁷ and without effective care, almost half will die before their third birthday.¹⁸ In this study, because of a household approach to HIV testing, we identified many children with HIV infection—half of whom needed and were provided ART at the time of testing. Only 1 of the 238 children whose mothers were HIV negative had HIV, but 6% of the children with HIV-infected or deceased mothers were infected with HIV. Prevalence was very high, nearly 18%, among those aged younger than 5 years but was also high for older children of HIV-infected and deceased mothers. It would likely be most cost-effective to limit child VCT to all children whose mothers died or who are HIV infected.

The implementation of home-based VCT is operationally feasible in rural Uganda. At the time of enrollment in this study, we conducted laboratory testing in the study laboratory and made a return visit to homes for results counseling. However, at The AIDS Support Organization centers and several community-based programs, trained lay providers are now conducting rapid finger stick testing in client homes, and this is supported by the new Ugandan Ministry of Health counseling and testing guidelines.¹⁹ Over 200,000 individuals in various communities of Uganda have received VCT in their homes. Dried blood spots are routinely collected for quality control using a parallel EIA testing algorithm (Virinostika Uniform II plus 0 and Murex HIV 120). Cost-utility analyses will be important to help compare the potential benefits of a home-based approach, including coverage, disclosure, and couples counseling with more traditional facility-based and referral approaches.

It would be useful to evaluate this type of intervention in urban settings where acceptance may be different. Concern

has been raised about possible negative social consequences that may occur with partner VCT,^{20,21} but in follow-up studies of the population in this study, we found substantial increases in positive social events such as strengthened relationships and community support and no increase in negative events during the 3 months after home-based VCT as compared with 3 months before enrollment.²² Our high acceptance rates were in the context of provision of ART and may not be applicable to other settings. However, similarly, acceptance rates have been demonstrated in this same population and several other home-based VCT programs in Uganda even before the availability of ART.^{10,13}

Provision of VCT for family members of people in HIV care and treatment programs is an important intervention for both case finding and for prevention of HIV transmission. Providing couples with HIV testing and counseling decreases high-risk sexual behavior and HIV transmission,^{23,24} particularly among HIV-discordant couples.^{25–27} Many persons with HIV believe that their partners are already infected and therefore do not avoid high-risk practices; however, in our study, 43% of the spouses of HIV-infected married participants were HIV negative. Reduction of HIV transmission within HIV-discordant couples should also help control the spread of ARV-resistant virus from persons taking ARVs. Integration of family VCT as a routine part of HIV care and treatment programs will be necessary for public health efforts to control the HIV epidemic and support people with HIV to live longer and healthier lives.

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