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Predictors of Attrition among High Risk HIV-Infected Participants Enrolled in a Multi-Site Prevention Trial

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Abstract

Objective—Recruiting and retaining high-risk individuals is critical for HIV prevention trials.

Design—The current analyses addressed predictors of trial dropout among high-risk HIV-infected men and women.

Results—Trial dropouts (n=74) were more likely to be younger, depressed, and not taking antiretroviral therapy than those who continued (n=815). No other background, substance use, or transmission risk differences were found, suggesting no dropout bias on key risk outcomes.

Conclusions—Efforts are warranted for early detection and treatment of depression and for improving retention of younger participants.

Keywords

Clinical Trials; Prevention; Retention; Depression

Background

Recruiting and retaining high risk participants is critical for the implementation of behavioral trials in HIV primary and secondary prevention (1-4). Attrition or dropout of participants threatens internal and external validity and, if attrition is associated with levels of risk, can impact study outcomes (5).

Purpose

The current analyses explore predictors of attrition in the Healthy Living Project randomized controlled trial of HIV-infected persons at risk for sexual transmission of HIV in four US cities that resulted in an overall decrease in HIV transmission risk (6). In this report, we explore whether differences exist between those who failed to return past randomization compared

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with those who remained in this successful trial on multiple factors measured at baseline, including demographics, clinical status, depression, substance use, and level of transmission risk.

Methods

Details of trial procedures are provided elsewhere (6-8). 3808 individuals were screened with 936 meeting inclusion criteria enrolled in the trial: risk for transmitting HIV to uninfected persons through unprotected sexual activity. In-person assessments were conducted at baseline and every five months for 25 months (total of 6 assessment points). Approximately half 467 (49.9%) were randomized to the immediate intervention of 15 individual 90 minute sessions and the other 469 (50.1%) were assigned to wait-list control/ lagged intervention. Standardized retention procedures were implemented across sites, including monthly phone calls, mailings, and in-person tracking through contacts identified at baseline.

Assessments included psychosocial (e.g., self-reported depressive symptoms on the Beck Depression Inventory), treatment (e.g., CD4, viral load, receipt of antiretroviral therapy), demographic (race, ethnicity, age, homelessness), and behavioral variables including substance use, number and serostatus of sexual partners, and transmission risk acts (unprotected vaginal or anal intercourse with HIV negative or unknown status partners).

Data analysis

A dropout was defined as a participant who did not return past the baseline assessment at which he/she was randomized. Participants who died (n=47) were not included in analysis. Of the remaining 889 participants, 74 (8.3%) did not return past the first assessment and are defined as dropouts. Bivariate logistic regressions of dropout (0 = no; 1 = yes) on explanatory variables were conducted; explanatory variables with $p < .25$ were retained for backward elimination multivariate logistic regression analysis (9). In multivariate analysis, explanatory variables with $p < .05$ were retained. The Hosmer-Lemeshow goodness-of-fit test was used to evaluate the overall fit of the final model.

Results

Baseline characteristics are provided in Table 1. Multivariate analyses revealed that dropouts were more likely to be younger, depressed, and less likely to be taking antiretroviral therapy (Table 2). There were no differences based on gender, race/ethnicity, clinical status, antiretroviral adherence, housing status, substance use, or level of HIV transmission risk behavior. The Hosmer-Lemeshow goodness-of-fit test showed excellent fit for this model (χ^2 (5) = 1.58, p = 0.90).

Discussion

The strongest predictor of dropout was a baseline level of self-reported depressive symptoms consistent with severe depression (10). Given the higher likelihood of mortality and treatment non-adherence associated with depression (11,12) and the higher rates of dropout found in this and other health-related programs (13), early screening for depression in clinical trials is warranted and can provide opportunity for immediate treatment referral and follow-up. While good clinical research practices include maximizing retention in clinical trials, and exclusion of individuals with depression may help meet retention goals, in the absence of safety concerns, fairness considerations would suggest inclusion of such individuals because of the potential for benefit to the individuals in studies like this one. Moreover, inclusion of individuals with depression, to the extent to which they are present in the population of persons living with HIV/AIDS, increases generalizability findings. Thus, the benefit in terms of knowledge,

protection and fair treatment of human participants would outweigh the potential advantages to research design.

That younger age was predictive of dropout is not surprising given the documented challenges of recruiting and retaining younger participants in research studies (13-21). The link between ART receipt and better retention suggests that individuals receiving stable ongoing medical care may have less chaotic personal circumstances. It is also possible that routine medical appointments associated with ART delivery may facilitate adherence to ancillary services.

Dropout was unrelated to level of transmission risk at baseline and to randomization status. This finding provides evidence against the possible effects of selective dropout bias on primary risk study outcomes. If those who dropped out were at higher risk for transmitting HIV and this were related to randomization status (e.g., feeling discouraged by the demands of the intervention), there would be concerns regarding the trial outcomes. Instead, the current analyses provide evidence of the feasibility of retaining high-risk participants in behavioral intervention trials of public health significance.

Limitations of note in the current analyses include the use of a convenience, non-probability-based sample and the use of self-reported data for several key variables, including depression and substance use.

In summary, self-reported depressive symptoms, younger age, and non-receipt of antiretroviral therapy were predictive of attrition in a trial of high-risk HIV-infected men and women. Drug use and HIV transmission risk were unrelated to dropout, supporting the focus on high-risk individuals for risk-reduction interventions.

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Table 1

Baseline Characteristics

	Whole Sample (*n*=889) ***n* (%)**	**Lost After 1st Interview (*n*=74)** ***n* (%)**
Race		
White	292 (32.9)	21 (28.4)
Latino	123 (13.9)	18 (24.3)
Black/AA	401 (45.2)	29 (39.2)
Other	71 (8.0)	6 (8.1)
Age *mean (SD)*	40.3 (7.4)	37.8 (7.7)
Female Gender	185 (20.8)	14 (18.9)
HS Graduate or more	717 (80.7)	57 (77.0)
Employed	331 (37.3)	32 (43.2)
Years Since HIV+ Diagnosis		
0−7 years	372 (41.8)	36 (48.7)
7−13 years	359 (40.4)	29 (39.2)
13+ years	158 (17.8)	9 (12.2)
Biomarker CD4 *mean (SD)*	433.1 (274.3)	458.6 (350.8)
Detectable viral load	549 (63.8)	52 (74.3)
Lagged Randomization status	451 (50.7)	29 (39.2)
Recent homelessness	202 (22.8)	26 (35.1)
Lifetime homelessness	419 (47.2)	35 (47.3)
Antiretroviral Therapy (ARV) Use	620 (69.8)	41 (55.4)
100% adherent to ARV medication	248 (27.9)	17 (23.0)
BDI score range		
Minimal	509 (57.3)	33 (44.6)
Mild	161 (18.1)	14 (18.9)
Moderate	143 (16.1)	11 (14.9)
Severe	75 (8.5)	16 (21.6)
Site χ^2 *(DF)*		
Los Angeles	316 (35.6)	21 (28.4)
Milwaukee	82 (9.2)	12 (16.2)
New York	228 (25.7)	17 (23.0)
San Francisco	263 (29.6)	24 (32.4)
Transmission Risk Acts		
0	234 (26.4)	16 (21.6)
1−5	381 (43.1)	33 (44.6)
6−10	127 (14.4)	13 (17.6)
11−20	69 (7.8)	6 (8.1)
21+	74 (8.4)	6 (8.1)
2+ HIV−/Unknown Partners	497 (55.9)	45 (60.8)
Any IDU (past year)	125 (14.1)	12 (16.2)
Alcohol Frequency		
None	288 (32.5)	21 (28.8)
< 4−6 times/week	537 (60.7)	46 (63.0)
>= 4−6 times/week	60 (6.9)	6 (8.2)
Marijuana Frequency		
None	456 (51.4)	30 (40.5)
< 4−6 times/week	295 (33.2)	32 (43.2)
>= 4−6 times/week	137 (15.4)	12 (16.2)
Drugs Frequency		
None	323 (36.5)	26 (35.1)
< 4−6 times/week	396 (44.8)	32 (43.2)

	Whole Sample (*n*=889) *n* (%)	**Lost After 1st Interview (*n*=74) *n* (%)**
>= 4−6 times/week	165 (19.0)	16 (21.6)
Lifetime Drug Seriousness		
Low — Marijuana/alcohol only	98 (11.2)	9 (12.5)
Med — Other drugs, no IDU	40 (4.6)	4 (5.6)
High — Hard drugs or IDU	739 (84.3)	59 (81.9)

Note: † Drug frequency includes the use of any of the following: cocaine, crack, speedball, MDMA, opiates, methamphetamine, heroin, methadone, inhalants, stimulants, ketamine, GHB, hallucinogens, sedatives, barbiturates, and steroids.

Table 2

Predictors of drop-out

	N	Bivariate Odds Ratio (95% CI)	Multivariate Odds Ratio (95% CI) *n* = 887
Race χ^2 *(DF)*	887	6.5 (3) *	—
White		—	—
Latino		2.2 (1.1, 4.3) **	—
Black/AA		1.0 (0.6, 1.8)	—
Other		1.2 (0.5, 3.1)	—
Median Age or older	889	0.5 (0.3, 0.9) **	0.6 (0.4, 0.98) **
Female Gender	889	0.9 (0.5, 1.6)	—
HS Graduate or more	889	0.8 (0.4, 1.4)	—
Employed	887	1.3 (0.8, 2.1)	—
Years Since HIV+ Diagnosis χ^2 *(DF)*	889	2.5 (2)	—
0−7 years		—	—
7−13 years		0.8 (0.5, 1.4)	—
13+ years		0.6 (0.3, 1.2) *	—
CD4	808	1.0 (1.0, 1.0)	—
Detectable viral load	860	1.7 (1.0, 3.0) *	—
Lagged randomization status	889	0.6 (0.4, 1.0) **	—
Recent homelessness	888	2.0 (1.2, 3.3) ***	—
Lifetime homelessness	888	1.0 (0.6, 1.6)	—
Antiretroviral Therapy (ARV) Use	888	0.5 (0.3, 0.8) ***	0.6 (0.3, 0.9) **
100% adherent to ARV medication	620	1.1 (0.6, 2.0)	—
BDI score range χ^2 *(DF)*	888	14.6 (3) ***	12.6 (3) ***
Minimal		—	—
Mild		1.4 (0.7, 2.6)	1.3 (0.7, 2.5)
Moderate		1.2 (0.6, 2.4)	1.2 (0.6, 2.5)
Severe		3.9 (2.0, 7.5) ****	3.6 (1.8, 7.0) ****
Site χ^2 *(DF)*	889	5.2 (3) *	—
Los Angeles		—	—
Milwaukee		2.4 (1.1, 5.1) **	—
New York		1.1 (0.6, 2.2)	—
San Francisco		1.4 (0.8, 2.6)	—
Transmission Risk Acts χ^2 *(DF)*	885	1.4 (4)	—
0		—	—
1−5		1.3 (0.7, 2.4)	—
6−10		1.6 (0.7, 3.3)	—
11−20		1.3 (0.5, 3.5)	—
21+		1.2 (0.5, 3.2)	—
2+ HIV−/Unknown Partners	889	1.2 (0.8, 2.0)	—
Any IDU (past year)	887	1.2 (0.6, 2.3)	—
Alcohol Frequency χ^2 *(DF)*	885	0.7 (2)	—
None		—	—
< 4−6 times/week		1.2 (0.7, 2.0)	—
>= 4−6 times/week		1.4 (0.5, 3.7)	—
Marijuana Frequency χ^2 *(DF)*	888	4.3 (2) *	—
None		—	—
< 4−6 times/week		1.7 (1.0, 2.9) **	—
>= 4−6 times/week		1.4 (0.7, 2.7)	—
Drugs Frequency χ^2 *(DF)*	884	0.5 (2)	—
None		—	—

	N	**Bivariate Odds Ratio (95% CI)**	**Multivariate Odds Ratio (95% CI) *n* = 887**
< 4−6 times/week		1.0 (0.6, 1.7)	—
>= 4−6 times/week		1.2 (0.6, 2.4)	—
Lifetime Drug Seriousness χ^2 *(DF)*	877	0.3 (2)	—
Low — Marijuana/alcohol only		—	—
Med — Other drugs, no IDU		1.1 (0.3, 3.8)	—
High — Hard drugs or IDU		0.9 (0.4, 1.8)	—

Note

For multi-category explanatory variables, multi-parameter Wald chi-square tests, degrees of freedom, and p-values are reported; the first category listed is the reference group.

* $p < 0.25$

** $p < 0.05$

*** $p < 0.01$

**** $p< 0.001$.