Letter to the Editor: Treatment as Prevention: Are HIV Clinic Patients Interested in Starting Antiretroviral Therapy to Decrease HIV Transmission?

Julia C. Dombrowski, M.D., M.P.H., Robert D. Harrington, M.D., Mark Fleming, B.A., and Matthew R. Golden, M.D., M.P.H., 2

Dear Editor:

HIV prevention research is increasingly focused on a strategy of case finding and early initiation of antiretroviral therapy (ART) to prevent HIV transmission, known as the "Test and Treat" or "Enhanced Test, Link to Care Plus Treat (TLC+)" strategy. The TLC+ strategy is predicated on the idea that diagnosing persons with HIV earlier in the course of infection will lead to substantial changes in sexual risk behavior and to earlier initiation of ART, both of which will result in diminished HIV transmission. Recently adopted HIV treatment guidelines expand the indications for ART to include all persons with CD4 counts of 500 or less, and leave open the option of treating those with higher CD4 counts.² The new guidelines also suggest that some persons might elect to start ART, at least in part, to diminish the risk of transmitting HIV. Little is known, however, about the acceptability of offering patients ART to prevent HIV transmission or whether persons living with HIV/AIDS (PLWHA) would be willing to consider starting ART early, in part, to decrease the likelihood that they will pass the virus to others.

We surveyed PLWHA who were not taking ART in order to evaluate the acceptability of including prevention considerations in decision-making about ART initiation and to gauge the population's interest in starting ART for prevention. We recruited patients from the Harborview Medical Center HIV clinic in Seattle, Washington (the largest HIV clinic in the Pacific Northwest of the United States) in three phases for a written, anonymous, self-administered survey. Phases 1 and 3 were conducted in May 2008 and 2009, respectively, as part of an annual risk surveillance program described previously.^{3,4} Potential participants were chosen using a random number table to select 50% of patients with a scheduled appointment during the survey period. Between the annual surveys (phase 2; October 2008 to January 2009), we recruited an additional population of persons who were not taking ART and did not meet CD4 count criteria for ART initiation based on US treatment guidelines in place at that time (CD4 count \leq 350). We conducted phase 2 specifically for this analysis with the aim of increasing the number of survey participants who would be potentially eligible to initiate ART

to prevent HIV transmission. A study nurse determined participant eligibility for phase 2 by reviewing medical records. The University of Washington Institutional Review Board approved all study procedures.

The survey included questions about HIV transmission risk behaviors and interest in starting ART to decrease HIV transmission risk. In each of the three phases, participants were asked to respond to the following: "Right now, doctors usually start people on HIV medications when their CD4 count drops below 350 cells/mm³. However, no one knows when the best time is to start medication. Some studies suggest that people who are taking HIV medicines are less likely to give HIV to their sex partners. This is not known for sure. Would you want to take HIV medicines in order to make it less likely that you would pass the virus to your sex partner(s)?" Following that, we asked, "Do you think that doctors should offer patients HIV medications to decrease the chance that they will infect other people?" Prior to the questions above (≤ 1 page earlier), we asked, "Do you think that people who take medications for HIV are less likely to give the infection to their sex partners if they have unprotected sex?" For the analysis, we dichotomized responses ("yes" versus "no," "don't know," or "maybe"). In phase 3 only, we asked if respondents had participated in the past year. We did not ask questions to assess patients' understanding of the details of ART use. We used Pearson χ^2 tests to compare results between phases and log-binomial regression⁵ to assess associations between interest in starting ART and the variables listed in Table 1. We used Stata 10.1 (StataCorp, College Station, TX) for all analyses.

In phases 1 and 3, we randomly selected 711 patients with scheduled clinic appointments as potential participants (393 in phase 1; 318 in phase 3). Of these, 199 (28%) did not attend their appointments, 52 (7%) did not speak English, 7 (1%) were too ill to participate, and 9 (1%) had completed the survey in the same year. After excluding those persons, the recruiter offered the survey to the remaining 442 persons (62% of those randomly selected) and missed 2 persons (<1%). Of those offered the survey, 408 (92%) completed it. A total of 102 (25%) participants were not taking ART; 94 (92%) of whom answered the question about interest in ART to decrease HIV

²Public Health-Seattle & King County, Seattle, Washington.

¹Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington.

748 LETTER TO THE EDITOR

Table 1. Factors Associated with Interest in Starting Antiretroviral Therapy to Decrease HIV Transmission Risk Among 136 HIV Clinic Patients not Taking Antiretroviral Therapy

Variable	Overall population n = 136		Interested in ART to decrease HIV transmission n=76 (56%)		Not interested in ART to decrease HIV transmission n = 60 (44%)		Unadjusted
Variable	N	% of total ^a	N	% of each group ^b	N	% of each group ^b	relative risk (95% CI)
Survey phase							
Phase 1	48	35	25	52	23	48	Reference
Phase 2	42	31	24	57	18	43	1.1 (0.8–1.7)
Phase 3	46	34	27	59	19	41	1.1 (0.8–1.7)
Gender ^c							
Male	101	74	56	56 50	45	45	Reference
Female	33	24	19	58	14	42	1.0 (0.7–1.5)
Missing	1	1	0	0	1	100	
Age	101	74	(1	(2	27	27	D = f =
< 50 years	101	74 22	64	63 25	37	37	Reference
≥50 years	31	23 3	11 1	35 25	20	65 75	0.6 (0.3–0.9)
Missing Race ^d	4	3	1	23	3	75	
White	75	55	11	55	34	45	Reference
White African American	75 41	55 30	41 24	55 59	34 17	45 41	1.1 (0.8–1.5)
	5			40		60	1.1 (0.6–1.3)
Missing	12	4 9	2 5	40 42	3 7	58	07(0414)
Hispanic ethnicity ^e Education	12	9	3	42	/	36	0.7 (0.4–1.4)
High school or less	65	48	39	60	26	40	Reference
	66	49	34	52	33	48	0.9 (0.6–1.2)
Beyond high school Missing	5	4	3	60	2	40	0.9 (0.0–1.2)
Income	3	7	3	00	2	10	
Less than \$15,000	89	65	51	57	38	43	Reference
\$15–30,000	25	18	14	56	11	44	1.0 (0.7–1.4)
More than \$30,000	20	15	10	50	10	50	0.9 (0.5–1.4)
Missing	2	1	1	50	1	50	0.5 (0.5 1.1)
Time since diagnosis of HIV	_	1		00		00	
<1 year	15	11	11	73	4	27	Reference
1–5 years	35	26	19	54	16	46	0.7 (0.5–1.1)
5–10 years	28	21	18	64	10	36	0.9 (0.6–1.3)
>10 years	48	35	26	54	22	46	0.7 (0.5–1.1)
Missing	10	7	2	20	8	80	,
Sexual identity ^d							
Gay or bisexual man	72	53	41	57	31	43	Reference
Heterosexual man	24	18	14	58	10	42	1.0 (0.7–1.5)
Heterosexual woman	27	20	16	59	11	41	1.0 (0.7–1.5)
Missing	3	2	1	33	2	67	
Number of anal or vaginal							
sex partners in the past year							
0	43	32	24	56	19	44	Reference
1	31	23	18	58	13	42	1.0 (0.7–1.6)
2 to 5	25	18	16	64	9	36	1.1 (0.8–1.7)
6 to 10	11	8	6	55	5	45	1.0 (0.5–1.8)
>10	16	12	7	44	9	56	0.8 (0.4–1.5)
Missing	10	7	5	50	5	50	
Reported nonconcordant							
unprotected anal or							
vaginal intercourse							
in the past year	07	<i>C</i> 1	40	EE	20	45	Dofamen
No Vos	87 47	64 25	48	55 55	39	45 45	Reference
Yes	47	35	26	55 100	21	45	1.0 (0.7–1.4)
Missing	2	1	2	100	0	0	
Nonconcordant primary							
partner No	91	67	50	55	41	45	Reference
Yes	44	32	25	57	19	43	1.0 (0.8–1.4)
Missing	1	1	1	100	0	0	1.0 (0.0-1.4)

(continued)

LETTER TO THE EDITOR 749

Table 1. (Continued)

Variable	Overall population n = 136		Interested in ART to decrease HIV transmission n=76 (56%)		Not interested in ART to decrease HIV transmission $n=60\ (44\%)$		Unadjusted
	N	% of total ^a	N	% of each group ^b	N	% of each group ^b	relative risk (95% CI)
Always disclose HIV status to anal/vaginal sex partners							
No	53	39	31	58	22	42	Reference
Yes	69	51	38	55	31	45	0.9(0.7-1.3)
Missing	14	10	7	50	7	50	, ,
Believed that ART decreases HIV transmission ^f							
No/don't know	110	81	64	58	46	42	Reference
Yes	25	18	12	48	13	52	$0.8 \ (0.5-1.3)$
Missing	1	1	0	0	1	100	
Believed providers should offer ART to prevent transmission							
No/don't know	50	37	16	32	34	68	Reference
Yes	79	58	56	71	23	29	2.2 (1.4–3.4)
Missing	7	5	4	57	3	43	,
Diagnosed with gonorrhea, chlamydial infection, or syphilis in the past year ^g	33	24	21	64	12	36	1.2 (0.9–1.6)
Methamphetamine use							
No	70	51	42	60	28	40	Reference
Yes	34	25	18	53	16	47	0.9 (0.6–1.3)
Missing	32	24	16	50	16	50	
Current or past injection							
drug use							
No	85	63	48	56	37	43	Reference
Yes	48	35	26	54	22	46	1.0 (0.7–1.3)
Missing	3	2	2	67	1	33	

^aPercentages sum to 100% across rows.

transmission. Of the 50 participants in phase 2, 42 (84%) answered the ART interest question. Thus, the final study population comprised 48 persons from phase 1, 42 from phase 2, and 46 from phase 3 ($N\!=\!136$). Respondent demographics, risk behaviors, interest in starting ART, and belief that ART reduces HIV transmission did not differ significantly between the phases (data not shown). Six participants in phase 3 (13%) indicated that they had participated in the previous year (because responses were anonymous, we were unable to link data from individuals across phases).

Of 136 respondents, 76 (56%) expressed definite interest in starting ART specifically to decrease the risk of transmitting HIV to their sexual partners. The majority believed that doctors should offer patients ART for this purpose (61%; 79 of 129 persons who answered the question). Table 1 presents the population's sociodemographic characteristics, sexual behavior, and drug use, dividing participants based on interest in ART to prevent transmission. Forty-seven (35%) respon-

dents reported having unprotected anal or vaginal intercourse (UAVI) with a partner of negative or unknown HIV status (nonconcordant UAVI) in the preceding year. Of those 47 persons, 26 (55%) were interested in starting ART to decrease transmission risk. Respondents who believed that ART decreases HIV transmission were more likely to report nonconcordant UAVI (relative risk [RR] 2.1 [95% confidence interval {CI}: 1.4–3.2)]. Age 50 years or older was associated with a lower likelihood of interest in starting ART to decrease HIV transmission (RR 0.6 [95% CI: 0.3–0.9]), and remained associated after adjustment for number of sex partners and time since HIV diagnosis (RR 0.5 [95% CI: 0.3–0.9]). Of the six respondents in phase 3 who reported completing the survey in the previous year, 3 (50%) were interested in starting ART and 3 (50%) were not.

We found that many HIV clinic patients are interested in starting ART to decrease the risk of transmitting HIV and that most patients believe that their medical providers should offer

^bPercentages sum to 100% across columns (within variable groups).

^cData from one transgendered patient were excluded from the gender analysis.

^dData from participants of other races and sexual identities were omitted from this table due to small sample sizes.

^eHispanic ethnicity data were missing from 8 (6%) surveys.

^fThis question was asked prior to the question about interest in ART to prevent transmission.

^gWe could not distinguish missing data from "no" due to the way this question was asked in the survey.

ART, antiretroviral therapy.

750 LETTER TO THE EDITOR

patients ART for this purpose. It does not appear that knowledge about the effect of ART on HIV transmission was widespread in the population at the time of our survey. The higher likelihood of nonconcordant UAVI among persons who believed that ART decreases HIV transmission is consistent with previous studies and highlights the importance of coupling sexual risk reduction counseling with education on the effect of ART on transmission. The generalizability of our results may be limited by the inclusion of patients from a single clinic that primarily serves socially disadvantaged patients, who may not be representative of all people living with HIV in King County or elsewhere. This study was a first step in assessing patient interest in taking ART to prevent transmission, and we did not assess participants' understanding of or levels of commitment to taking ART, nor can we be certain how important a role possible prevention benefits might play in patients' decision to initiate and continue treatment. Finally, we could not deduplicate data from 6 persons who reported completing the survey twice. However, that group was small and evenly distributed between "interested" and "not interested" in ART, suggesting that our inability to exclude duplicate responses did not affect our main finding.

Increasing evidence supports both the clinical and public health benefits of initiating ART early in the course of HIV infection. $\overline{\mbox{\it T-9}}$ The decision to initiate ART is complex and must include a consideration of the patient's stage of infection, commitment and ability to adhere to treatment, toxicities of ART, and potential consequences of imperfect adherence. In this context, the idea of starting ART for the primary purpose of preventing transmission is controversial. Nonetheless, the development of better tolerated, more convenient ART regimens and evidence of clinical benefits associated with ART initiation at higher CD4 counts favor more widespread use of ART. Our results suggest that most patients with HIV infection believe that their providers should offer patients ART as a means to decrease the risk of transmitting HIV and that many are interested in starting ART for the purpose of prevention. This study adds to the existing clinical and prevention rationale for clinicians to discuss the timing of ART initiation with patients at all stages of HIV infection, and suggests that a public health effort designed to ensure that patients have an opportunity to consider early initiation of ART, including the potential prevention benefits of treatment, would be acceptable to many PLWHA.

Acknowledgments

The authors thank Carol Glenn for participant recruitment and Timothy Menza for review of the survey instrument.

Supported by Public Health–Seattle & King County. J.C.D was supported by a National Institutes of Health (NIH)-funded training grant to the University of Washington (T32 A107140).

References

- Dieffenbach CW, Fauci AS. Universal voluntary testing and treatment for prevention of HIV transmission. JAMA 2009; 301:2380–2382.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1infected adults and adolescents. Department of Health and Human Services. December 1, 2009:1–161.
- Golden MR, Stekler J, Kent JB, Hughes JP, Wood RW. An evaluation of HIV partner counseling and referral services using new disposition codes. Sex Transm Dis 2009;36:95–101.
- Golden MR, Wood RW, Buskin SE, Fleming M, Harrington RD. Ongoing risk behavior among persons with HIV in medical care. AIDS Behav 2007;11:726–735.
- McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. Am J Epidemiol 2003;157:940–943.
- Crepaz N, Hart TA, Marks G. Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review. JAMA 2004;292:224–236.
- Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: A prospective cohort analysis. Lancet 2010;375:2092–2098.
- Kitahata MM, Gange SJ, Abraham AG, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med 2009;360:1815–1826.
- Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: A collaborative analysis of 18 HIV cohort studies. Lancet 2009;373:1352–1363.

Address correspondence to: Julia Dombrowski, M.D., M.P.H. 325 Ninth Ave Box 359777 Seattle, WA 98104

E-mail: jdombrow@uw.edu