Estimates of Prevalence of Cognitive Impairment From Research Studies Can Be Affected by Selection Bias

To the Editors:

We read with interest the commentary on cognitive impairment in a clinical setting presented by Ferretti et al[1] in the January issue of the journal. We agree with the observation by the authors that biased estimates of prevalence of HIV-associated cognitive impairment can occur with research samples. A source of bias in research samples arises from the requirement that the patients must consent to be studied. Unless careful documentation of the source population is performed, selection bias cannot be ruled out. In addition, documentation of reasons for nonconsent is essential to understand who is excluded from the study and how this exclusion may bias the estimates of prevalence. Such documentation has not systematically been done in neuro HIV research.

We had the opportunity to study the potential impact of selection bias on estimates of prevalence of HIV-associated cognitive impairment in our Positive Brain Health Now Cohort that recruited participants from 5 Canadian sites from 2013 to 2017. The protocol for this study has been published.[2] Ethical permission was obtained to carefully document rates of refusal and query people on reasons for refusing cohort entry at one of the study sites. Briefly, all eligible participants at the McGill University Health Centre were systematically invited to participate in the cohort. Selection criteria were: age ≥35, HIV+ ≥1 year, and absence of dementia or neurological disorder likely to affect cognition. All persons approached for recruitment were asked to complete a brief questionnaire designed to estimate the potential for selection bias; the questions were about age, sex, working status, reason for refusal, and on the frequency of experiencing 2 specific cognitive difficulties.

TABLE 1. Characteristics of Those Agreeing and Refusing Study Entry

	Agreeing (n = 148)	Refusing (n = 261) With Data (n = 182)	χ^2 Test (*P*)
Age (yr)			9.6 (0.022)
<45	22 (14.9%)	55 (30.2%)	
45–54	58 (39.2%)	67 (36.8%)	
55—59	26 (17.6%)	22 (12.1%)	
≥60	30 (20.3%)	38 (20.9%)	
Sex			11.3 (<0.001)
Men	125 (84.5%)	124 (68.5%)	
Women	23 (15.5%)	57 (31.5%)	
Working			9.4 (0.002)
Yes	66 (44.6%)	112 (61.5%)	
No	82 (55.4%)	70 (38.5%)	
Difficulty remembering names of people			33.6 (<0.00001)
Never	22 (14.9%)	80 (44.7%)	
Rarely to almost always	126 (85.1%)	99 (55.3%)	
Forget to turn off stove or on alarm clock			10.5 (0.001)
Never	73 (49.3%)	120 (67.4%)	
Rarely to almost always	74 (50.7%)	58 (32.6%)	

A total of 410 eligible patients were approached for participation: 261 refused (64%), with 182 of those (70%) completing the refuser's questionnaire. The most common reason for not participating was lack of time (34% of those declaring a reason); other reasons were unrelated to cognitive status. Table 1 presents selected characteristics of those agreeing and refusing study entry. Refusers were more likely than acceptors to be working, younger, and women. Refusers were also less likely to report cognitive difficulties. Assuming that cognitive impairment was present in 50% in those enrolled and in 0% of the refusers, the adjusted prevalence of cognitive impairment would be 22% in the full sample. A rate of cognitive impairment as high as 20% in refusers would yield an adjusted prevalence in the full sample of 35%.

In summary, there was a high rate of refusal to enter our study. Although this resulted in a sample of persons more relevant to our study aims on understanding brain health in people with HIV, generalizing the results to the wider HIV community is a concern. Although refusers had a different profile from participants, they differed in a predictable manner that will permit estimates of cognitive impairment derived from the participants to apply to refusers. The prevalence inflation factor would range from 1.4 to 2.3, depending on the assumed prevalence of cognitive impairment in the refusers. The results of this analysis reinforce the need to systematically document key variables for those refusing entry into studies to have accurate estimates of prevalence.

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Willingness to Pay for HIV Self-Tests Among Women in Kenya: Implications for Subsidy and Pricing Policies

To the Editors:

INTRODUCTION

With roughly 30% of all people living with HIV globally remaining undiagnosed, innovative HIV testing approaches are essential for meeting the first of the UNAIDS "90-90-90" targets and achieving the benefits of treatment as prevention.[1] HIV self-testing (HIVST) is increasingly being recognized as an HIV testing approach that may appeal to hard-to-reach or high-risk individuals who would benefit from frequent HIV testing.[2] Based on research showing high acceptability and interest in HIVST across a wide range of populations and settings,[3–8] the WHO issued guidelines in December 2016 to support implementation and scale-up evidence-based HIVST approaches.[9] Several countries in sub-Saharan Africa (SSA), including Kenya, have included HIVST in their testing guidelines and are currently developing plans to implement HIVST.[9,10] Governments and donors are now exploring HIVST distribution strategies—including retail distribution—that are best suited to enhance HIV testing access among those who are not reached by existing HIV testing services (HTS).

Although self-test kits may become available in private sector pharmacies and other retail outlets, the extent to which they must be subsidized remains unknown. High prices in the retail sector may impede access in target populations, but very low prices or free distribution would require larger public subsidies and potentially misallocate resources by targeting those who already seek existing HTS. There have been few studies that have assessed individuals' willingness to pay (WTP) for self-tests in SSA. Recent agreements between foundations and self-test manufacturers to achieve prices below current levels underscore the need for WTP data. To inform pricing policies for self-tests, we assessed WTP for self-tests among Kenyan women participating in a randomized trial.

METHODS

Data were collected as part of a randomized trial to evaluate whether secondary distribution of self-tests can promote partner and couples testing (ClinicalTrials.gov NCT02386215).[11] Participants were 18-39-year-old women recruited between June 11, 2015 and January 16, 2016 from antenatal and postpartum clinics in 3 urban and peri-urban health centers in Kisumu, Kenya. Participants were randomized to either an HIVST group that received 2 HIV self-tests free-of-charge or to a comparison group that received invitation cards for the male partner to come for clinic-based HIV testing. Self-tests given to participants in the HIVST group were oral fluid-based HIV test kits (OraQuick Rapid HIV-1/2 antibody tests; OraSure Technologies, Bethlehem, PA).

At the time of enrollment, participants were administered a baseline questionnaire that collected information on socioeconomic characteristics and health-related behaviors. Follow-up surveys were conducted with participants at 3 months to learn whether participants' primary partner had an HIV test and whether the couple tested together. The follow-up survey also asked participants in the HIVST group whether they would be willing to pay for HIV self-tests, and if yes, what amount of money they would be willing to pay.

The primary outcome in this substudy was a binary indicator of whether participants were willing to pay a nonzero amount for self-tests (ie, WTP > 0). We made the conservative assumption that participants who reported that they were "not sure if they would pay for a self-test" had WTP $= 0$. The secondary outcome was the amount, in Kenyan Shillings (KSH), that participants were willing to pay for self-tests. We assumed that participants who were willing to pay something but reported either "don't know" for the WTP amount or refused to answer had a WTP equal to the median value among those with a WTP > 0. Various baseline characteristics of participants were used in our analyses. Categorical variables measured at baseline included educational attainment, occupation, self-reported chance of acquiring HIV in the future, and partner's HIV testing history in the past year. Participants' age, monthly income, and number of times tested for HIV in the past year were measured as continuous variables. Participants' marital status, condom use at last sex, and intimate partner violence history in the year before were classified as binary variables.

Statistical Analyses

We used a modified Poisson regression model to identify predictors of whether participants had a WTP $>$ 0 for self-tests[12] and an ordinary least squares linear regression to identify predictors of the amount that participants were willing to pay for HIV self-tests. All models included robust

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