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# Tobacco use among adults initiating treatment for HIV infection in rural Uganda

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## Abstract

We conducted a longitudinal study of tobacco use among adults initiating antiretroviral therapy (ART) in Mbarara, Uganda where 11% of men and 3% of women use tobacco according to the 2011 Demographic and Health Survey. In a prospective cohort, self-reported tobacco use was assessed before starting ART and reassessed every 3–4 months. Plasma cotinine, a nicotine metabolite, was measured in a subset of adults pre-ART to verify self-report. Among 496 subjects, 50 (10%) reported current tobacco use (20% of men, 6% of women). Most (53%) adults with elevated cotinine levels (>15 ng/mL) reported no tobacco use. By 6 months after ART initiation, 33% of tobacco users had quit (95% CI=20–46%). By 5 years, 64% quit (95% CI=47–77%). Self-reported tobacco use among rural Ugandans starting ART was twice as common as among the local background population and use may be underreported. ART initiation could be an opportunity for tobacco cessation interventions.

### Keywords

Tobacco use; smoking cessation; socioeconomic status; resource-limited setting; antiretroviral treatment initiation

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## BACKGROUND

Tobacco use is a leading cause of preventable death, projected to claim one billion lives in the 21st century [1]. Of the six million deaths per year that are attributed to tobacco globally, 80% occur in resource-limited countries. At the same time, 97% of HIV-infected persons live in resource-limited countries. In resource-rich countries in the era of potent antiretroviral therapy (ART), people living with HIV have a prevalence of tobacco use that is two to three times higher than among people without HIV [2–8] even after accounting for sociodemographic characteristics [9]. The high prevalence of smoking among people infected with HIV has not been well-studied. It is likely related to multiple factors including socioeconomic disadvantage, comorbid substance use disorders, psychiatric disorders, physical or mental distress, or health beliefs about living with HIV [10]. High rates of tobacco use leads to a high burden of tobacco related illness with an estimated one out of four deaths among people with HIV attributable to smoking [11, 12]. In resource-rich nations, where coordinated care for HIV and treatments for cancer and cardiovascular disease are available, tobacco use accounts for more years of life lost among people with HIV than HIV itself [13].

Sub-Saharan Africa (SSA) has relatively low tobacco use prevalence in the general population ranging from 8.0% in low prevalence countries to 27.3% in high prevalence countries [14, 15]. There are few studies of the prevalence of tobacco use among HIV-infected individuals in resource-limited settings. When tobacco use has been examined in cross-sectional studies, it appears the prevalence of tobacco use among HIV-infected individuals is higher than the general population [16–19]. In prevalence studies, tobacco use can be measured by self-report or with biochemical measures. Cotinine is a metabolite of nicotine that can be measured in the urine, saliva and serum of people exposed to nicotine through personal tobacco use, environmental tobacco smoke exposure or use of nicotine containing medications. Validation of self-reported tobacco use by cotinine levels from resource rich settings shows little underreporting [20–22]. However, the accuracy of self-report in resource-limited settings has not been well studied.

In contrast to resource-rich settings, people in resource-limited settings may not have access to treatments for cardiovascular disease or cancer. The burden of tobacco-related illness among tobacco users with HIV may be even greater in these settings. We do not know how tobacco use changes over time as patients engage in HIV care and treatment programs in resource limited settings. For many people, particularly young people in settings where primary care is limited, starting treatment for HIV may be the first sustained interaction they have with the healthcare system. Starting treatment is also a time when people may feel especially vulnerable with regard to their health. This may be a time when they are particularly receptive to health promoting messages like advice to abstain from tobacco. In resource rich settings, people with HIV infection are interested in quitting [23], but less successful at achieving abstinence from tobacco than smokers without HIV [24]. The patterns of tobacco use and cessation among people with HIV infection in resource limited settings, where there are few or no treatment services for tobacco cessation, is not known. The aim of this study is to measure the prevalence and patterns of tobacco use over time among adults initiating treatment for HIV in rural southwest Uganda.

# METHODS

## Subjects

The Uganda AIDS Rural Treatment Outcomes (UARTO) study is a prospective cohort of HIV-infected adults (≥18 years old) who are initiating antiretroviral treatment (ART) at the Immune Suppression Syndrome Clinic in Mbarara University of Science and Technology. Participants were approached for recruitment if they were ART-naïve, over 18 years of age, and lived within 20 miles of the clinic. Other study details have been described in detail elsewhere [25]. Mbarara is a rural district in southwestern Uganda, located five hours by automobile from Kampala. Current tobacco use in the general population in southwestern Uganda is estimated to be 11% in men and 3% in women according to the national Demographic and Health Survey in 2011 [26]. We included subjects enrolled in UARTO starting in 2005 and followed through 2011. The loss to follow-up rate in the UARTO cohort (participants for whom researchers were unable to confirm vital status after 180 days without cohort follow-up) was 2% at one year and 5% at two years [27].

## Measurements

At both baseline visits and every three to four months at routine follow-up, subjects undergo structured interviews and provide blood for routine HIV-related monitoring. Data collected prior to ART initiation include demographic traits, household characteristics, and socioeconomic measures of educational attainment, monthly income, and occupation. We categorized occupation according to groupings defined in other tobacco prevalence studies using national demographic and health surveys in Africa [15]. We used the same four categories as these prior studies (1) managers, professionals, technicians, sales, and clerical workers, (2) household, domestic, service, craftsmen, tradesmen and other manual workers, (3) self-employed or informal agricultural workers (including subsistence farmers), or (4) unemployed or not working. Educational attainment was categorized as less than primary school, completed primary school, or some secondary school or more. Health status was assessed by history of HIV with lab results, tuberculosis, and the MOS-HIV summary scores for physical and mental health and subscales for social functioning, mental health, and health distress [28].

Tobacco use is assessed by self-report by asking participants if they have ever used smoking tobacco/cigarettes or chewing tobacco and if they have used these tobacco products in the past 30 days. Alcohol use is assessed using the three questions about alcohol consumption from the of the Alcohol Use Disorders Identification Test (AUDIT-C) [29]. The AUDIT-C has been evaluated as a brief screening test to detect heavy drinking and/or alcohol abuse or dependence among primary care patients [30]. Patients who screen positive were considered to have problem alcohol use. In our population, an option is added for patients to report they are unable to quantify alcohol use due to consuming homemade alcohol. The AUDIT-C was not calculated for these patients.

In a subset of patients, baseline plasma samples were tested for cotinine using Salimetrics Saliva Cotinine ELISA kit (State College, PA) to confirm self-reported tobacco use. Cotinine is a nicotine metabolite measurable among individuals who smoke, use smokeless

tobacco, use nicotine products (i.e. nicotine patch, nicotine gum), or are exposed to environmental tobacco smoke. The subset was a purposive sample selected as part of an analysis of biochemical confirmation of alcohol use [31]. The subset included patients who reported alcohol use in the prior year as well as a random sample of patients with no reported alcohol use. When cotinine was detectable, levels were repeated for confirmation. We used the average of the repeated measures as the cotinine level.

## Statistical Analysis

We estimated baseline prevalence of current tobacco use. Current use was defined as self-reported use of smoked tobacco/cigarettes or chewing tobacco products in the last 30 days at time of enrollment. We identified subjects who reported no tobacco use in their lifetime as never users at baseline. We identified those who reported any lifetime tobacco use but no current use as former users.

Among the subset of patients with baseline plasma cotinine levels, we compared cotinine levels by reported tobacco use with the Kruskal-Wallace chi-square test. We further measured the accuracy of self-reported tobacco use compared to cotinine level as the gold-standard indicating current tobacco use. We calculate the sensitivity, specificity, negative and positive predictive value of self-reported tobacco use. We used cotinine greater than 15 ng/mL as the cutpoint for current tobacco use [32]. This is a widely cited cutpoint based on data from the United Kingdom in the 1980s. Saliva or plasma cotinine measures at optimal cut-points have been measured at 96–97% sensitivity and 99–100% specificity compared to known smoking behavior [33]. Lower cutpoints have been recommended for U.S. samples based on recent population surveys. This decrease in optimal cotinine cutpoint is attributed to decreasing secondhand smoke exposure. These recommendations are further tailored to racial differences in cotinine metabolism [34]. Some racial groups and pregnant women metabolize cotinine more slowly which leads to longer cotinine half-life. In Uganda, however, we opted for the higher 15 ng/mL cutpoint because of reported high rates of environmental tobacco exposure [35] more similar to the 1980s U.K. environment than current U.S. environmental tobacco exposure.

Baseline associations between current tobacco use and demographic characteristics, socioeconomic status, and health status are calculated using log-binomial regression to calculate unadjusted and adjusted prevalence ratios. If a model failed to converge, we instead used Poisson regression with robust variance estimates to calculate prevalence ratios [36]. In multivariable models, we included all variables associated with self-reported tobacco use in unadjusted models at $p<0.05$. We had few missing data (8%) and used complete case analysis, excluding subjects missing any model variable. To evaluate for violation of the positivity assumption, we cross-tabulated our categorical variables of gender, alcohol use, education, and occupation to ensure there were subjects at all categories of exposure at every combination of confounders [37].

We used self-reported tobacco use at follow-up to calculate two time to event outcomes. First, we measured the time to initiation of tobacco use among never and former tobacco users. Time to initiation of tobacco use was calculated as number of days from enrollment to the date of the visit when tobacco use was first reported. Tobacco cessation was defined as

no tobacco use reported in the last 30 days at two or more consecutive visits. This definition has been used in other longitudinal studies of tobacco use [38] and is highly correlated with other self-reported tobacco cessation outcomes [39, 40]. Using this definition, we measured time to cessation among baseline tobacco users. Time to cessation was calculated as number of days from enrollment to the first of the two consecutive visits with no reported tobacco use. If tobacco use status was not documented at a visit, the status from the prior visit was used. Subjects who did not start or stop tobacco use were censored at their last study visit.

We compared time to initial use or time to cessation using cumulative incidence functions [41]. We considered death a competing event. Cumulative incidence functions were compared by gender, alcohol use, and socioeconomic status. We used Gray's test for equality of cumulative incident functions to compare differences in time to event between groups [42].

All analyses were conducted using SAS version 9.3 (Cary, NC). UARTO's procedures were approved by ethical review boards at the University of California at San Francisco, Partners HealthCare, and Mbarara University of Science and Technology. All subjects gave informed consent to participate in the study.

## RESULTS

Among 508 ART-naïve adults who were enrolled in the cohort during the analysis period, 503 completed baseline interviews. This includes 496 who provided information about their cigarette/smoked tobacco or chewing tobacco use that comprises our study sample. The population was mostly female (69%), with a median age of 35 years (interquartile range [IQR]: 29–40, Table I). More than one-half (51%) were married, 23% completed primary school, and 26% completed secondary school or more. The most common occupational class was non-manual workers (professionals, managers, technicians, sales and clerical workers) who comprised 30% of the sample. Another 28.4% were informal agricultural workers or self-employed (including subsistence farmers), 16.3% were household, domestic, service, craftsmen, tradesmen and other manual workers and 25.2% reported unemployment. The median income was 40,000 Ugandan schillings, or approximately US$16, (IQR 15,000–95,000). Almost one-half (48%) reported fair or poor health, 11% had a prior history of tuberculosis, 22% screened positive for alcohol use problems, and the median CD4+ T-cell count was 133 cells/$mm^3$ (IQR 76–201 cells/$mm^3$).

In this group, 20% of men and 6% of women reported tobacco use in the 30 days prior to starting treatment with ART. The vast majority of tobacco use was smoked tobacco products/cigarettes (90%, N=45). Only four (8%) patients used chewing tobacco and one (2%) used both cigarettes/smoked tobacco and chewing tobacco products. Former tobacco use was reported among 75 adults including 69 people who had previously smoked tobacco or cigarettes, three who had previously used chewing tobacco, and three who had used both smoking and chewing tobacco.

In our subset of patients with baseline cotinine (the nicotine metabolite) measurements (N=128), the median cotinine level for patients who reported tobacco use in the past 30 days

was 580.3 ng/mL (IQR 205.7–1140.1 ng/mL) compared to 10.0 ng/mL (IQR 6.0–10.0 ng/mL) among those who reported no baseline tobacco use (Kruskal-Wallis $\chi^2$ 29.82, p<0.001). Cotinine was above our cutpoint of 15 ng/mL for current tobacco use in 27% of samples (Table II). This includes 11% of never users (N=9/80), 32% of former tobacco users (N=10/31), and 88% of current tobacco users (N=15/17) (Pearson $\chi^2$ 43.29, p<0.001). Self-report of current (past 30-day) tobacco use had a sensitivity of 44% and a specificity of 98% compared to plasma cotinine >15 ng/mL as the measure of biochemically-confirmed tobacco use. The median cotinine level among our 19 false negative tobacco users—those who reported no tobacco use in the past 30 days but who had elevated cotinine levels >15 ng/mL)--was 286.3 ng/mL (IQR 154.3–379.1 ng/mL). The positive predictive value of self-report of tobacco use was 88% and the negative predictive value of reporting no tobacco use was 83%.

In unadjusted models examining the predictors of self-reported tobacco use prior to starting ART we included 456 subjects with no missing independent variables in the models. This included 45 current tobacco users. Marital status, income, general health, physical health, mental health, social functioning, and health distress were not associated with tobacco use (Table III). Being older, male, reporting problem alcohol use, and having less education were positively associated with tobacco use. By occupational status, self-employment/informal agricultural workers and being employed as a manual worker (household, domestic, service, craftsmen, tradesmen and other manual workers), compared to those who were unemployed, were also positively associated with tobacco use.

We included 456 subjects with no missing data in our multivariable log-binomial regression model. Forty-five of these patients were current tobacco users. Age, gender, occupation, education, and problem alcohol use met our criteria for inclusion. A cross-tabulation of these categorical covariates had empty cells for women in the highest education category and men in the second highest education category. To prevent violation of the positivity assumption, we combined the two highest educational categories for the multivariable model. Male gender, problem alcohol use, employment as manual worker (household, domestic, service, craftsmen, tradesmen and other manual workers), and less education were independently associated with tobacco use.

Our longitudinal data included 453 patients with one or more follow-up visits. The median follow-up time from date of enrollment to date of last visit was 3.7 years (Range: 0.2–5.9; IQR 2.5–4.4). Thirty-eight patients died including one tobacco user, two former users who restarted during follow-up, and 35 never users. Initial tobacco use was reported among six of 340 adults with no prior tobacco use. Another seven of the 67 former tobacco users reported resuming tobacco use during follow-up. Initial tobacco use was higher among men compared to women (cumulative incidence function [CIF] at five years, 0.08, 95% confidence interval [CI] 0.04–0.15 vs. CIF 0.02, 95% CI 0.01–0.04, Gray's test for equality of CIF $\chi^2$=8.58, p=0.004, Figure 1) and former tobacco users compared to never users (CIF 0.10, 95% CI 0.04–0.18 vs. CIF 0.02, 95% CI 0.01–0.05, Gray's test for equality of CIF $\chi^2$=8.23, p=0.004).

Among 46 baseline tobacco users seen in follow-up, 28 reported no tobacco use for two consecutive visits. The cumulative incidence of quitting among baseline tobacco users was 0.64 by 5 years (95% CI=0.47–0.77) with one-third quitting in the first six months after follow-up (cumulative incidence at 6 months: 0.33, 95% CI: 0.20–0.46). Nine patients made two or more attempts before quitting. We did not detect a difference in tobacco cessation by gender (Figure 2), alcohol use, education, or occupation.

## DISCUSSION

In this resource-limited setting, tobacco use was roughly twice as common among people with HIV as among the population in general. In the Southwest region of Uganda, according to the most recent Ugandan national Demographic and Health Survey, 3% of women and 11% of men aged 15–49 use tobacco [26]. In our population of HIV-infected adults who were initiating ART, we found that 6% of women and 20% of men with HIV were currently using tobacco. This relatively high self-reported tobacco use is similar to that found in resource-rich settings where people with HIV infection are two to three times more likely to use tobacco than people without HIV [2–4, 24, 43]. Additionally, biochemical verification of tobacco use with a nicotine metabolite suggests that tobacco use is underreported in this setting.

Managing traditional risk factors for cardiovascular disease [44] and malignancy [45], like tobacco use, could greatly impact morbidity and mortality among people infected with HIV. Therefore, even in this low prevalence setting, tobacco use is an important risk factor that should be assessed among every patient. The impact of tobacco cessation may be greater in resource-limited regions where secondary and tertiary treatment services are largely unavailable than in resource-rich settings.

Our finding that higher rates of tobacco use are concentrated among adults with manual labor jobs and lower educational attainment is consistent with prior work in SSA [19] as well as resource rich settings. Efforts to promote cessation should be targeted toward these groups.

The large proportion of patients who quit after initiating ART suggest that initial engagement in healthcare services may be an important time to promote cessation. In other regions of SSA, where tobacco use is more common, the majority of tobacco users in HIV care report receiving advice to quit [46]. Subjects in this study may be particularly interested in improving their health, as evidenced by staring treatment and engaging in HIV care. They may therefore be particularly receptive to health promoting advice. Capitalizing on this opportunity to deliver evidence-based tobacco cessation counseling might yield large effects on smoking cessation. Further reducing tobacco use among people infected with HIV could impact morbidity and mortality of patients in HIV care and treatment programs.

We acknowledge several limitations in our study. First, although self-reported tobacco use has been shown to correlate highly with cotinine levels in other settings [21], we found underreporting of tobacco use at baseline. There may also have been underreporting in follow-up and this could have contributed to the high cessation rate. We do not have data on

cotinine levels at follow-up to assess potential underreporting at that point. We do not know if social pressures to underreport increase as patients engage in treatment or decrease as they become more comfortable with their providers. Therefore we do not know how misrepresentation of tobacco use changes over time. More work is needed to understand the social desirability and stigma associated with reporting tobacco use in SSA and other resource poor settings.

Second, in defining cessation, we relied on a measure of use in the last 30 days. It may be that many tobacco users are not daily smokers, they use tobacco only very intermittently and we cannot definitively distinguish these intermittent users from those who smoke regularly and then quit. However, the mean cotinine of self-reported smokers is at least consistent with daily smoking patterns with cotinine of 694 ng/mL which is well above levels typically seen in daily smoker (e.g. 300 ng/mL) [33]. We did not detect a difference in cessation over time among our self-reported smokers by demographic or socioeconomic characteristics. We may have been underpowered to compare these groups. Finally, we did not have information about tobacco use patterns such as quantity and frequency of use. Prior studies suggest quantity smoked is relatively low in SSA ranging from only four to eight cigarettes per day on average [15, 19]. This information is important to understand the impact of tobacco use in this population and to help design tobacco cessation interventions.

In conclusion, 20% of men and 6% of women initiating treatment for HIV report current tobacco use in a region where there is little tobacco use in the general population. Tobacco use is a modifiable risk factor for cardiovascular disease and cancer among people with HIV which could threaten the ongoing success of HIV care and treatment programs in resource-limited settings. Tobacco use also disproportionately affects patients with low socioeconomic status. Engagement in care at the time of HIV treatment initiation offers an opportunity to address tobacco and this should be explored and leveraged to further reduce tobacco use in this population.

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## References

1. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2011: Warning about the dangers of tobacco. Geneva, Switzerland: 2011. http://whqlibdoc.who.int/publications/2011/9789240687813_eng.pdf [Accessed October 24, 2013]
2. Crothers K, Griffith TA, McGinnis KA, Rodriguez-Barradas MC, Leaf DA, Weissman S, et al. The impact of cigarette smoking on mortality, quality of life, and comorbid illness among HIV-positive veterans. J Gen Intern Med. 2005; 20:1142–1145. [PubMed: 16423106]

3. Palella FJ, Baker RK, Buchacz K, Chmiel JS, Tedaldi EM, Novak RM, et al. Increased mortality among publicly insured participants in the HIV Outpatient Study despite HAART treatment. AIDS. 2011; 25:1865–1876. [PubMed: 21811144]
4. Vidrine DJ, Arduino RC, Lazev AB, Gritz ER. A randomized trial of a proactive cellular telephone intervention for smokers living with HIV/AIDS. AIDS. 2006; 20:253–260. [PubMed: 16511419]
5. Wallace JM, Rao AV, Glassroth J, Hansen NI, Rosen MJ, Arakaki C, et al. Respiratory illness in persons with human immunodeficiency virus infection. The Pulmonary Complications of HIV Infection Study Group. Am Rev Respir Dis. 1993; 148:1523–1529. [PubMed: 8256894]
6. Royce RA, Winkelstein W. HIV infection, cigarette smoking and CD4+ T-lymphocyte counts: preliminary results from the San Francisco Men's Health Study. AIDS. 1990; 4:327–333. [PubMed: 1972021]
7. Niaura R, Shadel WG, Morrow K, Tashima K, Flanigan T, Abrams DB. Human immunodeficiency virus infection, AIDS, and smoking cessation: the time is now. Clin Infect Dis. 2000; 31:808–812. [PubMed: 11017836]
8. Greenwood GL, Paul JP, Pollack LM, Binson D, Catania JA, Chang J, et al. Tobacco use and cessation among a household-based sample of US urban men who have sex with men. Am J Public Health. 2005; 95:145–151. [PubMed: 15623875]
9. Stall RD, Greenwood GL, Acree M, Paul J, Coates TJ. Cigarette smoking among gay and bisexual men. Am J Public Health. 1999; 89:1875–1878. [PubMed: 10589323]
10. Reynolds NR. Cigarette smoking and HIV: more evidence for action. AIDS Educ Prev. 2009; 21:106–121. [PubMed: 19537958]
11. Lifson AR, Neuhaus J, Arribas JR, van den Berg-Wolf M, Labriola AM, Read TR, et al. Smoking-related health risks among persons with HIV in the Strategies for Management of Antiretroviral Therapy clinical trial. Am J Public Health. 2010; 100:1896–1903. [PubMed: 20724677]
12. Marshall MM, McCormack MC, Kirk GD. Effect of cigarette smoking on HIV acquisition, progression, and mortality. AIDS Educ Prev. 2009; 21:28–39. [PubMed: 19537952]
13. Helleberg M, Afzal S, Kronborg G, Larsen CS, Pedersen G, Pedersen C, et al. Mortality Attributable to Smoking Among HIV-1-Infected Individuals: A Nationwide, Population-Based Cohort Study. Clin Infect Dis. 2012
14. Townsend L, Flisher AJ, Gilreath T, King G. A systematic literature review of tobacco use among adults 15 years and older in sub-Saharan Africa. Drug Alcohol Depend. 2006; 84:14–27. [PubMed: 16442750]
15. Pampel F. Tobacco use in sub-Sahara Africa: estimates from the demographic health surveys. Soc Sci Med. 2008; 66:1772–1783. [PubMed: 18249479]
16. Desalu OO, Oluboyo PO, Olokoba AB, Adekoya AO, Danburam A, Salawu FK, et al. Prevalence and determinants of tobacco smoking among HIV patients in North Eastern Nigeria. Afr J Med Med Sci. 2009; 38:103–108. [PubMed: 20175412]
17. Iliyasu Z, Gajida AU, Abubakar IS, Shittu O, Babashani M, Aliyu MH. Patterns and predictors of cigarette smoking among HIV-infected patients in northern Nigeria. Int J STD AIDS. 2012; 23:849–852. [PubMed: 23258822]
18. Martinson, NA.; Golub, JE.; Chaisson, R., et al. TB risk and smoking in HIV-infected adults: a prospective cohort. Paper #998. 15th Conference on Retroviruses and Opportunistic Infections; 2008; Boston, MA, USA. 2008. http://www.retroconference.org/2008/PDFs/998.pdf
19. Munyati SS, Redzo N, Dauya E, Matambo R, Makamure B, Bandason T, et al. Human immunodeficiency virus, smoking and self-rated health in Harare, Zimbabwe. Int J Tuberc Lung Dis. 2006; 10:1279–1285. [PubMed: 17131789]
20. Yeager DS, Krosnick JA. The validity of self-reported nicotine product use in the 2001–2008 National Health and Nutrition Examination Survey. Med Care. 2010; 48:1128–1132. [PubMed: 20940652]
21. Caraballo RS, Giovino GA, Pechacek TF, Mowery PD. Factors associated with discrepancies between self-reports on cigarette smoking and measured serum cotinine levels among persons aged 17 years or older: Third National Health and Nutrition Examination Survey, 1988–1994. Am J Epidemiol. 2001; 153:807–814. [PubMed: 11296155]

22. Wong SL, Shields M, Leatherdale S, Malaison E, Hammond D. Assessment of validity of self-reported smoking status. Health Rep. 2012; 23:47–53. [PubMed: 22590805]
23. Mamary EM, Bahrs D, Martinez S. Cigarette smoking and the desire to quit among individuals living with HIV. AIDS Patient Care STDS. 2002; 16:39–42. [PubMed: 11839217]
24. Tesoriero JM, Gieryic SM, Carrascal A, Lavigne HE. Smoking among HIV positive New Yorkers: prevalence, frequency, and opportunities for cessation. AIDS Behav. 2010; 14:824–835. [PubMed: 18777131]
25. Weiser SD, Tsai AC, Gupta R, Frongillo EA, Kawuma A, Senkungu J, et al. Food insecurity is associated with morbidity and patterns of healthcare utilization among HIV-infected individuals in a resource-poor setting. AIDS. 2012; 26:67–75. [PubMed: 21904186]
26. Uganda Bureau of Statistics and ICF International. Uganda Demographic and Health Survey 2011. Kampala, Uganda and Calverton, Maryland: 2012. http://www.ubos.org/onlinefiles/uploads/ubos/UDHS/UDHS2011.pdf [Accessed October 24, 2013]
27. Kaida A, Matthews LT, Kanters S, Kabakyenga J, Muzoora C, Mocello AR, et al. Incidence and predictors of pregnancy among a cohort of HIV-positive women initiating antiretroviral therapy in Mbarara, Uganda. PLoS One. 2013; 8:e63411. [PubMed: 23704906]
28. Wu AW, Rubin HR, Mathews WC, Ware JE, Brysk LT, Hardy WD, et al. A health status questionnaire using 30 items from the Medical Outcomes Study. Preliminary validation in persons with early HIV infection. Med Care. 1991; 29:786–798. [PubMed: 1875745]
29. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Arch Intern Med. 1998; 158:1789–1795. [PubMed: 9738608]
30. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. Alcohol Clin Exp Res. 2007; 31:1208–1217. [PubMed: 17451397]
31. Hahn JA, Bwana MB, Javors MA, Martin JN, Emenyonu NI, Bangsberg DR. Biomarker testing to estimate under-reported heavy alcohol consumption by persons with HIV initiating ART in Uganda. AIDS Behav. 2010; 14:1265–1268. [PubMed: 20697796]
32. Jarvis MJ, Tunstall-Pedoe H, Feyerabend C, Vesey C, Saloojee Y. Comparison of tests used to distinguish smokers from nonsmokers. Am J Public Health. 1987; 77:1435–1438. [PubMed: 3661797]
33. SRNT Subcommittee on Biochemical Verification. Biochemical verification of tobacco use and cessation. Nicotine Tob Res. 2002; 4:149–159. [PubMed: 12028847]
34. Benowitz NL, Bernert JT, Caraballo RS, Holiday DB, Wang J. Optimal serum cotinine levels for distinguishing cigarette smokers and nonsmokers within different racial/ethnic groups in the United States between 1999 and 2004. Am J Epidemiol. 2009; 169:236–248. [PubMed: 19019851]
35. Musoke, F. The Uganda Global Youth Tobacco Survey Report (2008) - Tobacco Control Policy Implications. Brazzaville: 2008. http://www.who.int/tobacco/surveillance/Uganda__Brazzaville08.pdf [Accessed October 31, 2013]
36. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol. 2005; 162:199–200. [PubMed: 15987728]
37. Westreich D, Cole SR. Invited commentary: positivity in practice. Am J Epidemiol. 2010; 171:674–677. discussion 678–681. [PubMed: 20139125]
38. Vijayaraghavan M, Penko J, Vittinghoff E, Bangsberg DR, Miaskowski C, Kushel MB. Smoking Behaviors in a Community-Based Cohort of HIV-Infected Indigent Adults. AIDS Behav. 2013
39. Velicer WF, Prochaska JO. A comparison of four self-report smoking cessation outcome measures. Addict Behav. 2004; 29:51–60. [PubMed: 14667420]
40. Hughes JR, Carpenter MJ, Naud S. Do point prevalence and prolonged abstinence measures produce similar results in smoking cessation studies? A systematic review. Nicotine Tob Res. 2010; 12:756–762. [PubMed: 20504946]
41. Satagopan JM, Ben-Porat L, Berwick M, Robson M, Kutler D, Auerbach AD. A note on competing risks in survival data analysis. Br J Cancer. 2004; 91:1229–1235. [PubMed: 15305188]

42. Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. Annals of Statistics. 1988; 16:1141–1154.

43. Marshall MM, Kirk GD, Caporaso NE, McCormack MC, Merlo CA, Hague JC, et al. Tobacco use and nicotine dependence among HIV-infected and uninfected injection drug users. Addict Behav. 2011; 36:61–67. [PubMed: 20875704]

44. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab. 2007; 92:2506–2512. [PubMed: 17456578]

45. Krishnan S, Schouten JT, Jacobson DL, Benson CA, Collier AC, Koletar SL, et al. Incidence of non-AIDS-defining cancer in antiretroviral treatment-naïve subjects after antiretroviral treatment initiation: an ACTG longitudinal linked randomized trials analysis. Oncology. 2011; 80:42–49. [PubMed: 21606663]

46. Shapiro AE, Tshabangu N, Golub JE, Martinson NA. Intention to quit smoking among human immunodeficiency virus infected adults in Johannesburg, South Africa. Int J Tuberc Lung Dis. 2011; 15:140–142. [PubMed: 21276312]

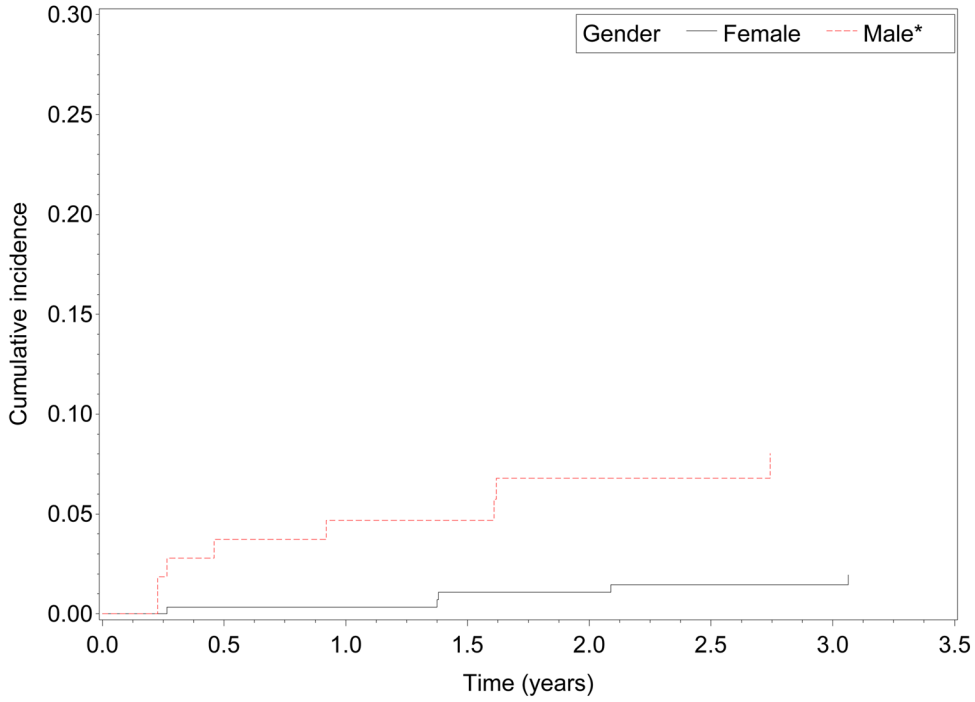


**Figure 1.**
Cumulative Incidence of New Tobacco Use
Legend: * p=0.004.

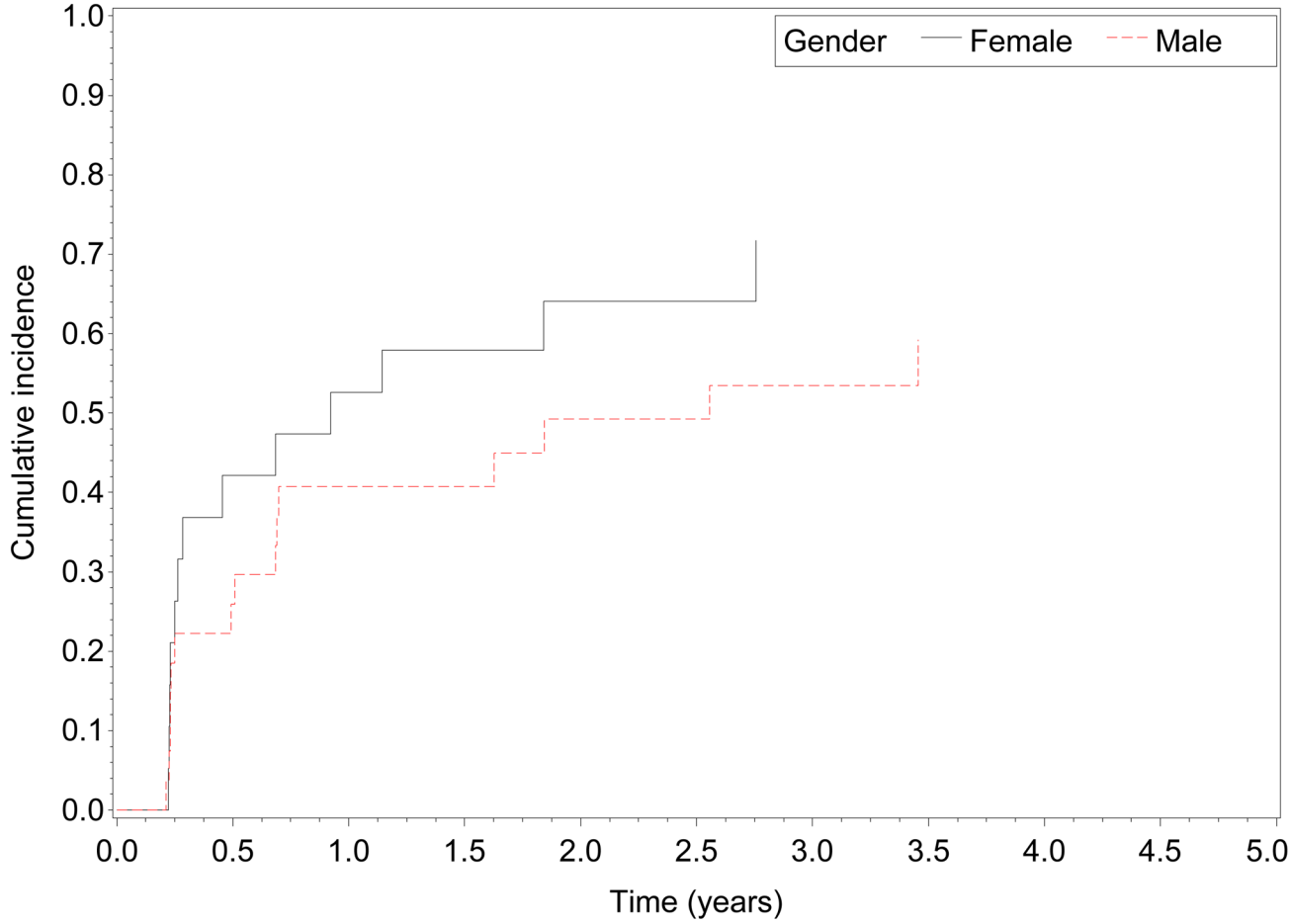


**Figure 2.**
Cumulative Incidence of Tobacco Cessation Among Pre-ART Tobacco Users

## Table I

Baseline characteristics of UARTO cohort

| | Total | N | % |
|---|---|---|---|
| DEMOGRAPHICS | | | |
| Age (median, IQR) | 496 | 35 | 29–40 |
| Gender | 496 | | |
| Male | | 154 | 31.1 |
| Female | | 342 | 68.9 |
| SOCIOECONOMIC STATUS | | | |
| Marital status | 496 | | |
| Married and living together | | 251 | 50.6 |
| Widowed | | 110 | 22.2 |
| Divorced/single/separated | | 135 | 27.2 |
| Education | 467 | | |
| Did not complete primary school | | 238 | 51.0 |
| Completed primary school | | 109 | 23.3 |
| Secondary school or more | | 120 | 25.7 |
| Occupation (4 class) | 496 | | |
| Managers, professionals, technicians, sales, and clerical workers | | 149 | 30.0 |
| Household, domestic, service, craftsmen, tradesmen and other manual workers | | 81 | 16.3 |
| Informal or self-employment including subsistence farming | | 141 | 28.4 |
| Unemployed | | 125 | 25.2 |
| Household monthly income (Ugandan shilling) (median, IQR) | 332 | 40,000[a] | 15,000–95,000 |
| Missing household income | | 164 | 33.1 |
| HEALTH STATUS | | | |
| Overall health | 483 | | |
| Excellent | | 20 | 4.1 |
| Very good | | 57 | 11.8 |
| Good | | 151 | 31.3 |
| Fair | | 189 | 39.1 |
| Poor | | 66 | 13.7 |
| MOS-HIV | 470 | | |
| Social functioning (median, IQR) | | 100 | 80–100 |
| Mental health (median, IQR) | | 76 | 60–92 |
| Health distress (median, IQR) | | 95 | 75–100 |
| Physical health summary score (median, IQR) | | 53 | 44–58 |
| Mental health summary score (median, IQR) | | 52 | 45–57 |
| History of tuberculosis | 496 | 54 | 10.9 |
| Baseline CD4 (median, IQR) | 496 | 133 | 76–201 |
| SUBSTANCE USE | | | |

| | Total | N | % |
|---|---|---|---|
| Problem alcohol use (AUDITC) | 483 | 105 | 21.7 |
| Current tobacco smoker | 496 | 46 | 9.3 |
| Current chewing tobacco user | 496 | 5 | 1.0 |
| Former chewing tobacco user | 496 | 6 | 1.2 |
| Former tobacco smoker | 496 | 72 | 14.5 |

Abbreviations: UARTO, Uganda AIDS Rural Treatment Outcomes study; IQR, interquartile range; AUDIT-C, Alcohol Use Disorders Identification Test; MOS-HIV, Medical Outcomes Study HIV Health Survey.

[a] 40,000 Uganda Shillings is approximately equal to US$16.

**Table II**

Validation of self-reported tobacco use at baseline

| | **Cotinine>15 ng/mL N (row %) [col %]** | **Cotinine≤ 15 ng/mL N (row %) [col %]** | **TOTAL** |
|---|---|---|---|
| Reported tobacco use | 15 (88%) [44%] | 2 (12%) [2%] | 17 (13%) |
| No reported tobacco use | 19 (17%) [56%] | 92 (83%) [98%] | 111 (87%) |
| TOTAL | 34 (27%) | 91 (71%) | 128 |

Sensitivity of self-reported tobacco use=44%

Specificity of self-reported tobacco use=98%

Positive predictive value of self-reported tobacco use=88%

Negative predictive value of no self-reported tobacco use=83%

**Table III**

Predictors of self-reported tobacco use at time of ARV initiation, log binomial multivariable regression (n=456)

| | PR | 95% CI | p-value | APR | 95% CI | p-value |
|---|---|---|---|---|---|---|
| DEMOGRAPHICS | | | | | | |
| **Age (years)** | **1.03** | **1.00–1.05** | **0.03** | 1.00 | 0.97–1.04 | 0.83 |
| **Male (vs. female)** | **3.53** | **2.01–6.19** | **<0.01** | **2.57** | **1.41–4.70** | **0.002** |
| SOCIOECONOMIC STATUS | | | | | | |
| Marital status | | | | | | |
| Divorced/single/separated | REF | -- | -- | -- | -- | -- |
| Married and living together | 0.71 | 0.32–1.55 | 0.39 | -- | -- | -- |
| Widowed | 0.75 | 0.40–1.41 | 0.37 | -- | -- | -- |
| **Education** | | | | | | |
| **Did not complete primary school** | **2.63** | **1.40–4.97** | **0.003** | **2.65** | **1.43–4.91** | **0.002** |
| **Completed primary school or more** | REF | -- | -- | REF | -- | -- |
| **Occupation (3 class)** | | | | | | |
| **Unemployed** | REF | | -- | REF | -- | -- |
| **Managers, professionals, technicians, sales, clerical jobs** | 1.76 | 0.54–5.71 | 0.34 | 1.49 | 0.46–4.86 | 0.51 |
| **Household, domestic, service, craftsmen, tradesmen and other manual jobs** | **4.52** | **1.51–13.51** | **0.007** | **3.07** | **1.04–9.04** | **0.04** |
| **Informal agricultural workers or self-employment including subsistence farming** | **5.08** | **1.80–14.36** | **0.002** | 2.81 | 0.99–7.96 | 0.05 |
| Household monthly income (per 10,000 shilling) [a] | 1.00 | 0.98–1.02 | 0.94 | -- | -- | -- |
| HEALTH STATUS | | | | | | |
| Overall health | | | | | | |
| Excellent | REF | -- | -- | -- | -- | -- |
| Very good | 0.27 | 0.05–1.40 | 0.12 | -- | -- | -- |
| Good | 0.89 | 0.32–2.44 | 0.82 | -- | -- | -- |
| Fair | 0.87 | 0.32–2.34 | 0.78 | -- | -- | -- |
| Poor | 0.12 | 0.01–1.05 | 0.06 | -- | -- | -- |
| MOS-HIV | | | | | | |
| Social functioning | 1.00 | 0.99–1.01 | 0.48 | -- | -- | -- |
| Mental health | 1.00 | 0.99–1.02 | 0.73 | -- | -- | -- |

| | PR | 95% CI | p-value | APR | 95% CI | p-value |
|---|---|---|---|---|---|---|
| Health distress | 1.02 | 0.99–1.04 | 0.05 | -- | -- | -- |
| Physical health summary score | 1.00 | 0.98–1.03 | 0.92 | -- | -- | -- |
| Mental health summary score | 1.01 | 0.98–1.04 | 0.39 | -- | -- | -- |
| History of tuberculosis | 0.85 | 0.32–2.27 | 0.74 | -- | -- | -- |
| Baseline CD4 | 1.00 | 0.99–1.00 | 0.24 | -- | -- | -- |
| SUBSTANCE USE | | | | | | |
| **Problem alcohol use (AUDIT-C)** | **3.46** | **2.03–5.94** | **<0.001** | **2.62** | **1.50–4.58** | **0.001** |

Abbreviations: PR, Unadjusted prevalence ratio; CI, Confidence interval; APR, Adjusted prevalence ratio; REF, Reference group; AUDIT-C, Alcohol use disorders identification test consumption items. MOS-HIV, Medical Outcomes Study HIV Health Survey.

[a] 40,000 Uganda Shillings is approximately equal to US$16.