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Smoking cessation after engagement in HIV care in rural Uganda

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Abstract

People living with HIV (PLWH) are more likely to smoke compared to HIV-uninfected counterparts, but little is known about smoking behaviors in sub-Saharan Africa. To address this gap in knowledge, we characterized smoking cessation patterns among people living with HIV (PLWH) compared to HIV-uninfected individuals in rural Uganda. PLWH were at least 40 years of age and on antiretroviral therapy for at least three years, and HIV-uninfected individuals were recruited from the clinical catchment area. Our primary outcome of interest was smoking cessation, which was assessed using an adapted WHO STEPS smoking questionnaire. We fit Cox proportional hazards models to compare time to smoking cessation between PLWH pre-care, PLWH in care, and HIV-uninfected individuals. We found that, compared to HIV-uninfected individuals, PLWH in care were less likely to have ever smoked (40% vs. 49%, p=0.04). The combined sample of 267 ever-smokers had a median age of 56 (IQR 49–68), 56% (n=150) were male, and 26% (n=70) were current smokers. In time-to-event analyses, HIV-uninfected individuals and PLWH prior to clinic enrollment ceased smoking at similar rates (HR 0.8, 95% CI 0.5–1.2). However, after enrolling in HIV care, PLWH had a hazard of smoking cessation over twice that of HIV-uninfected individuals and three times that of PLWH prior to enrollment (HR 2.4, 95% CI 1.3–4.6, p=0.005 and HR 3.0, 95% CI 1.6–5.5, p=0.001, respectively). In summary, we observed high rates of smoking cessation among PLWH after engagement in HIV care in rural

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Author Contributions

JAM, MJS and CMN conceived of the study design and planned the data analysis. OS, DV and BK led study procedures and data collection. JAM and CMN conducted all data analyses and wrote the first draft of the manuscript. MJS and ACT provided methodological guidance. All authors reviewed and critiqued the final manuscript.

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Uganda. While we hypothesize that greater access to primary care services and health counseling might contribute, future studies should better investigate the mechanism of this association.

Keywords

Africa; tobacco; primary care

Introduction

Smoking was responsible for over 6 million deaths globally in 2015 (GBD, 2016, 2017). People living with HIV (PLWH) are more likely to smoke compared to HIV-uninfected counterparts in high (Mamary, Bahrs, & Martinez, 2002; Mdodo et al., 2015) and low-income countries (Mdege, Shah, Ayo-Yusuf, Hakim, & Siddiqi, 2017). Smoking-related morbidity and mortality are particularly high among PLWH on antiretroviral therapy (ART) (Crothers et al., 2009), for whom smoking contributes to a greater decrement in life expectancy than HIV infection (Helleberg et al., 2013; Helleberg et al., 2015; Reddy et al., 2017; Reddy et al., 2016). For PLWH who quit smoking, health outcomes improve with continued cessation (Petoumenos et al., 2011).

Almost 70% of PLWH in the world live in sub-Saharan Africa (SSA) (UNAIDS, 2017), where smoking prevalence is increasing due to limited governmental legislation and expanding tobacco marketing campaigns (Blecher and Ross, 2013; Brathwaite, Addo, Smeeth, & Lock, 2015; Sreeramareddy, Pradhan, & Sin, 2014). Nearly 10% of the adult Ugandan population smokes (Kabwama et al., 2016). Tobacco control programs (WHO, 2003) can improve smoking behaviors, but require primary care access and/or developed health systems. In SSA, HIV care provides millions of people with access to routine medical care, and some have hypothesized that this additional access to care has positively impacted non-HIV health outcomes including blood pressure control and diabetes management (Feinstein et al., 2017; Manne-Goehler et al., 2017). Thus, the HIV care platform may provide a framework for smoking cessation interventions (Gupta and Bukhman, 2015; Niaura et al., 2000).

To address this gap in knowledge, we quantified smoking patterns in a clinic-based cohort of PLWH on stable ART and compared them to smoking patterns in a population-based, HIV-uninfected group residing in the clinic catchment area in rural Uganda. We hypothesized that PLWH who are engaged in HIV care would be less likely to smoke and more likely to quit smoking than HIV-uninfected controls.

Methods

We analyzed data from two cross-sectional samples. PLWH were enrolled using convenience sampling into the Ugandan Non-Communicable Diseases and Aging Cohort (UGANDAC; NCT02445079), a cohort study of older-aged PLWH on ART in rural Uganda. All UGANDAC study participants were at least 40 years old, had received ART for at least three years from the Mbarara Regional Referral Hospital HIV clinic (North et al., 2017) – which is one of the largest clinics in the region and provides much of the HIV care for

PLWH in southwestern Uganda – and all lived within approximately 130 km of the HIV clinic. Eligible participants were approached for study participation after having voluntarily arrived at the HIV clinic for routine HIV-related care, and study enrollment had no impact on their medical care. Per clinic protocols, in-person, 1-on-1 smoking cessation counseling is provided by trained HIV testing counselors for all clinic patients who screen positive for smoking and are referred by treating physicians at their initial intake and/or quarterly follow-up clinic appointments. Counseling includes teaching on the health risks of smoking and advice on lifestyle modifications for successful smoking cessation, tailored to the needs of each patient. Written educational materials are not present due to resource constraints.

Data from HIV-uninfected comparators were collected during one of five health screening events in the Nyakabare parish, a cluster of 8 villages within the HIV clinic catchment area, located approximately 20 kilometers from the HIV clinic. Eligible participants were approached for research data collection after voluntarily arriving for a free health screening, and consent to allow data collection had no bearing on whether they could complete the health screening. Interested community members who were unable to travel to the health screening locations due to physical ailments were identified in pre-event informational meetings, and free transportation was arranged. We included HIV-negative participants if they were over 40 years of age and tested negative for HIV at the health fair.

Smoking behaviors were characterized in both cohorts with an adapted WHO STEPS questionnaire (WHO, 2017) (See Online Supplement). HIV testing was conducted according to Ugandan Ministry of Health guidelines (*Uganda National Policy Guidelines for HIV Counseling and Testing*, 2005). For PLWH, CD4+ T-cell count and HIV viral load within one year of study visits were obtained from clinical record abstraction. We defined virologic suppression as a viral load below the limit of assay detection (dried blood spot: <550 copies/μL; plasma: <40 copies/μL). Participants gave written informed consent in both the UGANDAC study and the health screening events, and study procedures for both studies were approved by the Partners Healthcare and Mbarara University of Science and Technology human studies ethics committees, as well as by the Ugandan National Council for Science and Technology.

Statistical Analysis

We compared demographic characteristics by HIV serostatus using chi-squared for categorical variables or Fisher's exact tests for any variables with a cell size of less than 5 participants. To asses for selection bias, we compared characteristics of participants with and without complete smoking data, and between HIV-uninfected participants who did or did not attend the health screenings. Data from those who did not attend the health fairs were available from a population census collected the prior year. Our primary outcomes of interest were (1) cessation of smoking and (2) time from smoking initiation to cessation. The primary exposure of interest was HIV serostatus. We estimated the association between HIV serostatus and smoking cessation by constructing multivariable logistic regression models including all covariates with a $p \leq 0.2$ in unadjusted analyses. Age was explored as a non-linear covariate, and the joint statistical significance of the regression coefficients of categorical variables was tested using an F-type Wald test. We conducted a sensitivity

analysis by excluding smoking duration from regression models to limit missingness. For our secondary outcome, we fit Cox proportional hazard models with robust standard errors to account for clustering within individuals. We considered HIV clinic enrollment as a time varying exposure by dividing smoking duration among PLWH into two observation periods using the stsplit command in Stata: time before and time after enrollment in HIV care, and compared each group separately to HIV-uninfected comparators. We tested proportionality of hazard estimates with log-log plots and assessed for time varying effects. Potential confounders in both the regression and time to event analyses included age, gender, household asset wealth (Filmer and Pritchett, 2001), education and medical comorbidities, with smoking duration additionally included as a covariate in the correlates of smoking cessation analysis. Data were analyzed with Stata 13 (StataCorp, College Station, TX).

Results

Baseline Characteristics

Among 574 total participants in both cohorts (154 PLWH and 420 HIV-uninfected), 267 (47%) ever smoked (Table 1). Ever-smoking was less prevalent among PLWH (40%) than HIV-uninfected participants (49%, p=0.045). Among ever-smokers, PLWH were more commonly men (72% vs. 52%, p<0.001) and had higher educational attainment (p=0.002). Most PLWH were virologically suppressed (88%), and 81% had CD4+ counts ≥350 cells/mm^3 at last measurement. Nearly all PLWH (92%) were taking non-nucleoside reverse transcriptase inhibitor-based ART for a median of nine years (IQR 8–10).

HIV-uninfected participants who attended the health screening were older (55 vs. 50, p<0.001) than those who did not attend. Smoking duration data were missing in 30% of HIV-uninfected participants. Those with complete smoking data were younger and were more educated than those with incomplete data (eTable 1).

Correlates of Smoking Cessation

In unadjusted analyses, there was no difference in likelihood of having quit smoking or smoking duration by HIV serostatus. Most PLWH (68%) quit smoking prior to entry into HIV care, at a median of 14 years (IQR 6–18) after smoking initiation. Those who quit after care entry did so within a median of 2 years (IQR 0–6). In multivariable logistic regression models adjusted for confounders, HIV serostatus was associated with a non-significant doubling of the odds of smoking cessation (AOR 2.6, 95% CI 0.9–7.4) (Table 2). Older individuals (AOR 1.2 per year, 95% CI 1.1–1.3), men (AOR 3.1, 95% CI 1.2–8.1) and those with ≥1 medical condition (AOR 4.1, 95% CI 1.1–15.1) were more likely to cease smoking. Longer smoking duration was associated with decreased odds of quitting (AOR 0.9 per year, 95% CI 0.8–0.9). Results were similar in models restricted to participants with complete smoking duration data.

Time to Cessation

In time-to-event analyses, there was no difference in time to cessation between PLWH and HIV-uninfected participants prior to entry into HIV care (HR 0.8, 95% CI 0.5–1.2). However, the hazard of smoking cessation among PLWH after care entry was significantly

higher than that for HIV-uninfected individuals (HR 2.4, 95% CI 1.3–4.6, p=0.005) and for PLWH prior to care entry (HR 3.0, 95% CI 1.6–5.5, p=0.001) (Figure 1, eTable 2). Asset index was the only covariate that violated proportionality assumptions (eTable 3). In analyses stratified by asset index, the comparative hazard of cessation for PLWH versus HIV-negatives was higher in the wealthier subsample (HR 4.0, 95% CI 1.6–9.9, p=0.003) as compared to the less wealthy subsample (HR 1.9, 95% CI 0.7–4.6, p=0.18) (eTable 2).

Discussion

In rural Uganda, rates of smoking cessation among PLWH dramatically increase following engagement in HIV care, and are notably higher than cessation rates for population-based, HIV-uninfected comparators. Our study is among the first in SSA to compare smoking cessation patterns by HIV care engagement status, and lends support to the role of secondary health benefits afforded by HIV care programs.

Smoking prevalence was lower among PLWH than HIV-uninfected comparators in the current study, a finding that is consistent with data from SSA (Mutevedzi, Rodger, Kowal, Nyirenda, & Newell, 2013) but is contrary to much of the literature from other high-income settings (Mdege, et al., 2017; Mdodo, et al., 2015). The lower smoking prevalence among PLWH in our cohort may be due to the focus on PLWH in long-term care, who therefore have had repeated interactions with the healthcare system, while much of the data on HIV and smoking prevalence is focused on HIV cohorts that include participants at various stages along the HIV care continuum (Crothers, et al., 2009; Mdege, et al., 2017).

Several potentially complementary mechanisms may explain why engaging in HIV care may be associated with smoking behaviors. Firstly, in-person cessation counseling, which increases successful smoking cessation (Amiya et al., 2011; Berg et al., 2014; Chaiton et al., 2016; Louwagie, Okuyemi, & Ayo-Yusuf, 2014; Pacek, Rass, & Johnson, 2017; Ramon et al., 2013), is included as part of routine health counseling during initial enrollment at the Mbarara HIV clinic. Similar effects have been noted in the U.S., with one study showing a higher likelihood of smoking cessation among PLWH engaged in HIV care compared to the general population (Mdodo, et al., 2015). If these relationships are corroborated, our data support the expansion of smoking cessation programs both within HIV clinics and to other primary care delivery systems in the region.

Additional contributors to the observed phenomenon of smoking cessation among PLWH in clinical care could include changing social norms within social networks of PLWH (Christakis and Fowler, 2008) and changing perceived smoking norms (Perkins et al., 2017). For example, increasing media portrayal of binge drinking as socially undesirable contributed to decreasing binge drinking prevalence among youth in a longitudinal cohort study (Yanovitzky and Stryker, 2001). Alternatively, PLWH who present with co-infections or other severe comorbidities might have increased health-consciousness and/or be more apt to discontinue unhealthy behaviors (Kruse et al., 2014). Lastly, the advent of widespread ART has increased life expectancy among PLWH close to that of the HIV-uninfected community (Bor, Herbst, Newell, & Bärnighausen, 2013; Samji et al., 2013), which is known to change personal risk versus benefit calculations by attenuating the subjective

mortality expectations of PLWH engaging in care (Baranov and Kohler, 2018) or by modifying the competing mortality risks among PLWH engaged in care, for whom HIV may no longer be the most proximal health threat (Ganz, 2000). PLWH on ART, who can now reasonably expect to live a long life, may be more apt to stop smoking because they no longer interpret non-ART related health behaviors as futile.

Although time to smoking cessation decreased significantly after enrollment in care, the majority (68%) of PLWH who quit smoking did so before engaging in HIV care. Two potential hypotheses might explain this observation. PLWH who have enrolled in HIV care may be inherently more health-conscious and thus more likely to have quit smoking. Since we did not observe a group of PLWH not in care, we cannot test this hypothesis in this analysis. A diagnosis of HIV infection itself could also trigger increased health consciousness. This theory is supported by a study of PLWH in South Africa that found a higher odds of smoking cessation among PLWH versus uninfected individuals who participated in a smoking cessation program (Louwagie and Ayo-Yusuf, 2015). Alternatively, since PLWH in SSA present to care at more advanced stages of disease in comparison to PLWH in developed countries (Auld, 2017; Siedner et al., 2014), they may have quit smoking because they feel worse as their disease advances (Halpern and Warner, 1994; Wilkes and Evans, 1999).

Our study provides key data that can be used to identify predictors of smoking cessation for public health policy (Mohiuddin et al., 2007; Rahmanian et al., 2011; Rigotti, Munafo, & Stead, 2007). Notably, we found that, in addition to enrollment in HIV care, men and older individuals were more likely to cease smoking, which is consistent with prior literature (Abdullah, Driezen, Quah, Nargis, & Fong, 2015; Hymowitz et al., 1997; Lee and Kahende, 2007; Li et al., 2010). Such data can be used to target cessation interventions to populations in SSA with increasing tobacco consumption, and prevent smoking-related health outcomes.

The main strength of this analysis is the inclusion of a population-based, HIV-uninfected comparator group, which allows effect estimation by HIV serostatus. We additionally characterized smoking behaviors with a standardized, validated questionnaire, allowing for comparisons across cohorts. There are also several limitations. First, the cross-sectional design prevents assumptions regarding causality. Second, self-reported smoking data are subject to misclassification (Stuber, Galea, & Link, 2008), although some (Caraballo, Giovino, Pechacek, & Mowery, 2001; Vartiainen, Seppala, Lillsunde, & Puska, 2002) but not all (Kruse, et al., 2014) studies have shown correlation between self-report and objective measures of tobacco use. Third, data regarding cessation counseling among HIV-uninfected participants were not collected. Data on time of HIV diagnosis were not available, preventing analysis of the impact of HIV diagnosis on smoking behaviors. This analysis was also limited to one clinic, and the relationship between counseling and smoking cessation may differ based on resources and consistency of smoking cessation activities in HIV clinics. Missing data on smoking initiation and/or cessation times may have biased our results if smoking duration differed among those with missing data. Additionally, among HIV-uninfected participants, health screening attendees may not be representative of the larger population, which may have biased our results if attendance was associated with differences in smoking behaviors. Although analyses accounted for demographic differences

among study participants, unmeasured regional differences in cultural beliefs and/or practices throughout Uganda may have introduced bias into our estimates. Finally, this cohort was limited to older, rural Ugandans, so results are generalizable only to similar populations.

In conclusion, PLWH in rural Uganda who receive HIV care quit smoking faster than they do prior to engaging in care, and faster than HIV uninfected individuals. While further work is required to corroborate these findings and explore underlying mechanisms, this study suggests that integrating smoking cessation counseling into routine clinical care may decrease smoking among PLWH in SSA. Given the increased smoking prevalence and heightened risk of smoking-related morbidity and mortality among PLWH in SSA (Crothers, et al., 2009; Mdege, et al., 2017), broadening the integration of tobacco control interventions into existing HIV and general primary care could substantially improve health in the region.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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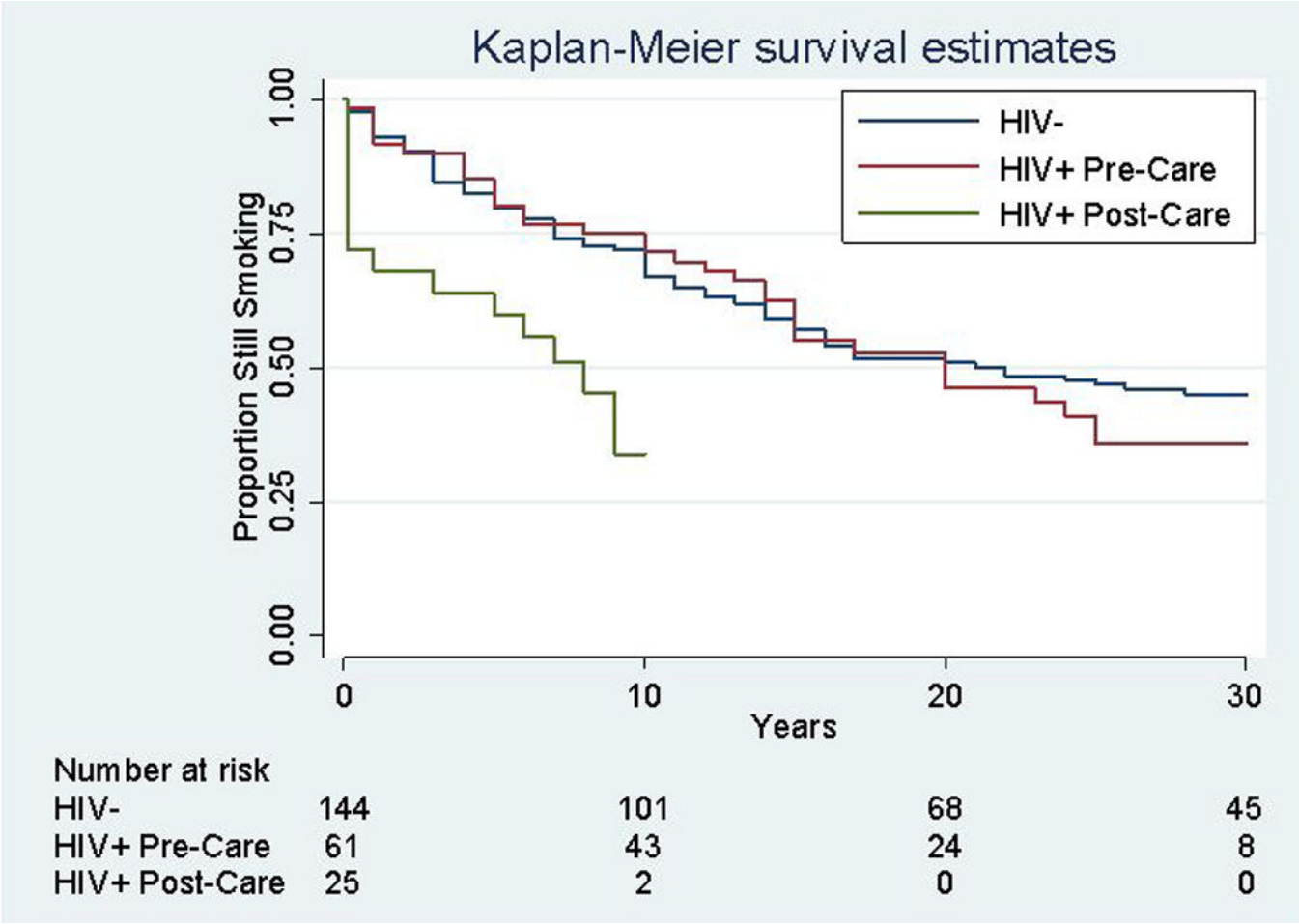

Figure 1:
Kaplan-Meier curve of time-to-smoking cessation for PLWH pre- and post-HIV care engagement vs. HIV-uninfected participants.

Table 1:

Baseline Cohort Characteristics of Current or Former Smokers

	Total (n=267)	HIV+ (n=61)	HIV- (n=206)	p-value
Age, years	56 [49, 68]	51 [49, 57]	60 [49, 71]	<0.001
Male	150 (56)	44 (72)	107 (52)	<0.01
1+ Medical Comorbidity [a]	72 (27)	11 (18)	61 (30)	0.07
Body Mass Index, kg/m2				0.29
Underweight (<18.5)	30 (11)	6 (10)	24 (12)	
Normal (18.5–24.9)	170 (65)	45 (74)	125 (62)	
Overweight (25–29.9)	41 (16)	8 (13)	33 (16)	
Obese (≥30)	22 (8)	2 (3)	20 (10)	
Education level				0.002
No school	92 (34)	11 (18)	81 (39)	
Any primary school	136 (51)	35 (57)	101 (49)	
More than primary school	39 (15)	15 (25)	24 (12)	
Farmer	193 (72)	38 (62)	155 (75)	0.05
Smoking status				0.10
Current smoker	70 (26)	11 (18)	59 (29)	
Former smoker	197 (74)	50 (82)	147 (71)	
Smoking duration, years [b]				
Current smoker	30 [22, 41]	35 [22, 42]	29 [21, 40]	0.73
Former smoker	13 [5, 24]	15 [6, 23]	11 [4, 26]	0.54
HIV Cohort				
Duration in HIV care, years		9 [8, 10]		
Baseline HIV viral load, copies/μL				
Undetectable		0 (0)		
Detectable, <10,000		1 (2)		
Detectable, ≥10,000		60 (98)		
Last HIV viral load, copies/μL				
Undetectable		51 (88)		
Detectable, <10,000		6 (10)		
Detectable, ≥10,000		1 (2)		
Baseline CD4+ count, cells/μm3				
<100		23 (38)		
100–349		37 (61)		
350–499		1 (2)		
≥500		0 (0)		
Last CD4+ count, cells/μm3				
<100		0 (0)		
100–349		12 (20)		
350–449		26 (43)		

	Total (n=267)	HIV+ (n=61)	HIV- (n=206)	p-value
≥500		23 (38)		
Current antiretroviral regimen [c]				
TDF/3TC/EFV		5 (8)		
AZT/3TC/EFV		13 (21)		
AZT/3TC/NVP		38 (62)		
TDF/3TC/LPV/r		5 (8)		

n (%) or median [IQR], unless otherwise noted

[a] Comorbidities include self-reported history of hypertension, hyperlipidemia, diabetes mellitus, renal disease, cancer, chronic obstructive pulmonary disease or asthma.

[b] Missing in 60 (19%) of study participants.

[c] AZT = zidovudine; 3TC = lamivudine; EFV = efavirenz; NVP = nevirapine; TDF = tadalfil; LPV/r = lopinavir/ritonavir.

Table 2:

Unadjusted and adjusted correlates of smoking cessation in rural Uganda

Characteristics	Unadjusted		Adjusted†	
	Odds Ratio	95% CI	Odds Ratio	95% CI
HIV Serostatus	1.8*	0.9 – 3.7	2.6	0.9 – 7.4
Age, per year	1.04***	1.02 – 1.07	1.2***	1.1 – 1.3
Male	2.9***	1.7 – 5.1	3.1*	1.2 – 8.1
1+ Comorbidities	3.7**	1.7 – 8.3	4.1*	1.1 – 15.1
Education				
None	REF			
Any primary school	0.5*	0.2 – 0.9	0.5	0.2 – 1.6
More than primary school	0.9	0.4 – 2.4	1.0	0.2 – 5.1
Asset Index				
Poorest	REF			
Poorer	1.3	0.7 – 2.5	1.1	0.3 – 3.6
Richer	2.6*	1.1 – 6.1	2.5	0.6 – 9.2
Richest	2.1	0.9 – 5.0	1.8	0.4 – 8.4
Smoking Duration, per year	0.94***	0.92 – 0.96	0.9***	0.8 – 0.9

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$

† n = 203