Sociobehavioral and community predictors of unsuppressed HIV viral load: multilevel results from a hyperendemic rural South African population

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Objective: Extensive antiretroviral therapy scale-up is expected to prevent onward transmission of HIV by reducing the overall community viral load. Despite multiple studies about predictors of detectable viral load derived from clinical setting, to date, no study has established such predictors using a population-based viral load survey in a sub-Saharan African hyperendemic setting to inform interventions designed to halt HIV transmission. We used one of Africa's largest prospective cohorts in rural KwaZulu-Natal Province, South Africa, to establish the key sociodemographic, behavioral and community predictors of unsuppressed viral load at the population level.

Methods: We collected 5454 viral load measurements from a population-based viral load survey of 3892 women living with HIV from a rural population during 2011, 2013 and 2014. Multilevel logistic regression models were fitted to examine the risk predictors of unsuppressed viral load.

Results: Among women living with HIV in this population, the prevalence of unsuppressed viral load was 69% in 2011, 58% in 2013 and 53% in 2014. Although time since HIV infection was associated with lower risk for virologic detection [adjusted odds ratio (aOR) = 0.91,0.87–0.94], young women (aOR = 2.59,1.47–4.55) with extensive external migration history (aOR = 1.25,1.02–1.54), greater number of sexual partners (aOR = 1.30,1.02–1.67), and longer history of residing in an HIV incidence hotspot community were more likely to experience unsuppressed viral load (aOR = 1.12,1.06–1.19).

Conclusion: Young women, number of sexual partners, transiency and longer residence in an HIV hotspot community are important determinants of unsuppressed viral load in a hyperendemic rural African setting. To substantially reduce the persistently high transmission potential in these settings, targeted interventions to address these risk factors will be essential for both individual and population health gains.

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Introduction

The ground-breaking research into the positive effects of preexposure prophylaxis, male circumcision and early antiretroviral therapy (ART) [1–3] provides hope for the possibility of reversing the HIV epidemic and moving gradually towards an HIV incident-free world. In particular, a population-based investigation [4] from an hyperendemic rural South African community demonstrated that extensive ART scale-up contributed to a significant decline in the risk of HIV acquisition, raising the possibility of achieving the ambitious goal of ending the HIV epidemic in developing countries by 2020 under the Joint United Nations Programme on HIV/AIDS Fast-Track strategies [5]. However, significant challenges remain to deliver on the promise of 90–90–90 targets (i.e. 90% of HIV-positive people will be diagnosed, 90% of whom will be on ART, and 90% of whom will be virally suppressed), particularly for women in sub-Saharan Africa. It is well established that the risk of HIV acquisition is high among women, particularly young women in South Africa [6,7], with a study suggesting no improvement in crude HIV incidence among this population in this hyperendemic rural community setting in KwaZulu-Natal, South Africa [8].

South Africa's HIV pandemic is one of the most extensive in the world, with approximately 7.0 and 3.4 million people living with HIV [9] and being on ART [10] respectively. The Universal Test and Treat strategy is a powerful concept, but its sustainability requires significant financial resources, which may be difficult to mobilize in financially stressed national health systems that are in the midst of declining HIV donor funding across resource-limited settings [11]. Its implementation, including any hope for successful treatment-as-prevention, requires intervention approaches at multiple levels, includes identifying subpopulations in which the bulk of the HIV transmission potential lies. The recent South African Treatment as Prevention trial [12] aimed to demonstrate the population HIV incidence impact of increasing ART coverage by opening HIV treatment eligibility to all the individuals irrespective of the stage of the disease. However, it failed to increase ART coverage in the intervention arm relative to the control arm, and thus could not show any population incidence impact. This failure underscores the limitations of evidenced-based biomedical HIV prevention strategies that neglect the social and cultural intricacies of real-world community settings.

Considered the gold standard for monitoring the response to ART [13], the viral load level is the single most important biological determinant of onward transmission [14]. Based on that population index, a recent study points to the disappointing trend among women in a hyperendemic rural South African community, where population prevalence of detectable viremia only decreased slightly [15], despite extensive ART scale-up efforts. The current evidence about the needs of women living with HIV demands further investigation to identify the wide-ranging predictors of unsuppressed viral load status across the individual-structural spectrum. To date, few studies from developing country settings [16,17] have investigated the individual sociodemographic, behavioral and nonbiological social predictors of unsuppressed viral load using clinical data. To our knowledge, no study has investigated predictors of unsuppressed viral load using population-based cohort data.

In the current study, we focused on the key individual sociodemographic, behavioral (shortened as 'sociobehavioral') as well as spatial predictors of chronic unsuppressed viral load among women residing in a rural hyperendemic South African community. Based on previous work that examined the risk of HIV acquisition, we choose three key sociobehavioral predictors, namely: number of sexual partners [18], contraception use [19] and external migration history [20,21]. The key community risk predictor considered was exposure to (or residing in) HIV hotspot (high incidence) communities. We previously argued empirically that HIV hotspot communities are a potential priority area for future ART scale-up interventions [22,23]. Hotspot communities are spatial clusters of HIV incidence, identified in previous large-population studies, in which HIV [24–26] and viral load tend to cluster in time and space [15,27]. The findings clearly demonstrated that the risk of HIV-related outcomes also varies in relation to context, warranting multilevel approaches that incorporate predictors across the individual-structural spectrum.

Despite the empirical rationale for studying the risk factors for HIV acquisition, there is little evidence, and no multilevel evidence, that identifies key predictors of unsuppressed viral load in women living with HIV in hyperendemic rural communities outside clinical settings. To find the evidence, we use population-based viral load data, which we have recently shown outperforms facility-based measures in predicting HIV incidence, as it accurately reflects the true underlying viral load distribution within communities [27]. We quantify the sociobehavioral and spatial predictors of unsuppressed viral load among women living with HIV in one of Africa's largest population-based HIV cohorts, which is located in a hyperendemic rural South African community.

Methods

Study area

The study was conducted in the Africa Health Research Institute (AHRI) surveillance area, which is situated in the southern part of the uMkhanyakude District in northern KwaZulu-Natal (KZN) Province, South Africa. The study area consists of 87 000 mainly isiZulu-speaking individuals who live within an area of 438 km^2 in a

predominantly poor rural setting. The area is adjacent to the national road that links the port city of Durban in the south, with South Africa's Mpumalanga Province, as well as Mozambique and Swaziland, to the north. It is a major corridor of both population movement and commercial transportation within South Africa and to southern African countries. The history of surveillance in the area dates back to 2000, this being the first comprehensive investigation designed to monitor the demographic, social and health impacts of the rapid HIV epidemic in rural KZN [28]. The surveillance area is characterized by a persistently high HIV burden among women, with the height of its epidemic in 2004 and 2014 reporting HIV incidence peaking at 7.8 per 100 person-years among women aged 20–24 years [29]. Since 2011, approximately one third of woman aged 15–49 years in the area have been living with HIV [4].

Study procedure

We collected HIV serology data from the AHRI Prevention Intervention Platform (AHRI PIP), which houses the demographic data of consenting adult participants at least 15 years of age who are enumerated annually by trained fieldworkers. Individuals are eligible to participate in the surveillance as long as they are members of a household within the surveillance area, which requires them to have spent at least one night in residence in the 12 months prior to the annual survey. Residents who meet the inclusion criteria are provided with a complete description of the study and are required to provide written informed consent (hereafter labeled the 'AHRI PIP cohort').

HIV serology data, consisting of a status test and viral load measures, were collected annually over 3 years (2011, 2013 and 2014), as was data from a sexual behavior questionnaire, the results of which were used for this current investigation. Approximately 80% of the female participants agreed to be tested and provided a dried blood spot (DBS) sample at least once during 2011, 2013 and 2014. The HIV status of the study participants was based on antibody testing with two parallel rapid tests using HIV-1/HIV-2 ELISA (Vironostika HIV-1 Microelisa System; Biomérieux, Durham, North Carolina, USA and Wellcozyme HIV 1 + 2 GACELISA; Murex Diagnostics Benelux B.V., Breukelen, The Netherlands). The study collected 1914 (2011), 1707 (2013), and 1833 (2014) DBS samples from all 3892 HIV-positive female participants (hereafter labeled 'HIV+ viral load cohort'). The overall proportion of women participated in all three rounds, two of the three rounds, or just one round were 7.5, 25.1 and 67.4%, respectively. Nucleic acid was extracted with NucliSENS EasyMag (bioMérieux, Bordeaux, France), and Generic HIV Viral Load (Biocentric, Bandol, France) was used to measure the viral load levels from the DBS sample participants with confirmed HIV. Separate written informed consent was obtained for specimen storage, with ethical approval being provided by the University of KwaZulu-Natal's Biomedical Research Ethics Committee.

Measures

The primary outcome of the study was virologic detection, defined as a viral load measurement at least 1550 copies/ml, which was analyzed with respect to key sociobehavioral and spatial risk predictors. The viral load cutoff was determined based on the minimum detection limit associated with the assay, as described in detail elsewhere [29]. The data on key sociobehavioral predictors (i.e. sociodemographic background, risky sexual behavior, contraception use, presence of extensive external migration history and number of sexual partners) were drawn from the demography and women general health survey within the AHRI PIP. Similar to a previous study [30], the presence of extensive external migration lifetime history is based on at least 50% of exposure time before HIV acquisition outside the surveillance area.

The main community risk predictor considered was exposure to (or living in) an HIV hotspot. The hypothesis is that neighborhood disadvantage associated with high risk of HIV acquisition is also inherently linked to having unsuppressed viral load. HIV hotspots were spatially constructed in the following steps, as performed previously [25,26]. First, HIV hotspot, or spatial clusters of excess incidence of HIV infection, were identified by summing the HIV incidence for individuals at least 15 years of age in each homestead (from the AHRI PIP cohort) and mapping them in a geographic information system to an accuracy of less than 2 m [25]. The Kulldorff elliptical spatial scan statistic was then used to identify high risk clusters (hotspots) of new infections at the micro-geographical level ($P < 0.05$) using the SaTScan software (Boston, Massachusetts, USA; version 9.1). The exposure to hotspot was also subsequently interacted with time since HIV acquisition to construct an individual-structural predictor that accounted for a person's clinical and community background. The HIV acquisition date was obtained by randomly selecting a time point between the last HIV− and first HIV+ test date, consistent with the previous investigations [30,31]. The first HIV+ test was used if the last HIV− was not available for the viral load cohort.

Analysis

There were three overarching analyses: first, summarizing individual baseline sociobehavioral and spatial characteristics of the HIV+ viral load cohort using descriptive statistics; second, identifying sociobehavioral and spatial predictors of unsuppressed viral load status, based on the cross-tabulation methods using standard Pearson's chi-square (χ^2) test by year; and third, multilevel mixed effects models to establish the above-mentioned risk predictors' link to unsuppressed viral load status over time. Four separate three-level random-intercept models were fitted for the multilevel analyses. Model 1 fitted a null model

without any explanatory variables, Model 2 considered the effect of individual sociobehavioral factors on virologic detection, whereas Model 3 fitted all explanatory variables. Model 4 is the full model that adjusted Model 3 by including interaction terms between time since HIV infection and exposure to hotspot community. Model fit was assessed using Akaike's Information Criterion [32] (AIC), in which the lower values indicate a better fit. Variance and the intraclass correlation coefficient (ICC), which explains the proportion of total variance, were computed for Models 1–4, with STATA 14 (StatCorp., College Station, Texas, USA) being used for all analyses.

Results

Baseline sociobehavioral and spatial characteristics

The baseline female cohort characteristics of the HIV+ viral load cohort ($N = 3892$) are presented in Table 1, with approximately one quarter of the participants ($n = 901$; 23.15%) being under the age of 25. Approximately half reported having 4+ or an unknown number of sexual partners ($n = 1823$; 46.84%), using contraception ($n = 2095$; 53.83%), and extensive external migration history ($n = 1560$; 49.08%). Most reported never being married ($n = 3188$; 81.91%) and having a history of pregnancy ($n = 3537$; 90.88%), with 6.94% ($n = 270$) reporting currently having tuberculosis (TB). As in previous studies [25,26], based on Kulldorff statistic ($P < 0.010$), two regions/sections were identified across the surveillance area [relative risk (RR) = 1.44 & 1.90], with a combined 641 cases (67.97% of all cases) over the 3 years, which showed significant spatial clustering for excess incidence of HIV infection in a peri-urban community living near the national highway (Fig. 1). Approximately one-third of the residents lived in the hotspot communities at baseline in 2011 ($n = 1438$). We detected a higher proportion of women with a greater number of lifetime (or unknown number of) sexual partners residing in hotspots ($P = 0.02$), but found no other baseline sociobehavioral differences in hotspot compared with nonhotspot areas.

Table 1. Cohort baseline characteristics of HIV+ women.

	Overall, $N = 3892$	
	n	%
Age category		
15–19	218	5.6
20–25	683	17.55
26–35	1236	31.76
36–45	887	22.79
46+	868	22.3
Extensive external migration history		
No (i.e. <50%)	2332	59.92
Yes	1560	40.08
Number of sexual partners in lifetime		
0–1	983	25.26
2–3	1086	27.90
4+ or unknown number	1823	46.84
Use of contraception in lifetime		
No	1797	46.17
Yes	2095	53.83
History of pregnancy		
No	355	9.12
Yes	3537	90.88
Marital history		
Marriage in the past	704	18.09
Never married	3188	81.91
Tuberculosis in the last 12 months		
No	3622	93.06
Yes	270	6.94
Residing in HIV hotspot		
No	2454	63.05
Yes	1438	36.95

Sociodemographic, behavioral and spatial predictors of unsuppressed viral load

Overall, the unsuppressed viral load status decreased from 69.02% in 2011, to 58.82% in 2013 and 53.30% in 2014. The risk predictors pertaining to the sociobehavioral and spatial characteristics of unsuppressed viral load status in 2011, 2013 and 2014 are provided in Table 2. During all 3 years, young women (ages 15–19) without a history of pregnancy or marriage consistently had a higher likelihood of unsuppressed viral load status. In contrast to 2011, women residing in spatially identified HIV hotspot communities were more likely to experience unsuppressed viral load status in the later years (2013 and 2014). Figure 2, drawn from Table 2 data, illustrates the unsuppressed viral load status percentage for the above-mentioned significant risk predictors (i.e. age, history of pregnancy and marriage, living in HIV hotspot) over time. These declined in all categories, with considerable improvements being evident among certain women [i.e. young women (ages 15–19), history of marriage, and living outside HIV hotspot]. However, the improvement in unsuppressed viral load status was small or nonexistent among women living in the HIV hotspot over time.

Multi-level analytical models (Models 0–3)

The results of the multilevel regression analyses are provided in Table 3. The ICC from the null model (Model 0) indicates that 7.48 and 65.44% of the variation in virologic detection outcomes are attributed to the differences between neighborhoods and individuals respectively. The results from Model 1, which incorporated only the behavioral explanatory variables, indicated that young women aged 15–19 [adjusted odds ratio (aOR) = 2.56, 95% confidence interval (CI): 1.46–4.50], number of lifetime sexual partners exceeding four (aOR = 1.32, 95% CI: 1.04–2.63), and extensive external migration history (aOR = 1.23, 95% CI: 1.01–1.69) were high risk factors for virologic detection. Time since HIV infection (aOR = 0.95, 95% CI: 0.92–0.98) and a history of pregnancy (aOR = 0.68, 95% CI: 0.48–0.98) were associated with lower risk of virologic detection.

Fig. 1. The study area with high-risk, overlapping elliptical clusters (relative risk = 1.44 and 1.9; $P \leq 0.011$) identified by the Kulldorff statistic in peri-urban communities near the national road [25]. The route continues along the eastern boundary of the surveillance area toward Mozambique. Peri-urban populations (gray-shaded diagonal lines) and urban populations (KwaMsane Township) are indicated on the map.

The results from Model 2, which incorporated both social and individual factors, indicated that exposure to hotspot community (aOR = 1.29, 95% CI: 1.05–1.56) was associated with a higher risk for virologic detection, with the significance of the findings from Model 1 remaining the same. The results of the full Model 3, which incorporated the interaction effects to Model 2, suggests that the effect of residing in hotspot communities

Table 2. Sociobehavioral and spatial predictors of unsuppressed viral load status by observation year.

	2011					2013					2014				
	No, *n*	No (%)	Yes, *n*	Yes (%)		No, *n*	No (%)	Yes, *n*	Yes (%)		No, *n*	No (%)	Yes, *n*	Yes (%)	
Age category					χ^2 (4) = 36.24*					χ^2 (4) = 32.5*					χ^2 (4) = 26.53*
15–19	10	10.53	85	89.47		21	22.83	71	77.17		40	41.67	56	58.33	
20–25	76	23.10	253	76.90		95	34.93	177	65.07		104	38.95	163	61.05	
26–35	199	32.46	414	67.54		199	38.87	313	61.13		242	43.29	317	56.71	
36–45	144	34.04	279	65.96		180	43.37	235	56.63		204	46.79	232	53.21	
46+	164	36.12	290	63.88		208	50.00	208	50.00		266	56.00	209	44.00	
Extensive external migration history					χ^2 (1) = 1.21					χ^2 (1) = 0.58					χ^2 (1) = 0.32
<50%	346	30.03	806	69.97		401	41.99	554	58.01		453	46.08	530	53.92	
≥50%	247	32.41	515	67.59		302	40.16	450	59.84		403	47.41	447	52.59	
Number of sexual partners in lifetime					χ^2 (2) = 4.11					χ^2 (2) = 0.78					χ^2 (2) = 21.53*
0–1	132	32.20	278	67.80		181	42.89	241	57.11		324	52.68	291	47.32	
2–3	166	27.81	431	72.19		210	41.18	300	58.82		240	44.36	301	55.64	
4+ or unknown number	295	32.52	612	67.48		312	40.26	463	59.74		292	43.13	385	56.87	
Use of contraception in lifetime					χ^2 (1) = 3.42					χ^2 (1) = 1.36					χ^2 (1) = 1.64
No	187	27.14	502	72.86		253	41.34	359	58.66		301	45.20	365	54.80	
Yes	276	31.44	602	68.56		256	38.15	415	61.85		320	41.83	445	58.17	
History of pregnancy					χ^2 (1) = 10.02*					χ^2 (1) = 6.57*					χ^2 (1) = 11.24*
No	34	20.00	136	80.00		39	30.00	91	70.00		47	32.87	96	67.13	
Yes	529	31.75	1137	68.25		561	41.56	789	58.44		779	47.44	863	52.56	
Marital history					χ^2 (1) = 9.32*					χ^2 (1) = 12.2*					χ^2 (1) = 18.82*
Marriage in the past	151	37.10	256	62.90		164	49.85	165	50.15		209	56.49	161	43.51	
Never married	428	29.20	1038	70.8		535	39.28	827	60.72		630	43.87	806	56.13	
TB in the last 12 months					χ^2 (1) = 1.93					χ^2 (1) = 0.01					χ^2 (1) = 1.67
No	497	30.18	1150	69.82		644	41.34	914	58.66		771	45.89	909	54.11	
Yes	66	35.11	122	64.89		48	41.38	68	58.62		54	52.43	49	47.57	
Residing in HIV hotspot					χ^2 (1) = 9.26*					χ^2 (1) = 4.19**					χ^2 (1) = 16.36*
No	339	28.75	840	71.25		436	43.21	573	56.79		588	50.30	581	49.70	
Yes	230	35.66	415	64.34		267	38.25	431	61.75		268	40.48	394	59.52	

() after χ^2 is degrees of freedom. TB, tuberculosis.
*$P < 0.01$.
**$P < 0.05$.

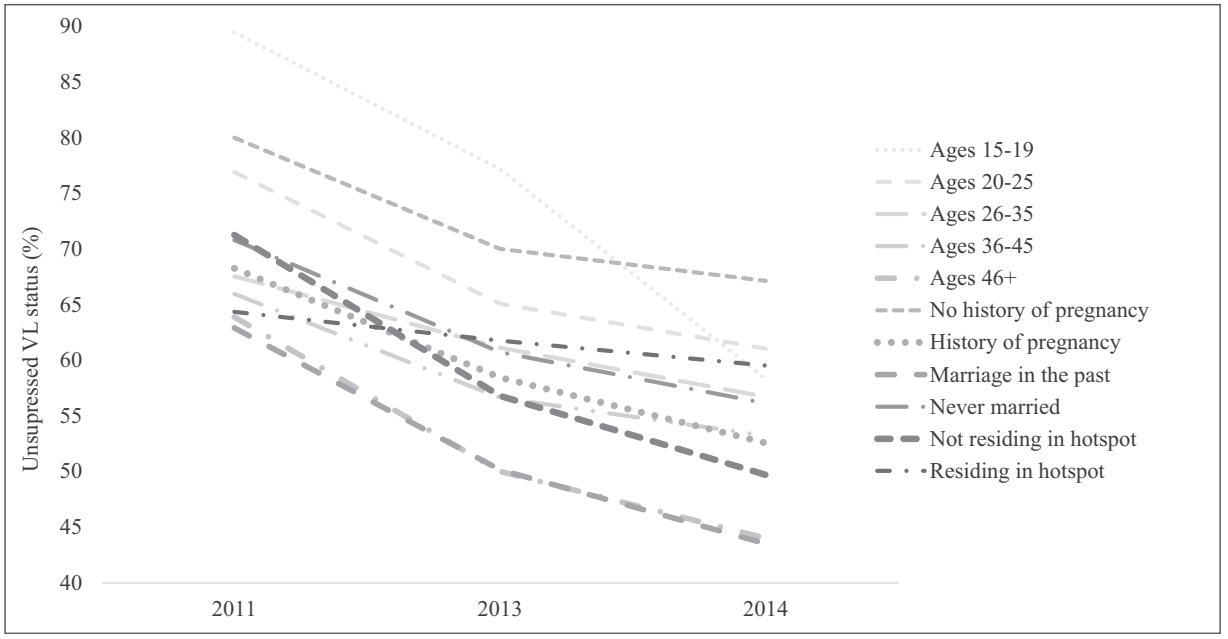

Fig. 2. Proportion of unsuppressed viral load by risk sociobehavioral and spatial categories over years 2011, 2013 and 2014.

is significantly different (aOR = 1.12,1.06–1.19) in those with longer time since HIV infection compared with those with less time from infection, as illustrated in Fig. 3. The ICC of the full model indicated that 19.78 and 50.18% of the variation in virologic detection outcomes are attributed to differences between neighborhoods and individuals respectively, whereas the AIC was the lowest in Model 3.

Discussion

We found certain large segments of the female HIV+ population (i.e. young, without history of marriage/pregnancy, and higher lifetime sexual partners) with high levels of unsuppressed viral load. Unsuppressed viral load poses a serious threat for perpetuating onward HIV transmission. Over 50% of these abovementioned risk subgroups identified in our study remain virally unsuppressed, a concerning figure in comparison with other Southern African Development Community countries, where the prevalence of viral load suppression has been estimated among female HIV+ community in Malawi [33] (72.9%, 95% CI: 69.9–75.9), Zambia [34] (61.3%, 95% CI: 58.7–63.8) and Zimbabwe [35] (64.5%, 95% CI: 62.2–66.7) to be much greater. Stark divergence in the viral load nonsuppression outcome was found, where onward disease transmission potential is perpetuated by individuals with a longer history of HIV who are living in hotspot communities. These findings highlight the importance of multilevel approaches that take individual and community context into consideration. It also necessitates giving urgent priority to providing care to women with at-risk sociobehavioral and spatial profiles to prevent onward disease transmission.

As in our previous studies, which dealt with the issue of the role of hotspot communities on influencing HIV acquisition risk [23,25,26], we found similar results related to viral load, raising further questions about hotspots, particularly regarding perpetuating the HIV challenges among individuals with a longer history of the disease in those communities. Such social challenges inevitably require discussion beyond the biomedical model of HIV. The theory of practice [36,37], also referred to as the theory of social and cultural reproduction, is one of the most influential empirically supported modern social theories on agency-structure dialectic dynamics in the behavior practices, including health-related behavior [38–40], in explaining the intergenerational persistence of social inequality [41]. According to this theory, practices are a consequence of *habitus,* this being the schema and disposition operating below the conscious level in individuals, which develops as a result of constant exposure to social conditions from one's social structural position, within the context of a given field that serves to reproduce existing social structures [38,42]. As described further below, *habitus,* or in this case, disposition for disengagement with local health system to access ART care, may partly help to explain the perpetuation or reproduction of the HIV challenge (i.e. detectable viral load).

The recent Treatment as Prevention trial in this population failed to reduce HIV incidence in the intervention arm likely due to poor linkage to HIV care [12]. This result attests to the complexity of ART uptake

Table 3. Multilevel mixed-effects logistic regression on unsuppressed viral load outcome.

		Bivariate analyses			Model 0 (null)			Model 1			Model 2			Model 3 (full)		
	[Reference]	OR	SE	95% CI	aOR	SE	95% CI	aOR	SE	95% CI	aOR	SE	95% CI	aOR	SE	95% CI
Age category	[46+]															
15–19		4.42*	0.98	[2.87,6.82]				2.56*	0.74	[1.46,4.50]	2.56*	0.74	[1.46,4.50]	2.59*	0.75	[1.47,4.55]
20–25		2.62*	0.37	[1.98,3.47]				2.00*	0.43	[1.32,3.04]	2.01*	0.43	[1.33,3.05]	2.03*	0.43	[1.33,3.08]
26–35		1.76*	0.21	[1.40,2.21]				1.46**	0.27	[1.01,2.11]	1.47**	0.27	[1.02,2.12]	1.47	0.28	[1.02,2.13]
36–45		1.42*	0.18	[1.12,1.81]				1.24	0.22	[0.87,1.76]	1.25	0.22	[0.88,1.77]	1.26	0.23	[0.89,1.80]
Extensive external migration history	Less than 50%															
≥50%		0.92	0.08	[0.78,1.09]				1.24**	0.13	[1.01,1.52]	1.24**	0.13	[1.01,1.51]	1.25**	0.13	[1.02,1.54]
Number of sexual partners in lifetime	[0–1]															
2–3		1.46*	0.17	[1.16,1.83]				1.22	0.16	[0.94,1.56]	1.21	0.15	[0.95,1.56]	1.22	0.15	[0.95,1.57]
4+ or unknown number		1.37*	0.14	[1.11,1.68]				1.32**	0.17	[1.04,1.69]	1.30*	0.16	[1.01,1.66]	1.30*	0.16	[1.02,1.67]
Use of contraception in lifetime	[No]	1.07	0.10	[0.90,1.28]												
Yes								1.09	0.10	[0.90,1.31]	1.08	0.10	[0.90,1.30]	1.07	0.10	[0.89,1.29]
History of pregnancy	[No]															
Yes		0.45*	0.07	[0.33,0.62]				0.68**	0.12	[0.48,0.98]	0.68**	0.12	[0.47,0.97]	0.69**	0.13	[0.48,0.98]
History of marriage	[No]															
Single		1.78*	0.19	[1.44,2.20]				1.19	0.19	[0.88,1.62]	1.16	0.18	[0.85,1.58]	1.15	0.18	[0.85,1.57]
TB in the last 12 months	[No]															
Yes		0.84	0.13	[0.62,1.12]				0.88	0.15	[0.63,1.23]	0.89	0.15	[0.63,1.24]	0.89	0.15	[0.64,1.25]
Time since HIV diagnosis	In years	0.91*	0.01	[0.88,0.93]				0.95*	0.01	[0.92,0.98]	0.95*	0.01	[0.92,0.98]	0.91*	0.02	[0.87,0.94]
Exposure to hotspot	[No]															
Yes		1.15	0.10	[0.97,1.38]							1.29**	0.13	[1.05,1.56]	0.84	0.13	[0.62,1.12]
Interaction (time since HIV and exposure to hotspot)														1.12*	0.03	[1.06,1.19]
Model fit (Models 0-3)																
Variance component for individual-level, σ2 (SE)					2.15 (0.40)			1.63 (0.47)			1.62 (0.47)			1.65 (0.47)		
ICC for individual-level					0.65			0.49			0.49			0.50		
Variance component for community-level, σ2 (SE)					0.25 (0.25)			0.69 (0.33)			0.66 (0.33)			0.65 (0.33)		
ICC for community-level					0.07			0.21			0.20			0.20		
AIC					7056.46			5376.29			5372.49			5359.71		

Reference category in bracket. AIC, Akaike's information criterion; aOR, adjusted odds ratio; CI, confidence interval; ICC, intraclass correlation coefficient; OR, odds ratio; SE, standard error; TB, tuberculosis.
*$P < 0.01$.
**$P < 0.05$.

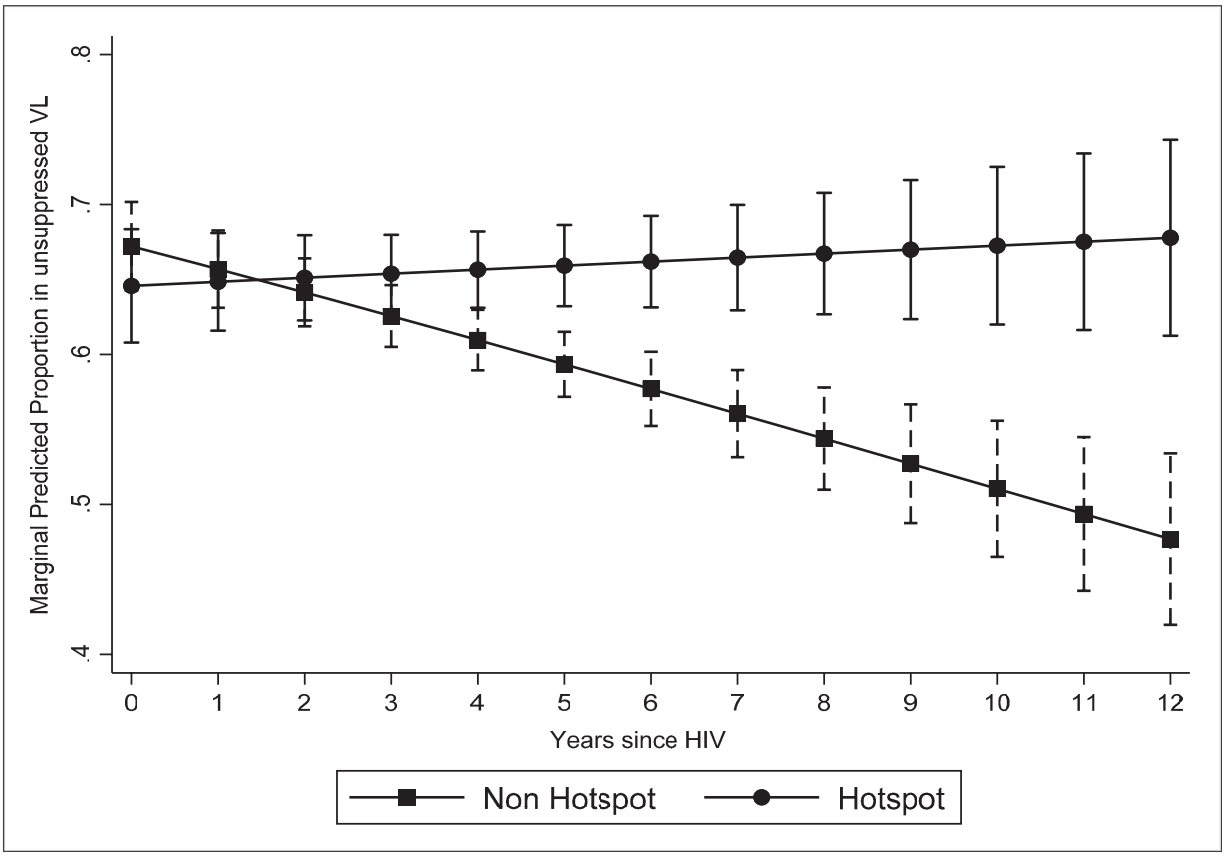

Fig. 3. Marginal predicted proportion with unsuppressed viral load.

in real world settings. Difficulties that impede individual linkages to care (and treatment maintenance [43]) in community settings are, in part, socially constructed factors outside individual's control. Social barriers include the experience of stigmatization of HIV and its treatment [44–46], perception of poor provider practices (e.g. communication, coordination and training) [47], locations of the HIV providers [48] and even sex inequality, which require women to set aside treatment to support their family's wellbeing [49]. *Habitus* is governed by socially and historically situated conditions [38], this being evidenced during the country's predemocracy apartheid era, when women in South Africa were subjected to consuetudinary norms that promoted disparate identities, roles and expectations. It is the persistence of sex inequality in hotspots, we argue, that socially disenfranchises women with a longer history of HIV from seeking obviously needed ART.

We found that sociodemographic (i.e. young women, never married), and behavior factors (i.e. no history of pregnancy, extensive external migration history, higher number of sexual partners) were also important predictors of unsuppressed viral loads. There are very few similar studies from developing countries to compare the results with, with the one from Vietnam drawing its participants from a large number of clinics, where the women were significantly more likely to be divorced/widowed, and less likely to be single [16]. This is in contrast with our study, which may suggest the opposite (i.e. younger, not married, no history of pregnancy), the difference possibly being a consequence of the fact that our study is based on community, not clinical samples. This speaks to potential selection bias, where the younger people in our study are less likely to be represented or connected to ART clinics, which may help to explain the lower likelihood of viral suppression found among young women and those engaged in higher numbers of sexual partners [27].

Our multilevel study is the first to empirically investigate the sociobehavioral and spatially-identified community risk predictors of unsuppressed viral load obtained from HIV hyperendemic rural population settings, which avoids the use of nonrepresentative facility-based sample data. Despite the significant findings, our study has some limitations surrounding ART. As previous investigations demonstrated, high ART coverage in a community contributed to a significant decline in an individual's risk of HIV acquisition [4]. ART coverage across the study area is characterized by spatial heterogeneity both within and outside the hotspot communities. For this current investigation, ART measures obtained through linkage to the health services have not been available since 2013, and we were thus unable to quantify the proportion of the

population that were on ART but had detectable viral load either as a result of drug resistance or poor treatment adherence.

We made the argument, driven by the theory of social and cultural reproduction (i.e. theory of practice), that there is a predisposition towards having an unsuppressed viral load in the hotspots. This raises further question as to whether *hotspots can be eradicated*, and *how policy makers can engage ART uptake among HIV+ women in these socially challenging communities.* One potential solution is to strengthen individual bonds with and integration into community programs that promote conventional activities and relationships [50]. Important explorative and intervention research is currently underway at the AHRI Surveillance Area site, specifically, an NIH-funded trial (Clinicaltrials.gov # NCT03757104) called HITS (Home-based Intervention to Test and Start). This study attempts to test the effect of a cash incentive intervention to improve the uptake of HIV testing and linkage to HIV care. It is theorized that cash transfer can be effective in changing social values and building community through social inclusion and interaction [51]. It is well known that sex inequality [52], including socioeconomic inequality and vulnerability of women [53], are closely linked to HIV. It is possible that empowering women through such community-based interventions can contribute towards addressing persistent HIV challenge in South Africa. Although much work remains to be done to develop appropriate and sustainable community-based interventions in the country, consistent with other studies [54,55], we highlight the need to focus on hotspots as a targeted approach to optimize the allocation of limited resources.

Although many studies of risk predictors of viral load have been derived from clinical settings, our current study is one of the few that identified them in a sub-Saharan African community. This information is crucial for effective population-based interventions to interrupt HIV transmission in hyperendemic community settings. We found that young age, number of sexual partners, transiency, and longer residence in an HIV hotspot community are important determinants of unsuppressed viral load in a hyperendemic rural African setting. To substantially reduce the persistently high transmission potential in these settings, targeted interventions for women living with HIV with these risk profiles will provide important opportunities for interventions to improve both individual and population health.

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Conflicts of interest

There are no conflicts of interest.

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