AIDS and Behavior (2019) 23:2558–2575
https://doi.org/10.1007/s10461-019-02523-7

ORIGINAL PAPER

The Impacts of Residential Location on the Risk of HIV Virologic Failure Among ART Users in Durban, South Africa

Yi-No Chen[1] · Daniella Coker[1] · Michael R. Kramer[1] · Brent A. Johnson[2] · Kristin M. Wall[1] · Claudia E. Ordóñez[3] · Darius McDaniel[4] · Alex Edwards[4] · Anna Q. Hare[5] · Henry Sunpath[6] · Vincent C. Marconi[3,7]

Published online: 2 May 2019

Abstract

Using a case–control study of patients receiving antiretroviral treatment (ART) in 2010–2012 at McCord Hospital in Durban, South Africa, we sought to understand how residential locations impact patients' risk of virologic failure (VF). Using generalized estimating equations to fit logistic regression models, we estimated the associations of VF with socioeconomic status (SES) and geographic access to care. We then determined whether neighborhood-level poverty modifies the association between individual-level SES and VF. Automobile ownership for men and having non-spouse family members pay medical care for women remained independently associated with increased odds of VF for patients dwelling in moderately and severely poor neighborhoods. Closer geographic proximity to medical care was positively associated with VF among men, while higher neighborhood-level poverty was positively associated with VF among women. The programmatic implications of our findings include developing ART adherence interventions that address the role of gender in both the socioeconomic and geographical contexts.

Keywords HIV virologic failure · Social determinants of health · Geographic access to care · Neighborhood socioeconomic status · Gender-specific risk

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10461-019-02523-7) contains supplementary material, which is available to authorized users.

✉ Yi-No Chen
yche465@emory.edu

[1] Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA

[2] Department of Biostatistics and Computational Biology, University of Rochester, Rochester, NY, USA

[3] Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA

[4] Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, GA, USA

[5] Department of Dermatology, Oregon Health and Sciences University, Portland, OR, USA

[6] Infectious Diseases Unit, Nelson Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa

[7] Division of Infectious Diseases, Emory University School of Medicine, Atlanta, GA, USA

Resumen

Utilizando un estudio de casos y controles de pacientes que estaban recibiendo terapia antiretroviral (TAR), llevado a cabo en el Hospital McCord en Durban Sudáfrica, entre 2010 y 2012, buscamos entender cómo el sitio de residencia impacta en el riesgo de falla virológica (FV) de los pacientes. Valiéndonos de ecuaciones estimativas generalizadas para ajustar los modelos de regresión logística, estimamos la asociación de FV con nivel socioeconómico (NSE) y accesibilidad geográfica a los servicios de salud. Luego determinamos si el nivel de pobreza del barrio modifica la asociación entre el NSE individual y la FV. Se observó que para los pacientes habitantes de barrios con niveles de pobreza moderada y severa dos factores se mantienen independientes en su asociación con mayores probabilidades de FV: para los hombres la propiedad de un automóvil y para las mujeres contar con familiares (no incluye la pareja) que pagan sus servicios salud. Para los hombres la cercanía geográfica a los servicios de salud tuvo una asociación positiva con FV mientras que para las mujeres la asociación positiva se dio con un mayor nivel de pobreza del barrio donde habitan. Entre las principales sugerencias programáticas resultantes de esta investigación esta el desarrollo de intervenciones para la adherencia a TAR que incluyan en su diseño las implicaciones del género en los contextos socioeconómico y geográfico.

Introduction

Preventing virologic failure (VF) among people living with HIV (PLHIV) is crucial for ensuring the success of antiretroviral therapy (ART) programs. Numerous studies have demonstrated that VF is associated with acquired drug resistance and adverse clinical outcomes, including mortality [1–3]. In South Africa, 8–23% of patients on first-line ART and 23–35.6% of patients on second-line ART experience treatment failure in 5 years [4–7] and 12 months [8–10], respectively. The number of PLHIV affected by VF is a growing problem in many sub-Saharan African countries due to the extent of the HIV epidemic and the increasing number of patients initiated on ART every year. ART coverage increased from 24% in 2010 to 66% in 2017 (12.9 million people) in eastern and southern Africa [11, 12].

Durban, situated in the South African province with the highest HIV prevalence (18.1%) [13], has one of the largest ART programs in the world. The physical and social environments of the greater Durban area are principally shaped by the lasting effects of discriminatory policies, forced relocation, and further marginalization experienced by Black Africans, Indians and Coloured before and during the Apartheid era [14–17]. Segregated townships created in the periphery of central Durban since the late nineteenth century until the end of Apartheid have been characterized by being impoverished, overcrowded, and deficient in proper housing, basic public services, road networks and public transportation [18–23]. Therefore, understanding how socioeconomic inequality contributes to health disparity is particularly crucial for informing impactful public health interventions [24].

Substantial research has described how socioeconomic status (SES) affects patient access to HIV care [25–27] and adherence to ART [28], a crucial behavioral risk factor for VF. Our previously published case–control study identified automobile ownership and having non-spouse family members pay for medical care as independent individual-level SES risk factors for VF among HIV-positive men and women receiving ART, respectively, in Durban [29]. A study in rural Zambia similarly found owning transportation-related assets to be a barrier to ART adherence [30]. Automobile ownership is often noted as a symbol of status and financial productivity among men [29, 31, 32], many of whom are socially conditioned to establish self-worth from the enactment of self-reliance, often described as hegemonic masculinity ideals, in sub-Saharan African contexts [33]. As a result, men who own automobiles and view it as a trait of masculinity may be less willing to accept their "sick role" of HIV patient, which in turn discourages ART adherence [34, 35]. Furthermore, owning automobiles could come with financial expenditures and social responsibilities that would compete with commitment to HIV care.

On the other hand, financially dependent women, indicated by having non-spouse family members pay for medical care, could experience greater difficulties paying for medications or transportation, which have been associated with decreased ART adherence [36–38]. From a psychosocial perspective, financially dependent women may suffer from depression and poor self-esteem [29, 39], which has also been shown to negatively affect ART adherence [38, 40]. Furthermore, ART adherence and clinic retention for financially dependent women could be limited if the family members financially supporting these women did not view their health as a priority [41].

In addition to individual-level SES, the geographic location of an individual's residence is intrinsically linked with their health. Residential location may not only influence geographic access to care, which in turn could affect utilization of HIV care services [42], but can also affect their social environment. Over the past 20 years, there has been an increased focus on understanding how neighborhood characteristics impact individual health using various nuanced statistical methods including multi-level modeling [43–45]. Although there are studies describing the role of neighborhood-level SES on HIV-related health outcomes [25, 46, 47], they remain limited.

Here, we sought to ascertain how residential location impacts VF risk of ART-treated men and women by determining (1) the associations of neighborhood-level SES and geographic access to care with VF, and (2) if neighborhood-level SES modifies the gender-specific individual-level SES risk factors of VF identified in our previous analysis. Ultimately, we hope to contribute to the growing body of evidence for developing public policies that address socioeconomic and contextual drivers of poor HIV outcomes.

Methods

Study Location, Population and Design

The Risk Factors for Virologic Failure (RFVF) study, a case–control study design with density-type control sampling, was launched between October 2010 and June 2012 at Sinikithemba Clinic (STC), an outpatient HIV clinic at McCord Hospital in Durban, South Africa. Detailed information about the clinic and patient care is described elsewhere [29, 48, 49]. HIV-positive adults (≥ 18 years of age) who received care at McCord Hospital and were on a first-line ART regimen for ≥ 5 months were enrolled [29]. Cases were identified as participants who developed VF (i.e., having a single viral load measurement of > 1000 copies/mL within 1–2 weeks of a visit to the clinic). Two controls were randomly selected for every case enrolled during the same week. Controls were not matched on any known predictors of VF [29, 50]. All participants in this study provided written informed consents upon enrollment.

A survey was administered at enrollment to collect information including demographics, socioeconomic status, and psychosocial factors. The collected data were managed using REDCap electronic data capture tools hosted at Emory University [51]. This study and the secondary analysis were approved by the Office for Human Research Protections-registered Institutional Review Boards at Emory University and the McCord Research Ethics Committee.

Demographic and Socioeconomic Characteristics

The present analysis included a set of individual-level characteristics that were significantly associated with VF in univariate logistic regression models from the previous analysis by Hare et al.: age, gender, non-spouse family members paying for care, automobile ownership, years on ART, education, unemployment, income, dependent living arrangement, and CD4 at enrollment. All selected variables followed the same categorization schemes as the previous analysis [29]. A categorical age variable was created based on tertile cutoffs.

In this study, the term "neighborhood" was used to describe a basic area unit by which the socioeconomic and demographic attributes of residents may be correlated due to mutual geographic proximity. The boundaries of Main Places of the 2011 South African Census were used to define the geographic extent of neighborhoods in this study. Main Place and Sub-Place were level-4 and level-3 geographic hierarchical entities, respectively, within the South African 2011 Census (Fig. 1). Main places generally covered cities, townships or villages, while Sub Places were located inside Main Places and corresponded to sub-villages or suburbs [52].

Neighborhood-level poverty was summarized as percent of households in each Main Place living under the annual income of R9600 (~ $1448 USD as of 1/1/2011), which was the income bracket created by the 2011 Census that was closest to the upper national poverty line—the annual household income of R7400 (~ $1116 USD as of 1/1/2011) after adjusting for the March 2011 inflation rates [53]. The values were populated among participants whose residences were located within the same Main Place. A trichotomous neighborhood-level poverty variable was created by using the tertile cutoffs of the neighborhood-level poverty percentage distribution (i.e., < 22.4%, 22.4–33.9%, > 33.9%). For convenience, these three levels were labeled as low-poverty, moderately poor, and severely poor neighborhoods, respectively.

In this analysis, automobile ownership, non-spouse family members paying for care and neighborhood-level poverty were treated as the SES exposure variables, while age, gender, years on ART, education, unemployment, income, dependent living arrangement, and CD4 at enrollment were treated as potential covariates to be controlled for during modeling.

Geographic Access to Care Indicators

Largely using Google's mapping Application Programming Interface (API), participants' residential addresses collected upon enrollment were initially geocoded to the residential streets whenever possible, or the centroid of the next larger localities (e.g., Sub-place or Main Place). Google Earth Pro was used to finalize the placement of the geographic

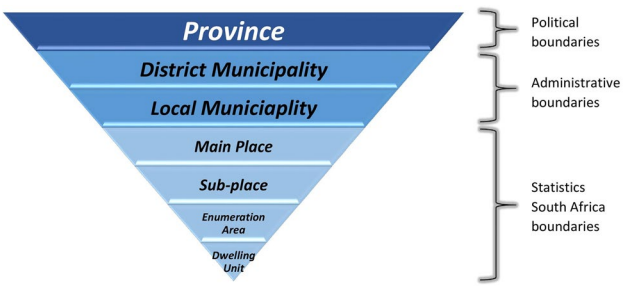

Fig. 1 Hierarchy of geographic frames used by Statistics South Africa in the 2011 Census

coordinates. ArcMap 10.2 was utilized to map the geocoded coordinates of each home residence and of McCord Hospital. The administrative boundary shapefiles of Durban were obtained through Open Africa, an independent open data repository for the African continent maintained and supported by Code for Africa, Amazon Web Services and the World Bank [54]. To reduce distance distortions within the study area, all shapefiles were projected to the Universal Transverse Mercator (UTM) Zone 36S projected coordinate system.

Several distance and time measurements were created to comprehensively indicate participants' geographic access to care. Euclidean distance was calculated as straight-line distances between each home residence and McCord hospital. Measurements of driving distance and time from residential locations to McCord Hospital based on road networks were obtained using the R package "gmapdistance". This package utilizes Google Map API capacities to estimate driving time and distance according to specified parameters including routing preference (i.e., inclusion or exclusion of highways), traffic condition, and departure date and time [55]. A total of two distance measurements and four time measurements were simulated: driving distance via highway-including routes, driving distance via highway-excluding routes, driving time via highway-including routes under pessimistic traffic, driving time via highway-including routes under optimistic traffic, driving time via highway-avoiding routes under pessimistic traffic, and driving time via highway-avoiding routes under optimistic traffic. Since departure date and time could not be set to the past due to technical limitation of the analytic package, it was set to 9/20/2017 at 12 pm, South Africa time. Categorical self-reported travel time (i.e., <30 min, 30–60 min, >60 min) was taken directly from survey responses. To be comparable with self-reported travel time, the Google Map simulated driving times were trichotomized accordingly.

Statistical Analysis

All data were analyzed using SAS 9.4 (Cary, NC). Descriptive statistics described the demographic and socioeconomic characteristics, and the geographic access to care indicators. Gender-stratified and unstratified frequency distributions were compared by case status: Chi square tests and Fisher's exact tests were applied to non-sparse and sparse categorical data, respectively, while two-sample equal variance t-tests and Mann–Whitney U tests were applied to continuous data.

Generalized estimating equations (GEE) fitting logistic regression models quantified associations between exposure and VF while accounting for the possible statistical non-independence among patients residing in the same Main Place. Confidence intervals (CIs) of 95% were used to assess statistical significance for all hypotheses. Collinearity in multivariate models was assessed using the definition of having condition indices ≥ 30 and at least two variables with variance decomposition proportions >0.5.

Univariate models assessed the crude associations of VF with demographic and socioeconomic characteristics and geographic access to care indicators. To further answer our a priori question on how neighborhood-level SES impacts the odds of VF, we developed the following three multivariate parsimonious models.

1. An unstratified model that included three interaction terms between SES exposure variables and gender to quantify the association of VF with neighborhood-level poverty in each gender, and conversely, the association of VF with gender in each neighborhood poverty level.
2. A women-stratified model that included an interaction term between non-spouse family members paying for care and neighborhood-level poverty to quantify the association of VF with non-spouse family members paying for care in each neighborhood poverty level among women.
3. A men-stratified model that included an interaction term between automobile ownership and neighborhood-level poverty to quantify the association of VF with automobile ownership in each neighborhood poverty level among men.

The three parsimonious multivariate models were each built using the following steps: a fully adjusted model was first established to include all ten or as many covariates (i.e., gender, categorical age, years on ART, education, unemployment, income, dependent living arrangement, CD4 at enrollment) as the requirement of non-collinearity would allow, in addition to the pre-specified interaction terms. The categorical age variable was used, in lieu of the continuous age variable, in multivariate modeling to not induce multicollinearity. The Quasi-likelihood under Independence Model Criterion (QIC) was used to assess model fitness. After building a fully adjusted model, we ran the baseline model, which only included the exposure variables and their interaction terms, adjusting for all combinations of covariates until we found the model with the lowest QIC while maintaining relevant effect estimates within 10% change from those from the fully adjusted model. We additionally adjusted for the continuous Euclidean distance to assess whether the association with SES variables were confounded by the geographic proximity to the ART service provider. Percent differences were computed to determine if the effect estimates from the parsimonious model were meaningfully different (i.e., percent difference $>10\%$) than those from the models that adjusted for geographic proximity.

To identify potential geographic predictors of VF, geographic access to care indicators with statistically

significant crude association with VF were selected for multivariate modeling, where the aforementioned modeling technique was followed to establish parsimonious models. Neighborhood-level poverty was included in all of the fully adjusted models that assessed geographic access to care.

Results

Characteristics of Study Participants

There were 457 participants (299 controls, 158 cases) living in 62 Main Places (Fig. 2). On average, each Main Place had 7.4 participants. One male participant's residential location was considered a geographic outlier and subsequently excluded when analyzing geographic access to healthcare

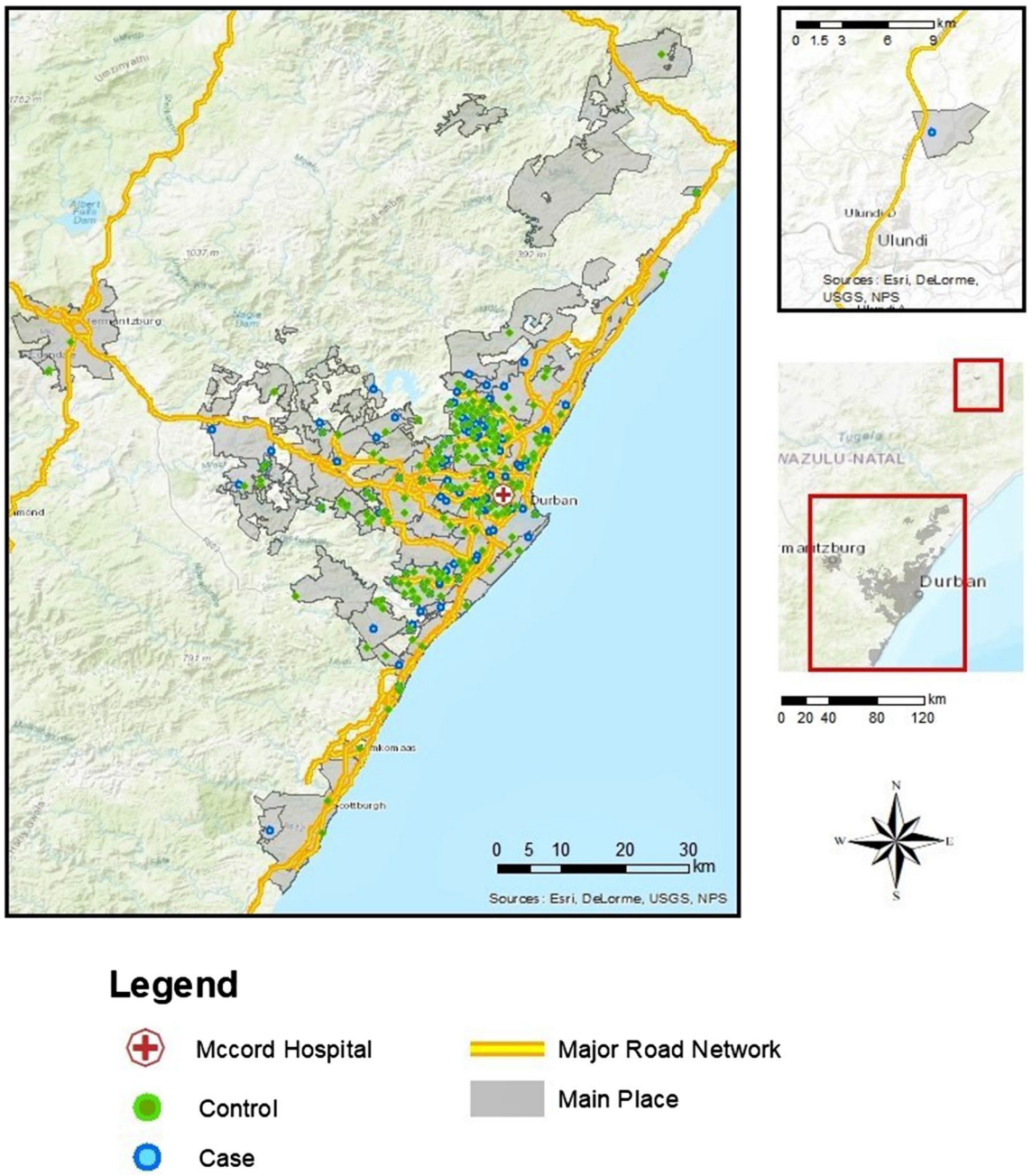

Fig. 2 Spatial distribution of RFVF study participants (n = 457) in Durban, South Africa

in relation to VF. Two large clusters of severely poor neighborhoods were visually identified in the north and south of McCord Hospital (Fig. 3).

On average, the participants lived in Main Places where 28.3% of households lived under the annual income of R9600 (~$1448 USD as of 1/1/2011). Among women, a significantly greater proportion of cases had their non-spouse family members pay for care (30% of cases vs. 13% of controls, $p < 0.001$), suffered from unemployment (31% of cases vs. 19% of controls, $p = 0.027$), had no income (36% of cases vs. 22% of controls, $p = 0.011$), and had dependent living situations (61% of cases vs. 45% of controls, $p = 0.010$) compared to controls. In addition, women cases on average lived in poorer neighborhoods (30.0% of the households in case-containing neighborhoods vs. 27.8% of the households in control-containing neighborhoods under the study-specific poverty threshold, $p = 0.041$). Among men, a significantly greater proportion of cases owned an

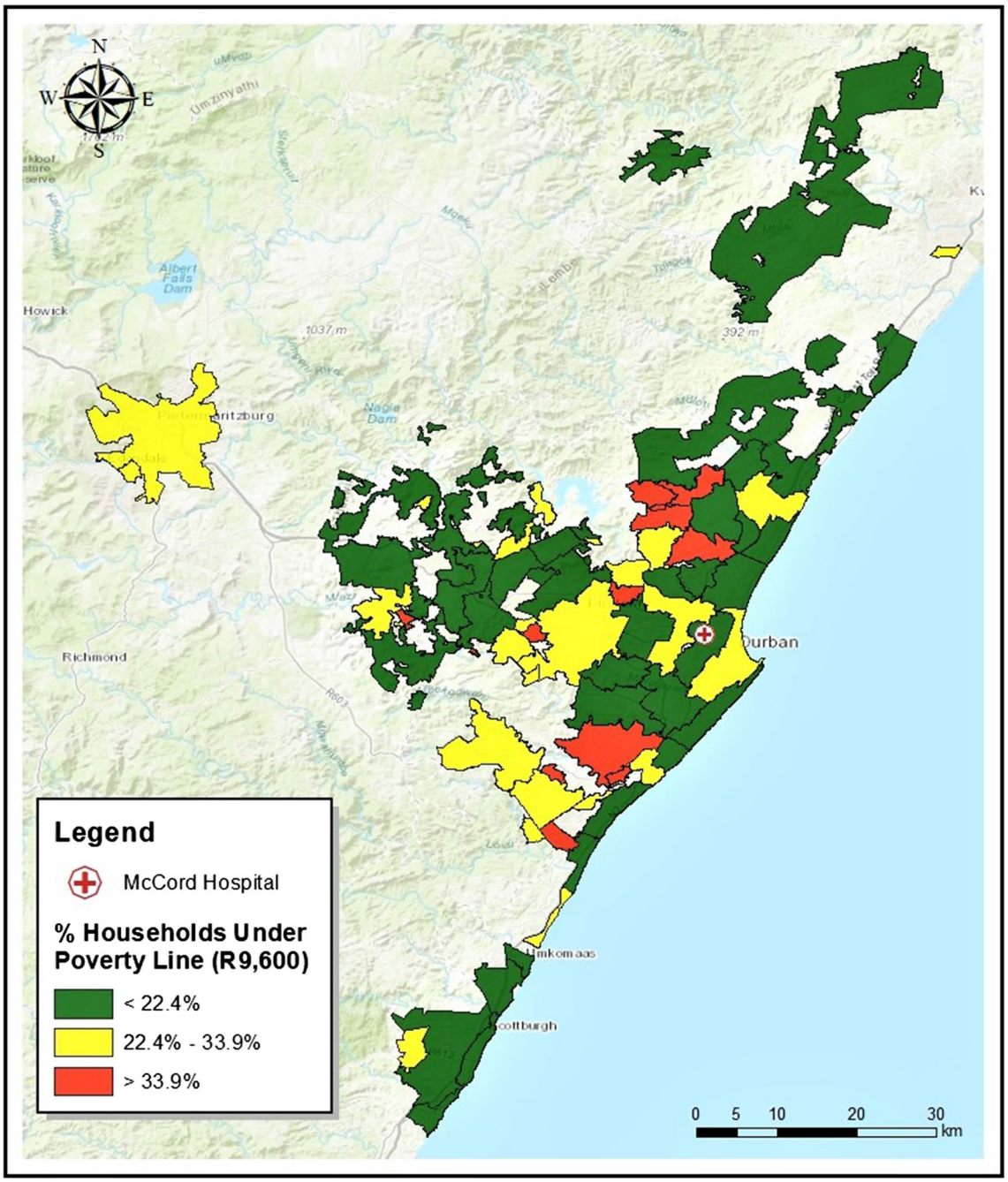

Fig. 3 Spaital distribution of neighnorhood-level poverty in Durban, South Africa (62 main places)

Table 1 Baseline demographic and socioeconomic characteristics stratified by HIV virologic failure status and gender, among RFVF[a] participants in Durban, South Africa

Variable name	Total (N = 457)		Men (N = 162)					Women (N = 295)				
	All (N = 457)		Control (N = 87)		Case (N = 75)			Control (N = 212)		Case (N = 83)		
	Mean/N	SD[a]/%	Mean/N	SD[a]/%	Mean/N	SD[a]/%	p	Mean/N	SD[a]/%	Mean/N	SD[a]/%	p
Gender: male	162	35%										
Non-spouse family members paying for care	67	15%	5	6%	10	13%	0.110*	27	13%	25	30%	< 0.001
Automobile ownership	77	17%	20	23%	31	41%	0.012	17	8%	9	11%	0.442
Neighborhood-level poverty: % poor household	28.3	8.7	28.5	8	27.2	10	0.434*	27.8	8	30.0	9	0.041*
Neighborhood-level poverty[b]							0.606					0.105
Low poverty	154	34%	28	32%	29	39%		77	36%	20	24%	
Moderately poor	143	31%	24	28%	21	28%		69	33%	29	35%	
Severely poor	160	35%	35	40%	25	33%		66	31%	34	41%	
Age	39.1	9.0	41.9	9.5	38.8	7.6	0.049*	40.5	8.90	35.5	8.79	<0.001*
Years on ARV	2.5	2.1	2.4	1.7	2.1	2.3	0.004*	2.9	2.11	2.1	1.95	<0.001*
Education: at least 12 years	242	53%	36	41%	40	53%	0.129	113	53%	53	64%	0.100
Unemployment	87	19%	7	8%	13	2%	0.073	41	19%	26	31%	0.027
No income	98	21%	8	9%	14	19%	0.079	46	22%	30	36%	0.011
Dependent living arrangement	206	45%	29	33%	31	41%	0.293	95	45%	51	61%	0.010
CD4 at enrollment							0.001					<0.001
> 500	87	19%	15	17%	7	9%		55	26%	10	12%	
350–500	105	23%	25	29%	7	9%		61	29%	12	14%	
200–350	138	30%	25	29%	23	31%		66	31%	24	29%	
< 200	127	28%	22	25%	38	51%		30	14%	37	45%	

[a]*RFVF* The Risk Factors for Virologic Failure study; *SD* standard deviation

[b]Low-poverty neighborhoods were defined as neighborhood with < 22.4% of poor households. Moderately poor neighborhoods had 22.4–33.9% poor households. Severely poor neighborhoods had > 33.9% poor households

*Fisher exact *p* value or Mann–Whitney U p-value

automobile than controls (41% of cases vs. 23% of controls, p = 0.012) (Table 1). Other trends and distributions of individual-level demographic and socioeconomic characteristics are described elsewhere [29].

Indicators of geographic access to HIV care did not generally differ by case–control status in either gender (Table 2). Participants, on average, lived about 14.9 km in straight-line distance from the STC at McCord hospital. They were estimated to travel 23.2 km or 21.5 km to reach the hospital on average when they included or avoided highways in their travel routes, respectively. Nearly 84% of the participants reported spending 31–60 min in transit. Depending on traffic conditions and routes (i.e., avoiding highways or not), the participants were estimated to spend 21.5–39.1 min in transit on average.

Associations of VF with Individual-Level and Neighborhood-Level SES Exposures and Gender

The univariate and adjusted associations between covariates and VF are described in Tables 3 and 4, respectively. Neighborhood-level poverty was not significantly associated with VF among men in both univariate and multivariate models. Living in severely poor neighborhood remained associated with increased odds of VF among women after adjusting for individual-level SES and the Euclidean distance to McCord Hospital (AOR 2.14, 95% CI 1.06–4.30, p = 0.033). Compared to women, men were more likely to have greater VF odds in low-poverty (AOR 3.24, 95% CI 1.35–7.75, p = 0.008) and moderately poor neighborhoods (AOR 2.39, 95% CI 1.11–5.12, p = 0.025), but not in severely poor neighborhoods (AOR 1.13, 95% CI 0.51–2.54, p = 0.761), after adjusting for individual-level SES and the Euclidean distance to healthcare (Table 4).

Automobile ownership and non-spouse family members paying for healthcare were independently associated with increased VF among men and women, respectively, in moderately poor ($AOR_{automobile\ ownership}$ 7.30, 95% CI 1.73–30.80, p = 0.007; $AOR_{non\text{-}spouse\ family\ paying\ care}$ 4.35, 95% CI 1.77–10.69, p = 0.001) and severely poor neighborhoods ($AOR_{automobile\ ownership}$ 6.33, 95% CI 4.08–9.82, p < 0.001; $AOR_{non\text{-}spouse\ family\ paying\ care}$ 4.50, 95% CI 2.42–8.33, p < 0.001). The associations between the gender-specific individual-level SES exposure and VF was attenuated in low-poverty neighborhoods (Table 4).

After adjustment of the Euclidean distance, the association size changed significantly between VF and non-spouse family members paying for care among women in moderately poor neighborhood (percent difference = 17%); and automobile ownership among men in low-poverty (percent difference = 10%) and moderately poor neighborhoods (percent difference = 17%) (Table 4).

The Association of VF with Geographic Access to Healthcare

Among men, decreasing continuous distance indicators were generally associated with increased odds of VF (Table 5). The categorical geographic access indicators that consistently showed significant association between VF and travel distance or time in both univariate and multivariate models included: (1) simulated distance with highways-avoiding routes, (2) simulated travel time with highways-avoiding routes under optimistic traffic, and (3) simulated travel time with highways-including routes under optimistic traffic (Table 5). The odd ratios that were related to those three indicators and were statistically significant similarly suggested that men with less travel distance or time had greater odds of VF. On the other hand, no statistically significant association of VF was observed with most of the travel time and distance indicators among women.

Discussion

In this analysis, we hypothesized that residential location affected VF among adults receiving ART and living in the metropolitan area of Durban via geographic access to care and socioeconomic characteristics of the neighborhoods. There were three important findings from this study. First, women living in very poor neighborhoods had an increased odds of VF compared to those living in low-poverty neighborhoods, independent of their geographic access to care and individual SES. Such an association is consistent with results from previous studies that examined neighborhood-level SES and adverse HIV outcomes [47, 56]. Secondly, contrary to our expectation, men with shorter travel distance or time to healthcare had relatively higher odds of VF. These results could imply gender-specific differences in the psychosocial experiences of PLHIV as they navigate their socioeconomic and spatial environments [57, 58]. Finally, we found that the larger socioeconomic contexts modifies the associations between VF and gender-specific individual-level SES risk factors, which attenuated with increasing neighborhood-level wealth.

A possible explanation behind the observed presence and absence of an association between neighborhood poverty and VF among women and men, respectively, could be the gender-based lifestyles and dispositions in South African urban settings, which may shape different responses to their socioeconomic environment [59, 60]. During Apartheid, successful employment for black men was greatly limited to pursuing formal sector jobs in urban areas away from their family members for an extended period of time (e.g. mines and service positions), leaving many black women alone to maintain the household and having to engage in

Table 2 Geographic access to care indicators by HIV virologic failure status and gender, among RFVF[a] participants in Durban, South Africa

Variable name	All (N = 456)		Men (N = 161)					Women (N = 295)				
	Mean/N	SD[a] /%	Control (N = 87)		Case (N = 74)[b]			Control (N = 212)		Case (N = 83)		
			Mean/N	SD[a]/%	Mean/N	SD[a]/%	p	Mean/N	SD[a]/%	Mean/N	SD[a]/%	p
Continuous euclidean distance (km)	14.9	11.0	16.8	13.5	14.0	8.3	0.277*	14.0	10.5	15.7	11.1	0.299*
Continuous simulated distance (km): including highways	23.2	14.0	25.5	16.7	22.0	11.0	0.290*	22.2	13.8	24.3	13.5	0.213*
Continuous simulated distance (km): avoiding highways	21.5	15.4	24.2	18.4	20.3	11.8	0.234*	20.3	15.4	22.5	14.6	0.274*
Euclidean distance							0.967					0.781
≤ 5 km	57	13%	11	13%	9	12%		29	14%	8	10%	
5.1–10 km	106	23%	16	18%	16	22%		52	25%	22	27%	
10.1–20 km	209	46%	44	51%	36	49%		93	44%	36	43%	
> 20 km	84	18%	16	18%	13	18%		38	18%	17	20%	
Simulated distance (including highways)							0.501*					0.031*
≤ 5 km	41	9%	8	9%	6	8%		24	11%	3	4%	
5.1–10 km	35	8%	6	7%	5	7%		13	6%	11	13%	
10.1–20 km	123	27%	19	22%	24	32%		61	29%	19	23%	
> 20 km	257	56%	54	62%	39	53%		114	54%	50	60%	
Simulated distance (excluding highways)							0.382					0.317*
≤ 5 km	42	9%	8	9%	6	8%		24	11%	4	5%	
5.1–10 km	43	9%	7	8%	7	9%		19	9%	10	12%	
10.1–20 km	168	37%	26	30%	31	42%		80	38%	31	37%	
> 20 km	203	45%	46	53%	30	41%		89	42%	38	46%	
Continuous travel time (min): avoiding highways, pessimistic traffic	39.1	20.5	42.6	23.9	37.9	17.3	0.240*	37.3	20.0	40.7	20.1	0.256*
Continuous travel time (min): avoiding highways, optimistic traffic	29.3	17.6	32.6	20.6	27.9	14.7	0.179 *	27.9	17.2	30.5	17.4	0.313*
Continuous travel time (min): including highways, pessimistic traffic	28.0	11.1	29.7	12.6	27.3	9.1	0.262*	27.2	11.5	28.9	10.0	0.238*
Continuous travel time (min): including highways, optimistic traffic	21.5	9.2	23.0	10.3	20.7	7.5	0.218*	20.9	9.5	22.3	8.3	0.205*
Self-report							0.736					0.383*
0–30 min	39	9%	12	14%	8	11%		11	5%	8	10%	
31–60 min	385	84%	69	79%	59	80%		187	88%	70	84%	
> 60 min	32	7%	6	7%	7	9%		14	7%	5	6%	
Categorical travel time: avoiding highways, pessimistic traffic							0.599					0.064
0–30 min	138	30%	26	30%	22	30%		69	33%	21	25%	
31–60 min	265	58%	47	54%	44	59%		126	59%	48	58%	
> 60 min	53	12%	14	16%	8	11%		17	8%	14	17%	
Categorical travel time: avoiding highways, optimistic traffic							0.371*					0.458
0–30 min	274	60%	46	53%	46	62%		133	63%	49	59%	
31–60 min	152	33%	32	37%	24	32%		69	33%	27	33%	
> 60 min	30	7%	9	10%	4	5%		10	5%	7	8%	

Table 2 (continued)

Variable name	All (N = 456)		Men (N = 161)					Women (N = 295)				
			Control (N = 87)		Case (N = 74)[b]			Control (N = 212)		Case (N = 83)		
	Mean/N	SD[a]/%	Mean/N	SD[a]/%	Mean/N	SD[a]/%	p	Mean/N	SD[a]/%	Mean/N	SD[a]/%	p
Categorical travel time: including highways, pessimistic traffic							0.281*					0.597*
0–30 min	272	60%	46	53%	46	62%		131	62%	49	59%	
31–60 min	179	39%	39	45%	28	38%		78	37%	34	41%	
> 60 min	5	1%	2	2%	0	0%		3	1%	0	0%	
Categorical travel time: including highways, optimistic traffic							0.312*					0.344*
0–30 min	381	84%	67	77%	63	85%		184	87%	67	81%	
31–60 min	73	16%	19	22%	11	15%		27	13%	16	19%	
> 60 min	2	0%	1	1%	0	0%		1	0%	0	0%	

[a]*RFVF* The Risk Factors for Virologic Failure study; *SD* standard deviation

[b]One geographic outlier (a male case) was removed

*Fisher exact p-value or Mann–Whitney U p-value

the informal economy in order to afford basic necessities. This trend has continued, in part, among black South Africans with the legacy of socioeconomic inequality inherited from the Apartheid era [61, 62]. Thus, women who spend relatively more time in their neighborhoods and are more financially dependent on individuals other than their spouse, compared to men, could be more affected by neighborhood-associated factors. Furthermore, because of fewer local resources (e.g., food supply, employment opportunities, transportation system, and education) in poorer neighborhoods [63–65], women who may have lower access to such resources than men, could experience greater anxiety and competing responsibilities related to housekeeping and securing a livelihood. This may contribute to women from poor neighborhoods deprioritizing health-seeking behaviors including ART adherence.

In addition, extensive violence in poorer neighborhoods [66] may have greater psychological toll (e.g., depression, fatalistic outlook) on women compared to men [67]. Women are also more likely to encounter sexual and intimate partner violence, which is linked with neighborhood poverty [68]. This could lead them to further acquire present-bias preference such that they overvalue physical safety and compromise the fulfillment of higher-order needs such as committing to ART services and other health-seeking behaviors [45, 50, 69, 70]. Moreover, HIV-positive women in poorer neighborhoods, where gender inequality may be worse, could experience a greater level of stigma—they may be perceived as sex workers or participants in an extramarital relationship [71]. As a result, those women may be more inclined to behaviors that lead to suboptimal ART adherence, such as hiding their HIV status and their medications or taking them inconsistently for fear of disclosure [71–73]. Further research would be required to describe the underlying psychosocial or clinical reasons behind the lack of association between VF and neighborhood-level poverty observed among men in our study.

The association between men and increased odds of VF observed in less poor neighborhoods in this study is consistent with previously published literature, which state that men tend to have worse HIV treatment outcomes than women in many populations [74–77]. Further research is needed to assess whether the attenuated association between men and VF in severely poor neighborhoods was influenced by the greater stigma against HIV-positive women in poorer neighborhoods, which could disproportionately drive up their likelihood of ART non-adherence and therefore narrow the gap of VF risk between men and women in severely poor neighborhoods.

In addition to demonstrating the direct impact of neighborhood-level poverty on VF risk, our study indicated that neighborhood-level SES modifies individual-level SES risk factors in both genders. The attenuated association between

Table 3 Crude association of HIV virologic failure with baseline characteristics

Variable type	Variable name	Men (n = 162)					Women (n = 295)				
		Event	OR[a]	95% CI[a]		p	Event	OR[a]	95% CI[a]		p
Exposure	Non-spouse family members paying for care	75	2.48	0.97	6.36	0.058	83	3.02	1.89	4.82	< 0.001
	Automobile ownership	75	2.31	1.16	4.59	0.017	83	1.36	0.66	2.84	0.406
	Neighborhood-level poverty[b]	75					83				
	Low poverty		ref					ref			
	Moderately poor		0.88	0.54	1.43	0.607		1.58	0.84	3.00	0.159
	Severely poor		0.71	0.35	1.48	0.365		1.98	0.97	4.03	0.059
Covariate	Age (yrs)	75					83				
	< 35		ref					ref			
	35–42		0.70	0.33	1.51	0.363		0.43	0.26	0.72	0.001
	> 42		0.26	0.10	0.72	0.010		0.24	0.12	0.51	< 0.001
	CD4 at enrollment	75					83				
	> 500		ref					ref			
	350–500		0.60	0.23	1.52	0.280		1.10	0.34	3.61	0.871
	200–350		1.95	0.83	4.58	0.123		2.05	0.92	4.56	0.079
	< 200		3.67	1.59	8.46	0.002		6.77	2.54	18.03	< 0.001
	Years on ARV	75	0.90	0.73	1.10	0.308	83	0.82	0.70	0.96	0.013
	Education: at least 12 years	75	1.68	1.09	2.59	0.018	83	1.52	0.85	2.71	0.155
	Unemployment	75	2.31	0.95	5.61	0.065	83	1.88	1.13	3.13	0.016
	No income	75	2.19	0.91	5.24	0.079	83	2.05	1.17	3.60	0.012
	Dependent living arrangement	75	1.49	0.93	2.38	0.094	83	1.95	1.31	2.91	0.001

[a] *OR* odd ratio; *CI* confidence interval

[b] Low-poverty neighborhoods were defined as neighborhood with < 22.4% of poor households. Moderately poor neighborhoods had 22.4–33.9% poor households. Severely poor neighborhoods had > 33.9% poor households

VF and non-spouse family members paying for care among women in low-poverty neighborhoods could suggest that there is no meaningful difference in general health status between financially dependent and independent women in such neighborhoods. Moreover, it could potentially imply that certain psychosocial pathways by which financial dependence influence health-seeking behaviors, such as adhering to ART, among women were limited in low-poverty neighborhoods. For instance, in low-poverty neighborhoods where financially dependent women may feel more empowered, they may not hold a meaningfully greater feeling of mistrust [78] of others including medical care providers, compared to financially independent women. In addition, family members of financially insecure HIV positive women could be more supportive of them utilizing HIV care services in low-poverty neighborhoods possibly due to some evidence of strong social cohesion in those contexts between individuals and their family and friends [79].

On the other hand, the attenuated association between automobile ownership and VF among men in low-poverty neighborhoods could be explained by several possibilities that would require further research. For example, HIV-positive men who owned automobiles in low-poverty neighborhoods may not feel as great of a need to uphold masculinity ideals. Or perhaps expenditures related to owning automobiles were less likely to compete with medical related expenditures among men in low-poverty neighborhoods. Nevertheless, the significant multiplicative and additive interaction between severe neighborhood-level poverty and automobile ownership in affecting VF odds among men as demonstrated in our supplementary analysis (Supplementary Table I) underscores the need for further investigation into the mechanism by which severe neighborhood poverty aggravated the impact of automobile ownership on VF among men. It also highlights the importance of developing effective interventions to target male automobile owners in poor neighborhoods.

In addition, increased effect sizes of the gender-specific individual-level SES risk factors in low-poverty and moderately poor neighborhoods after adjusting for the Euclidean distance suggests the negative confounding effect of geographic proximity to care on these associations in certain communities. Future research may be required to describe the mechanisms by which geographic proximity to care may confound the association between VF and individual-level SES, in relation to neighborhood-level poverty.

Table 4 The adjusted associations of HIV virologic failure with SES[a] exposures and gender

Parameters of parsimonious models[a]	Population	Effect variable	Parsimonious model				The euclidean distance adjustment				
			AOR[a]	95% CI		p	AOR[a]	95% CI		p	% Diff.
G, FPC, NP, AO, A, CE, G×FPC, G×NP, G×AO	Men	Neighborhood-level poverty									
		Low-poverty	ref				ref				
		Moderately poor	0.94	0.44	2.00	0.877	0.95	0.45	2.03	0.899	1%
		Severely poor	0.74	0.30	1.83	0.519	0.75	0.31	1.83	0.526	0%
	Women	Neighborhood-level poverty									
		Low-poverty	ref				ref				
		Moderately poor	1.27	0.61	2.66	0.526	1.29	0.60	2.79	0.515	2%
		Severely poor	2.12	1.07	4.20	0.031	2.14	1.06	4.30	0.033	1%
	Low poverty neighborhoods	Gender: male	3.20	1.36	7.55	0.008	3.24	1.35	7.75	0.008	1%
	Moderately poor neighborhoods		2.37	1.10	5.11	0.027	2.39	1.11	5.12	0.025	1%
	Severely poor neighborhoods		1.12	0.50	2.53	0.780	1.13	0.51	2.54	0.761	1%
A, CE, Y, FPC×NP	Women in low-poverty neighborhoods	Non-spouse family members paying for care	1.95	0.69	5.55	0.211	2.04	0.70	5.99	0.193	5%
	Women in moderately poor neighborhoods		3.72	1.55	8.93	0.003	4.35	1.77	10.69	0.001	17%
	Women in severely poor neighborhoods		4.20	2.27	7.75	< 0.001	4.50	2.42	8.33	<0.001	7%
AO, A, CE, I, AO×NP	Men in low-poverty neighborhoods	Automobile ownership	1.09	0.21	5.83	0.917	0.99	0.20	4.90	0.986	10%
	Men in moderately poor neighborhoods		6.25	1.30	29.96	0.022	7.30	1.73	30.80	0.007	17%
	Men in severely poor neighborhoods		6.03	4.09	8.89	< 0.001	6.33	4.08	9.82	< 0.001	5%

Three multivariate parsimonious models (1 unstratified and 2 gender-stratified models) were illustrated in this table to quantify associations of VF with socioeconomic and demographic risk factors across various travel time and distance adjustments. A geographical outlier (male case) was excluded in the multivariate modeling process

[a]*SES* socioeconomic status; *AOR* adjusted odds ratio; *A* categorical age; *AO* automobile ownership; *CE* CD4 at enrollment; *FPC* non-spouse family members paying for care; *G* gender; *I* income; *N* neighborhood-level poverty; *Y* years on ARV

Table 5 Associations of HIV virologic failure with geographic access to care

Variable name	Men (n = 161[b])									Women (n = 295)								
	Univariate				Multivariate					Univariate				Multivariate				
	OR[a]	95% CI[a]		p	AOR[a]	95% CI[a]		p	Covariates[a]	OR[a]	95% CI[a]		p	AOR[a]	95% CI[a]		p	Covariates[a]
Continuous euclidean distance (km)	0.98	0.95	1.00	0.035	0.97	0.94	1.00	0.036	A, AO, CE, I	1.01	0.99	1.04	0.285					
Continuous simulated distance (km): including highways	0.98	0.96	1.00	0.050	0.98	0.95	1.00	0.049	A, AO, CE, I	1.01	0.99	1.03	0.345					
Continuous simulated distance (km): avoiding highways	0.98	0.97	1.00	0.046	0.98	0.96	1.00	0.020	A, AO, CE, I	1.01	0.99	1.03	0.385					
Euclidean distance																		
≤ 5 km	1.11	0.57	2.20	0.756						0.63	0.09	4.41	0.639					
5.1–10 km	2.17	0.87	5.44	0.098						0.89	0.38	2.09	0.793					
10.1–20 km	0.96	0.38	2.41	0.924						0.86	0.41	1.78	0.678					
> 20 km	ref									ref								
Simulated distance (including highways)									A, AO, CE, N									A, AO, F, N, Y
≤ 5 km	1.16	0.86	1.56	0.332	0.93	0.34	2.51	0.887		0.32	0.03	3.62	0.357	0.51	0.06	4.73	0.556	
5.1–10 km	1.42	0.91	2.22	0.121	0.84	0.29	2.46	0.749		1.81	1.01	3.24	0.048	2.91	1.46	5.77	0.002	
10.1–20 km	2.34	1.20	4.57	0.013	1.57	0.61	4.02	0.345		0.64	0.32	1.26	0.196	0.70	0.37	1.35	0.288	
> 20 km	ref				ref					ref				ref				
Simulated distance (excluding highways)									A, AO, CE, I, N									
≤ 5 km	1.55	1.46	1.64	<0.001	1.23	0.51	2.99	0.650		0.41	0.03	4.92	0.483					
5.1–10 km	2.15	1.12	4.12	0.021	1.48	0.55	3.93	0.436		1.12	0.57	2.22	0.741					
10.1–20 km	3.10	2.43	3.94	<0.001	1.97	1.04	3.71	0.037		0.84	0.45	1.56	0.584					
> 20 km	ref				ref					ref								
Continuous travel time: avoiding highways, pessimistic traffic (per 15-min increment)	0.84	0.70	1.01	0.067						1.14	0.90	1.44	0.289					
Continuous travel time: avoiding highways, optimistic traffic (per 15-min increment)	0.79	0.63	1.00	0.046	0.74	0.56	0.96	0.024	A, AO, CE, I	1.14	0.87	1.50	0.333					
Continuous travel time: including highways, pessimistic traffic (per 15-min increment)	0.73	0.51	1.06	0.095						1.22	0.77	1.94	0.389					
Continuous travel time: including highways, optimistic traffic (per 15-min increment)	0.64	0.41	1.01	0.054						1.28	0.73	2.23	0.385					
Self-report																		
0–30 min	ref									ref								
31–60 min	1.20	0.59	2.46	0.610						0.45	0.16	1.30	0.142					
> 60 min	1.67	0.58	4.84	0.346						0.40	0.09	1.80	0.231					

Table 5 (continued)

Variable name	Men (n = 161[b])									Women (n = 295)								
	Univariate				Multivariate					Univariate				Multivariate				
	OR[a]	95% CI[a]		p	AOR[a]	95% CI[a]		p	Covariates[a]	OR[a]	95% CI[a]		p	AOR[a]	95% CI[a]		p	Covariates[a]
Categorical travel time: avoiding highways, pessimistic traffic																		A, CE, F, N
0–30 min	ref									ref				ref				
31–60 min	1.07	0.58	1.96	0.826						1.26	0.65	2.42	0.492	0.84	0.47	1.51	0.568	
> 60 min	0.70	0.32	1.52	0.368						2.77	1.16	6.59	0.022	2.94	0.95	9.11	0.061	
Categorical travel time: avoiding highways, optimistic traffic									A, AO, CE, Y, I, N									
0–30 min	ref				ref					ref								
31–60 min	0.39	0.27	0.57	<0.001	1.02	0.45	2.32	0.961		1.13	0.55	2.32	0.741					
> 60 min	0.42	0.15	1.19	0.101	0.16	0.04	0.65	0.010		1.93	0.82	4.56	0.134					
Categorical travel time: including highways, pessimistic traffic[c]									A, AO, CE, I									
0–30 min	ref				ref					ref								
31–60 min	0.49	0.31	0.78	0.003	0.67	0.37	1.21	0.189		1.15	0.52	2.54	0.722					
Categorical travel time: including highways, optimistic traffic[c]									A, AO, CE, I									
0–30 min	ref				ref					ref								
31–60 min	0.46	0.23	0.92	0.027	0.45	0.23	0.89	0.022		1.54	0.75	3.18	0.242					

[a]*OR* odds ratio; *AOR* adjusted odds ratio; *CI* confidence interval; *A* categorical age; *AO* automobile ownership; CE CD4 at enrollment; *F* non-spouse family members paying for care; *I* income; *N* neighborhood-level poverty; *Y* years on ARV

[b]One geographic outlier was removed from the men cohort (n = 162) when analyzing geographic access to care

[c]No cases travelled for > 60 min using highway-included routes, which led to technical error message(i.e., generalized Hessian matrix is not positive definite) when running the GENMOD procedures in SAS. Therefore, only two categorical levels (i.e., 0–30 min, > 30 min) were used for computing the corresponding odd ratios

Our study is also unique in that longer travel distance or time was found associated with decreased odds of VF among men. This finding of a so-called distance bias association (i.e., longer travel distance to care is associated with better health outcomes) is in contrast to much of the published literature on geographic determinants of health, which has observed positive relationships between poor geographic access and the risk for adverse health outcomes [80], including HIV VF [81, 82]. There are a few possible reasons that could explain the distance bias association observed in our study but would require further investigation. For instance, patients who were physically capable of traveling farther to access ART services could be healthier or more motivated to remain in care [80]. Moreover, because of prevalent social stigma against HIV patients, those living nearby McCord Hospital could be less willing to access ART services at the HIV clinic, where they risked being recognized by fellow community members [83, 84].

While women may also experience fear of being publicly recognized when accessing nearby health facilities, they could face greater constraints on physical mobility in many low- and middle-income countries [85–87]. For instance, women living further away from the hospital could experience financial constraint for long-distance commutes and thus may not have a greater incentive to access ART services than those living closer. Such a rationale could potentially explain the lack of consistent associations between travel distance or time and VF among women. On the other hand, we do not expect social and cultural norms in urban Durban to meaningfully discourage women's day-time travel to McCord Hospital as in rural regions based on our working experiences with the local populations.

From a programmatic perspective, our findings suggest that a holistic strategy for averting the risk of HIV VF should consider gender-specific barriers to ART adherence associated with one's individual and neighborhood SES. The appropriate short-term individual-level interventions could include providing financially dependent women with economic incentives (e.g., cash payments, prize systems) [88, 89] to encourage care retention and ART adherence. Future research on developing durable, scalable and cost-effective monetary incentives for complex socioeconomic and cultural settings will be required to take full advantage of the benefits of such an intervention on health-seeking behaviors. ART adherence programs in Durban may also benefit from interventions that empower patients to overcome gender-specific HIV-related stigma, sociocultural expectations and present bias preference behaviors due to stressors from the larger surrounding environments or life styles (e.g., gender-specific support groups and motivational counseling).

At a structural level, policy interventions should be developed to promote sociocultural awareness for gender equality, especially in impoverished neighborhoods, and expand vocational opportunities and trainings to encourage financial independence, especially among women. In addition, HIV-positive patients who live near HIV care facilities and are concerned with being stigmatized when accessing ART service could benefit from community-level education campaigns that raise awareness toward people living with HIV [90] and stigma-reduction programs among health workers [91], as well as establishing an ART delivery system that ensures patient confidentiality [92].

One possible limitation to our analysis is the non-differential misclassification bias of the neighborhood-level poverty categorization across the status of VF. Using R9600, as opposed to the published national poverty line (R7400), as the threshold for aggregating counts of poor households per Main Places may lead to the over-estimation of neighborhood-level poverty. Furthermore, the tertile cutoffs from the poor household percentage distribution used for categorizing neighborhood-level poverty may not necessarily reflect true qualitative differences in the neighborhood-level SES across Main Places in Durban. Moreover, the one-time RFVF questionnaire administered at enrollment may not account for possible evolution of patient socioeconomic characteristics during their ART period.

In addition, the accuracy of the geocoded coordinates was limited by Google's address data coverage in Durban at the time of our analysis, as well as participants' recall or data entry error. Subsequently, about 48% of the home residence data were not geocoded to the individual street level. Although such a geocoding uncertainty could lead to non-differential over-estimation or under-estimation of travel time and distance by VF status, overall about three-quarter of the residential addresses were still consistently approximated within the precision of 1 km.

Another limitation related to our GIS analysis is that travel times were simulated under direct, non-commercialized routes, which may not be consistent with the regular routes used by minibuses (the most prevalent transportation method) and may not account for waiting time between minibus stops. Moreover, the travel time simulation was based on the road network and traffic condition in September 2017, which may not reflect true commute experiences that took place before then. This could potentially lead to under-estimation of travel time in a few newly developed communities, such as those close to the M19 and N2 interchange, where viaduct bridges were built in 2012. However, we expect such impacts to be limited based on our field staff's personal commuting experiences in Durban over the past decade. Lastly, patients most likely made various trips to McCord Hospital over time, not necessarily all from their residential locations, after starting ART. Over-simplifying such commute experiences with one-time measurement of travel times may not reflect the true average commute experience.

Conclusions

Recognizing how socio-cultural contexts and the legacy of inequity from Apartheid influence and impact health in South Africa, our analysis aims to improve our understanding of the gender-specific relationship between certain characteristics (individual-level SES, neighborhood poverty and geographic access to care) and the risk of HIV VF among ART-initiated patients in urban Durban. Our findings suggest gender-specific risk factors for VF at both the individual level (i.e., automobile ownership among men in poorer neighborhoods, financial dependency among women in poorer neighborhoods) and contextual level (i.e., closer geographic proximity to medical care among men, higher neighborhood-level poverty among women).

Both structural and individual-level interventions should be considered to improve ART adherence and subsequent treatment outcomes by addressing the psychosocial experiences related to the aforementioned risk factors. Such interventions could include providing monetary incentives for financially dependent women, raising awareness on the gendered health effects of socio-culturally driven behaviors (e.g., toxic masculine behaviors), education campaigns against HIV-related stigma, and improving gender equality in poorer neighborhoods.

Acknowledgements The authors would like to express our utmost gratitude for the patients who participated in the study, our local collaborators (i.e., Sabelo Dladla, Roma Maharaj, Kristy Nixon, Melisha Pertab and Sifiso Shange) who provided crucial assistance for the data collection and analysis, and Dr. Mónica C. Méndez who kindly assisted with the Spanish translation of the manuscript's abstract. In addition, we thank the Sinikithemba Clinic at McCord Hospital in Durban, South Africa for their dedication to supporting research and enhancing the quality of patient care. The success of this study was made possible because of the meaningful contributions from their counsellors, medical records staff, nurses, and medical officers. Lastly, we also thank the Rollins School of Public Health at Emory University for providing technological capacity essential for performing related analyses. This work was supported by the Emory University Center for AIDS Research (CFAR) (V.C.M., P30AI050409); Research and Health Sciences IT Division grant support (V.C.M. UL1RR025008); NIH (V.C.M. R01 AI098558-01A1); Elizabeth Glaser Paediatric AIDS Foundation as part of Project HEART (H.S.); and The Gilead Foundation (H.S.).

References

1. Murphy RA, Sunpath H, Lu Z, Chelin N, Losina E, Gordon M, et al. Outcomes after virologic failure of first-line ART in South Africa. AIDS (London, England). 2010;24(7):1007–12.
2. Hassan AS, Nabwera HM, Mwaringa SM, Obonyo CA, Sanders EJ, Rinke de Wit TF, et al. HIV-1 Virologic failure and acquired drug resistance among first-line antiretroviral experienced adults at a rural HIV clinic in coastal Kenya: a cross-sectional study. AIDS Res Ther. 2014;11(1):9.
3. Petersen ML, Tran L, Geng EH, Reynolds SJ, Kambugu A, Wood R, et al. Delayed switch of antiretroviral therapy after virologic failure associated with elevated mortality among HIV-infected adults in Africa. AIDS (London, England). 2014;28(14):2097–107.
4. Boulle A, Van Cutsem G, Hilderbrand K, Cragg C, Abrahams M, Mathee S, et al. Seven-year experience of a primary care antiretroviral treatment programme in Khayelitsha, South Africa. AIDS (London, England). 2010;24(4):563–72.
5. Fox MP, Cutsem GV, Giddy J, Maskew M, Keiser O, Prozesky H, et al. Rates and predictors of failure of first-line antiretroviral therapy and switch to second-line ART in South Africa. J Acquir Immune Defic Syndr. 2012;60(4):428–37.
6. Nglazi MD, Lawn SD, Kaplan R, Kranzer K, Orrell C, Wood R, et al. Changes in programmatic outcomes during 7 years of scale-up at a community-based antiretroviral treatment service in South Africa. J Acquir Immune Defic Syndr. 2011;56(1):e1–8.
7. Onoya D, Nattey C, Budgell E, van den Berg L, Maskew M, Evans D, et al. Predicting the need for third-line antiretroviral therapy by identifying patients at high risk for failing second-line antiretroviral therapy in South Africa. AIDS Patient Care ST. 2017;31(5):205–12.
8. Fox MP, Ive P, Long L, Maskew M, Sanne I. High rates of survival, immune reconstitution, and virologic suppression on second-line antiretroviral therapy in South Africa. J Acquir Immune Defic Syndr. 2010;53(4):500–6.
9. Murphy RA, Sunpath H, Castilla C, Ebrahim S, Court R, Nguyen H, et al. Second-line antiretroviral therapy: long-term outcomes in South Africa. J Acquir Immune Defic Syndr. 2012;61(2):158–63.
10. Johnston V, Fielding K, Charalambous S, Mampho M, Churchyard G, Phillips A, et al. Second-line antiretroviral therapy in a workplace and community-based treatment programme in South Africa: determinants of virological outcome. PLoS ONE. 2012;7(5):e36997.
11. 17 million people with access to antiretroviral therapy [press release]. Geneva: UNAIDS Global AIDS; 2016.
12. UNAIDS Data 2018. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2018
13. South African national HIV prevalence, incidence and behaviour survey, 2017. Pretoria, South Africa: The Human Sciences Research Council; 2018.
14. Ordóñez CE, Marconi VC. Understanding HIV risk behavior from a sociocultural perspective. J AIDS Clin Res. 2012;3(7):e408.
15. Seekings J. Race, class, and inequality in the South African city. The new Blackwell companion to the city. Malden: Wiley-Blackwell; 2011. p. 532–46.
16. Maharaj B. Apartheid, urban segregation, and the local state: Durban and the group areas act in South Africa. Urban Geogr. 1997;18(2):135–54.
17. Rosenberg LG. A city within a city: vestiges of the socio-spatial imprint of colonial and Apartheid Durban, from the 1870s to 1980s: University of KwaZulu-Natal, Durban; 2012.
18. Mbonambi L, Dlamini Sb. Township renewal: ink case study. eThekweni Municipality, South Africa: Department of Provincial and Local Government, the Development P, Environment and Management Unit, INK Urban Renewal/ABM Programme; 2009.
19. Maharaji A. Umlazi local economic development plan. Ethekwini Municipality, South Africa: KA Economic Development Consulting CC; 2008.
20. Adebayo AA. The rhetoric of transformation and sustainable development in African cities in the era of change: the case of Durban, South Africa. Afr J Rhetor. 2016;2016(8):68–96.
21. Baars L. Township renewal: Kwamashu case study. Department of Provincial and Local Government, Senior Manager: Projects EDU; 2009.

22. Inanda, Ntuzuma, KwaMashu (INK) Nodal Economic Development Profile. KwaZulu Natal, South Africa: Department of Provincial and Local Government; 2006.
23. Marx C, Charlton S. The case of Durban. London: University College London; 2003.
24. Thornton RLJ, Glover CM, Cené CW, Glik DC, Henderson JA, Williams DR. Evaluating strategies for reducing health disparities by addressing the social determinants of health. Health Aff. 2016;35(8):1416–23.
25. Joy R, Druyts EF, Brandson EK, Lima VD, Rustad CA, Zhang W, et al. Impact of neighborhood-level socioeconomic status on HIV disease progression in a universal health care setting. J Acquir Immune Defic Syndr. 2008;47(4):500–5.
26. Walcott M, Kempf M-C, Merlin JS, Turan JM. Structural community factors and sub-optimal engagement in HIV care among low-income women in the Deep South of the USA. Cult Health Sex. 2016;18(6):682–94.
27. Young S, Wheeler AC, McCoy SI, Weiser SD. A review of the role of food insecurity in adherence to care and treatment among adult and pediatric populations living with HIV and AIDS. AIDS Behav. 2014;18(Suppl 5):S505–15.
28. Peltzer K, Pengpid S. Socioeconomic factors in adherence to HIV therapy in low- and middle-income countries. J Health Popul Nutr. 2013;31(2):150–70.
29. Hare AQ, Ordóñez CE, Johnson BA, Del Rio C, Kearns RA, Wu B, et al. Gender-specific risk factors for virologic failure in KwaZulu-Natal: automobile ownership and financial insecurity. AIDS Behav. 2014;18(11):2219–29.
30. Masa R, Chowa G, Nyirenda V. Barriers and facilitators of antiretroviral therapy adherence in rural Eastern province, Zambia: the role of household economic status. Afr J AIDS Res. 2017;16(2):91–9.
31. Hiscock R, Macintyre S, Kearns A, Ellaway A. Means of transport and ontological security: do cars provide psycho-social benefits to their users? Transp Res D. 2002;7(2):119–35.
32. Ellaway A, Macintyre S, Hiscock R, Kearns A. In the driving seat: psychosocial benefits from private motor vehicle transport compared to public transport. Transp Res. 2003;6:217–31.
33. Himmelstein MS, Sanchez DT. Masculinity impediments: internalized masculinity contributes to healthcare avoidance in men and women. J Health Psychol. 2016;21(7):1283–92.
34. Mburu G, Ram M, Siu G, Bitira D, Skovdal M, Holland P. Intersectionality of HIV stigma and masculinity in eastern Uganda: implications for involving men in HIV programmes. BMC Public Health. 2014;14:1061.
35. Nyamhanga TM, Muhondwa EP, Shayo R. Masculine attitudes of superiority deter men from accessing antiretroviral therapy in Dar es Salaam, Tanzania. Glob Health Act. 2013;6:21812.
36. Tuller DM, Bangsberg DR, Senkungu J, Ware NC, Emenyonu N, Weiser SD. Transportation costs impede sustained adherence and access to HAART in a clinic population in Southwestern Uganda: a qualitative study. AIDS Behav. 2010;14(4):778–84.
37. Afolabi MO, Ijadunola KT, Fatusi AO, Olasode OA. Determinants of adherence to antiretroviral drugs among people living with HIV/AIDS in the Ife-Ijesa zone of Osun state, Nigeria. Afr J Prim Health Care Fam Med. 2009;1(1):006.
38. Heestermans T, Browne JL, Aitken SC, Vervoort SC, Klipstein-Grobusch K. Determinants of adherence to antiretroviral therapy among HIV-positive adults in sub-Saharan Africa: a systematic review. BMJ Glob Health. 2016;1(4):e000125.
39. Martikainen P, Bartley M, Lahelma E. Psychosocial determinants of health in social epidemiology. Int J Epidemiol. 2002;31(6):1091–3.
40. Chen W-T, Wantland D, Reid P, Corless IB, Eller LS, Iipinge S, et al. Engagement with health care providers affects self-efficacy, self-esteem, medication adherence and quality of life in people living with HIV. J AIDS Clin Res. 2013;4(11):256.
41. Gugsa S, Potter K, Tweya H, Phiri S, Sande O, Sikwese P, et al. Exploring factors associated with ART adherence and retention in care under Option B + strategy in Malawi: a qualitative study. PLoS ONE. 2017;12(6):e0179838.
42. Lankowski AJ, Siedner MJ, Bangsberg DR, Tsai AC. Impact of geographic and transportation-related barriers on HIV outcomes in Sub-Saharan Africa: a systematic review. AIDS Behav. 2014;18(7):1199–223.
43. Closing the gap in a generation: health equity through action on the social determinants of health: Commission on Social Determinants of Health final report. Geneva: WHO Commission on Social Determinants of Health; 2008.
44. Harper S, Strumpf EC. Commentary: social epidemiology: questionable answers and answerable questions. Epidemiology. 2012;23(6):795–8.
45. Tomita A, Labys CA, Burns JK. A multilevel analysis of the relationship between neighborhood social disorder and depressive symptoms: evidence from the South African National Income Dynamics Study. Am J Orthopsychiatry. 2015;85(1):56.
46. Bloom SS, Urassa M, Isingo R, Ng'weshemi J, Boerma JT. Community effects on the risk of HIV infection in rural Tanzania. Sex Transm Infect. 2002;78(4):261–6.
47. Shacham E, Lian M, Önen N, Donovan M, Overton E. Are neighborhood conditions associated with HIV management? HIV Med. 2013;14(10):624–32.
48. Bateman C. Provincial policy death-knell for iconic McCord Hospital? S Afr Med J. 2013;103(3):140–2.
49. Giddy J. HIV care at McCord Hospital, Durban, South Africa. Ann Arbor, Michigan: Passages; 2005.
50. Marconi VC, Wu B, Hampton J, Ordóñez CE, Johnson BA, Singh D, et al. Early warning indicators for first-line virologic failure independent of adherence measures in a South African Urban Clinic. AIDS Patient Care ST. 2013;27(12):657–68.
51. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377–81.
52. Census 2011 Geography Metadata. World Bank; 2011.
53. Lehohla P. Poverty trends in South Africa: An examination of absolute poverty between 2006 and 2011. Pretoria 2014. Report No.: 03-10-06.
54. About openAFRICA: Code for Africa; 2013 – 2018. https://africaopendata.org/about.
55. Melo RA, Zarruk D. Distance and travel time between two points from Google Maps. 3.3 ed2017.
56. Sheehan DM, Trepka MJ, Fennie KP, Prado G, Madhivanan P, Dillon FR, et al. Individual and neighborhood predictors of mortality among HIV-positive Latinos with history of injection drug use, Florida, 2000–2011. Drug Alcohol Depend. 2015;154:243–50.
57. Denton M, Prus S, Walters V. Gender differences in health: a Canadian study of the psychosocial, structural and behavioural determinants of health. Soc Sci Med. 2004;58(12):2585–600.
58. Hunter M. The political economy of concurrent partners: toward a history of sex–love–gift connections in the time of AIDS. Rev Afr Polit Econ. 2015;42(145):362–75.
59. Strebel A, Crawford M, Shefer T, Cloete A, Henda N, Kaufman M, et al. Social constructions of gender roles, gender-based violence and HIV/AIDS in two communities of the Western Cape, South Africa. SAHARA J. 2006;3(3):516–28.
60. Mantell JE, Needham SL, Smit JA, Hoffman S, Cebekhulu Q, Adams-Skinner J, et al. Gender norms in South Africa: implications for HIV and pregnancy prevention among African and

Indian women students at a South African tertiary institution. Cult Health Sex. 2009;11(2):139–57.
61. Myroniuk TW. Gendered social capital in a Johannesburg Township. Sociol Focus. 2016;49(3):231–46.
62. Bak M. Townships in transition: women's caring keeps the township together. J S Afr Stud. 2008;34(2):255–68.
63. Yen IH, Kaplan GA. Neighborhood social environment and risk of death: multilevel evidence from the Alameda County Study. Am J Epidemiol. 1999;149(10):898–907.
64. Macintyre S, Ellaway A, Cummins S. Place effects on health: how can we conceptualise, operationalise and measure them? Soc Sci Med. 2002;55(1):125–39.
65. Stafford M, Marmot M. Neighbourhood deprivation and health: does it affect us all equally? Int J Epidemiol. 2003;32(3):357–66.
66. Graif C, Gladfelter AS, Matthews SA. Urban poverty and neighborhood effects on crime: incorporating spatial and network perspectives. Sociol Compass. 2014;8(9):1140–55.
67. Almeida Bentes A, Comini César C, Coelho Xavier C, Teixeira Caiaffa W, Proietti FA. Self-rated health and perceived violence in the neighborhood is heterogeneous between young women and men. BMC Public Health. 2017;17(1):967.
68. Copp JE, Kuhl DC, Giordano PC, Longmore MA, Manning WD. Intimate partner violence in neighborhood context: the roles of structural disadvantage, subjective disorder, and emotional distress. Soc Sci Res. 2015;53:59–72.
69. Hennink MM, Kaiser BN, Marconi VC. Pathways to retention in HIV care among U.S. veterans. AIDS Res Hum Retrovir. 2018;34(6):517–26.
70. Wright RJ, Mitchell H, Visness CM, Cohen S, Stout J, Evans R, et al. Community violence and asthma morbidity: the inner-city asthma study. Am J Public Health. 2004;94(4):625–32.
71. Herstad B. Addressing gender issues related to HIV treatment adherence programs. Washington, D.C.: Health Policy Initiative, Task Order I; 2010.
72. Katz IT, Ryu AE, Onuegbu AG, Psaros C, Weiser SD, Bangsberg DR, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. J Int AIDS Soc. 2013;16:1. https://doi.org/10.7448/IAS.16.3.18640.
73. Nyblade L, Pande R, Mathur S, MacQuarrie K, Kidd R, Banteyerga H, et al. Disentangling HIV and AIDS stigma in Ethiopia, Tanzania and Zambia. Washington, D.C.: International Center for Research on Women; 2003.
74. Druyts E, Dybul M, Kanters S, Nachega J, Birungi J, Ford N, et al. Male sex and the risk of mortality among individuals enrolled in antiretroviral therapy programs in Africa: a systematic review and meta-analysis. AIDS (London, England). 2013;27(3):417–25.
75. Barth RE, van der Loeff MF, Schuurman R, Hoepelman AI, Wensing AM. Virological follow-up of adult patients in antiretroviral treatment programmes in sub-Saharan Africa: a systematic review. Lancet Infect Dis. 2010;10(3):155–66.
76. Kipp W, Alibhai A, Saunders LD, Senthilselvan A, Kaler A, Konde-Lule J, et al. Gender differences in antiretroviral treatment outcomes of HIV patients in rural Uganda. AIDS Care. 2010;22(3):271–8.
77. Penot P, Héma A, Bado G, Kaboré F, Soré I, Sombié D, et al. The vulnerability of men to virologic failure during antiretroviral therapy in a public routine clinic in Burkina Faso. J Int AIDS Soc. 2014;17(1):18646.
78. Ross CE, Mirowsky J, Pribesh S. Powerlessness and the amplification of threat: Neighborhood disadvantage, disorder, and mistrust. Am Sociol Rev. 2001;66:568–91.
79. Chipkin I, Ngqulunga B. Friends and family: social cohesion in South Africa. J S Afr Stud. 2008;34(1):61–76.
80. Kelly C, Hulme C, Farragher T, Clarke G. Are differences in travel time or distance to healthcare for adults in global north countries associated with an impact on health outcomes? A systematic review. BMJ Open. 2016;6(11):e013059.
81. Taiwo BO, Idoko JA, Welty LJ, Otoh I, Job G, Iyaji PG, et al. Assessing the viorologic and adherence benefits of patient-selected HIV treatment partners in a resource-limited setting. J Acquir Immune Defic Syndr. 2010;54(1):85–92.
82. Terzian A, Younes N, Greenberg A, Opoku J, Hubbard J, Happ L, et al. Identifying spatial variation along the HIV care continuum: the role of distance to care on retention and viral suppression. AIDS Behav. 2018;22:1–15.
83. Adeneye AK, Adewole TA, Musa AZ, Onwujekwe D, Odunukwe NN, Araoyinbo ID, et al. Limitations to access and use of antiretroviral therapy (ART) among HIV positive persons in Lagos, Nigeria. World Health Popul. 2006;8(2):46–56.
84. Munyaneza F, Ntaganira J, Nyirazinyoye L, Birru E, Nisingizwe MP, Gupta N, et al. Community-based accompaniment and the impact of distance for HIV patients newly initiated on antiretroviral therapy: early outcomes and clinic visit adherence in rural Rwanda. AIDS Behav. 2018;22(1):77–85.
85. Mechakra-Tahiri SD, Freeman EE, Haddad S, Samson E, Zunzunegui MV. The gender gap in mobility: a global cross-sectional study. BMC Public Health. 2012;12(1):598.
86. Babinard J. World bank gender transportation surveys: an overview. Washington, D.C.: The International Bank for Reconstruction and Development, Development TIBfRa; 2011.
87. Jayachandran S. The roots of gender inequality in developing countries. Annu Rev Econ. 2015;7(1):63–88.
88. Bassett IV, Wilson D, Taaffe J, Freedberg KA. Financial incentives to improve progression through the HIV treatment cascade. Curr Opin HIV AIDS. 2015;10(6):451–63.
89. Alsan M, Beshears J, Armstrong WS, Choi JJ, Madrian BC, Nguyen MLT, et al. A commitment contract to achieve virologic suppression in poorly adherent patients with HIV/AIDS. AIDS (London, England). 2017;31(12):1765–9.
90. Unnikrishnan B, Mithra PP, Rekha T, Reshmi B. Awareness and attitude of the general public toward HIV/AIDS in Coastal Karnataka. Indian J Community Med. 2010;35(1):142–6.
91. Batey DS, Whitfield S, Mulla M, Stringer KL, Durojaiye M, McCormick L, et al. Adaptation and implementation of an intervention to reduce HIV-related stigma among healthcare workers in the United States: piloting of the FRESH Workshop. AIDS Patient Care ST. 2016;30(11):519–27.
92. Tran DA, Shakeshaft A, Ngo AD, Rule J, Wilson DP, Zhang L, et al. Structural barriers to timely initiation of antiretroviral treatment in Vietnam: findings from six outpatient clinics. PLoS ONE. 2012;7(12):e51289.