NEIGHBORHOOD-LEVEL DETERMINANTS OF HIV AND CHRONIC DISEASE COMORBIDITY IN A SOUTH AFRICAN URBAN INFORMAL SETTLEMENT

Amy N. Huber

A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Epidemiology in the Gillings School of Global Public Health.

Chapel Hill
2017

Approved by:

Allison E. Aiello

Michael E. Emch

William C. Miller

Audrey E. Pettifor

Annelies Van Rie

ABSTRACT

Amy N. Huber: Neighborhood-level determinants of HIV and chronic disease comorbidity in a South African urban informal settlement
(Under the direction of Allison E. Aiello)

INTRODUCTION

The prevalence of chronic disease and HIV comorbidity is increasing in South Africa and prevention strategies for this context are needed. In order to maintain the health of people living with HIV, it is necessary to move beyond the individual level and consider the characteristics of the neighborhoods and contexts to which the individual belongs.

METHODS

Using cross-sectional data from a randomized community survey conducted in Diepsloot, South Africa, we examined the distribution of HIV, hypertension, diabetes, and obesity, four highly prevalent chronic diseases at the neighborhood level. We mapped the distribution of each level of the HIV care cascade and each chronic disease using the Spatial Scan Statistic to identify hotspot areas. We then conducted a log binomial regression analysis to assess factors associated with 1) living in an area of higher than expected HIV infectiousness; and 2) prevalent chronic disease among those with and without HIV.

RESULTS

Sixteen percent of the study population were living with HIV, 3% (n=42) were diabetic, 29% (n=359) were hypertensive, and nearly 50% (n= 576) of the population was either overweight or obese, with women having a higher prevalence than men (66% vs. 26%). Overall, 9% of the sample was living with HIV and at least one other chronic disease. Overlapping hotspots of

hypertension, diabetes, and obesity prevalence were present and differed from the areas of high HIV prevalence. Individuals residing in a HIV infectiousness hotspot were more likely to be of higher education level (at least secondary school) (Prevalence Ratio=1.43, 95%CI: 1.14-1.78) and unemployed without government grant assistance (PR=1.21, 95%CI: 1.00-1.46). Controlling for other factors, HIV positive participants with a chronic condition were more likely to live less than 300 meters from the nearest supermarket (PR=1.21, 95% Confidence Interval(CI): 0.97-1.51).

CONCLUSIONS

Within a poor urban informal settlement in South Africa, we observed variation between neighborhoods in engagement in the HIV care cascade, level of HIV infectiousness, and chronic disease prevalence suggesting that these conditions have different drivers. Our findings support targeted interventions at the neighborhood level such as HIV testing programs and chronic disease screening as an efficient way to reach those in need of health outreach.

ACKNOWLEDGEMENTS

I would like to acknowledge and thank Dr. Allison Aiello, the chair of my dissertation committee. Dr. Aiello was supportive throughout the proposal and dissertation process and always pushed me by encouraging a high standard. Her support and flexibility to advise me after I left Chapel Hill for South Africa has allowed me to move my career forward while finishing up the PhD.

I would also like to thank my former advisor and committee member, Dr. Annelies Van Rie. Dr. Van Rie supported me during two summer practica at the Witkoppen Health and Welfare Centre where I was able to work with the Mapping Study team to implement a new data collection tool. This experience resulted in Aim 1 of my dissertation and facilitated my understanding of the different neighborhoods of Diepsloot, without which I would not have been able to fully understand the findings of this study.

I would also like to thank the members of my dissertation committee: Dr. Emch, Dr. Pettifor, and Dr. Miller for their time, guidance, and support during the dissertation process.

A special thank you to Jordan Cates, Ruth Link-Gelles, Nadja Violet, Liz Rogawski, Mag Assimon, Ricky Camplain, Sydney Jones, Nancy Colvin, and Valerie Hudock for all of their support during the PhD process.

I would like to thank the residents of Diepsloot for their participation in the study, the Diepsloot Mapping Team, especially Nora West, Colleen Hanrahan, Sheree Schwartz, Rachel Clad and Dr. Jean Bassett. I would also like to thank the Witkoppen Health and Welfare Centre, Right to Care and Clinical HIV Research Unit research team for their contributions.

This study was supported by the National Institute of Allergy and Infectious Diseases at the National Institutes of Health through the Training in Infectious Disease Epidemiology grant (2-T32-AI070114-06). The Diepsloot Household Mapping survey was funded by USAID (award number AID674-A-12-00033, PI: Dr. Jean Bassett).

TABLE OF CONTENTS

APPENDIX 2. FOOD AND ALCOHOL VENDOR ASSESSMENT TOOLé é é ..é é é é é é . 95

REFERENCESé é é é é é é

LIST OF TABLES

LIST OF FIGURES

LIST OF TERMS AND ABBREVIATIONS

ART	anti-retroviral therapy
GIS	geographic information system
GPS	global positioning system
HIV	human immunodeficiency virus
MSM	men who have sex with other men
PREP	Pre-exposure prophylaxis (for HIV)
RDP	Reconstruction and Development Programme
WHO	World Health Organization

CHAPTER 1: BACKGROUND

1. HIV burden (epidemiology of HIV)

Worldwide burden of HIV

HIV was first identified in the 1980s as a disease causing immune deficiency in humans. Untreated cases resulted in death due to opportunistic infections within an average of 5-10 years after acquisition. Transmission of HIV occurs when the virus enters the body and is able to replicate in the hostôs immune cells. Transmission can occur sexually, from mother to child, through untested blood transfusions, or via needle sharing. HIV was quickly identified as an epidemic in high-risk populations in the USA and by the mid-1990s a generalized epidemic was occurring in sub-Saharan Africa. Worldwide, there are an estimated 35.3 million people living with HIV [1].

Sub-Saharan burden of HIV

Sub-Saharan Africa is the region most heavily affected by the global HIV epidemic, resulting in an estimated 23.5 million people living with HIV, representing 69% of the global burden [2]. The sub-Saharan African epidemic is considered to be a generalized epidemic, defined as an epidemic that is self-sustaining through heterosexual transmission [3]. This results in HIV transmission occurring in the general population and not only high-risk groups such as men who have sex with men (MSM) and injection drug users. The majority of cases are transmitted via heterosexual sexual intercourse, with the minority of cases acquired though mother-to-child transmission, MSM sex, and drug use. Main sexual risk factors include inconsistent or incorrect condom use, multiple sex partners, alcohol use [4], intergenerational sex [5], and having

a sexually transmitted infection (STI) [6]. The sub-Saharan region contributes a high level of HIV cases to the world burden, but there is heterogeneity in country-level prevalences (Figure 1.1). Out of the 45 countries in sub-Saharan Africa, 20 have a national prevalence below 2%, 12 between 2% and 5%, 9 between 5% and 15%, and only Botswana, Lesotho, Swaziland and South Africa have national HIV prevalence above 15% [7]. Improvement in treatment access in the region has resulted in a 32% decline in the number of people dying from AIDS-related causes from 2005 to 2011 [2].

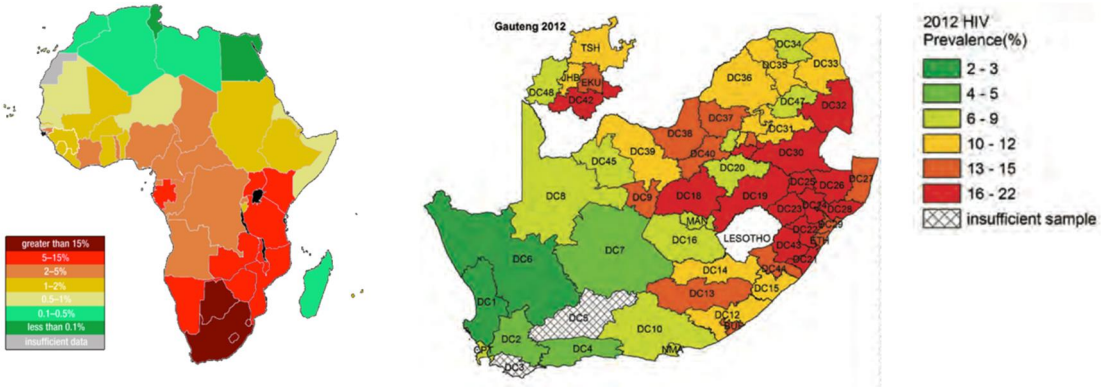


Figure 1.1 HIV prevalence across sub-saharan Africa and South Africa (HSRC, 2012).

South African burden of HIV

South Africa is experiencing one of the largest HIV epidemics in the world. In 2012, the South African Human Sciences Research Council [8] estimated the prevalence of HIV in adults aged 15 to 49 was 18.8%, which translates to over 5 million people living with HIV in South Africa [8]. HIV is most prevalent in black South Africans in early and mid-adulthood, and prevalence peaks at 25.8% in adults between the age of 30 and 34 [8]. Though anti-retroviral treatment is now available country-wide, as many as 64% of deaths for people between the age of 15 and 49 could be attributable to HIV [9].

South African HIV treatment cascade

HIV prevention and testing campaigns were implemented throughout the 2000ôs resulting in increased awareness of HIV status for South Africans. Combination antiretroviral therapy (ART) was made available at government clinics to patients with a CD4 count below 200 in 2004, below 350 in 2011, below 500 in 2015, and the current recommendation it to start ART for a patient regardless of CD4 count (from September 2016 onward).

However, only those who know their status can be treated, with 62% percent of male and 45% of female HIV positive South Africans unaware of their status [8], and many more known positives not receiving adequate treatment, there is a great opportunity to increase the life expectancy and quality of life of HIV positive South Africans. A success of the HIV response in South Africa is that 31.2% of HIV positive South Africans are now on treatment and people living with HIV are now consistently living past middle age. The South African Human Sciences Research Council estimates 43% of people living with HIV above the age of 50 are on ART, though testing rates remain low in this population, with only 55% of those over 50 ever testing for HIV. Among those aged 50+, prevalence of HIV in urban informal settlements is 10% [8].

The HIV treatment cascade provides a framework to quantify stages in HIV treatment service delivery and identify stages in the process from knowledge of HIV status to viral load suppression so that treatment providers can focus resources to areas where HIV positive individuals. Attrition from ART programs is a barrier to reducing community viral load and maximizing the health of those living with HIV. All stages of ART care are at risk for loss [10]. The HIV care cascade is defined inconsistently and includes up to six stages: 1) HIV infected; 2) HIV diagnosed; 3) linked to HIV care; 4) retained in care; 5) on ART; 6) suppressed viral load. Barriers to accessing treatment

need to be minimized in order to increase the number of HIV-positive individuals reaching and maintaining viral load suppression.

Geographical differences in HIV risk/treatment success

Sub-saharan Africa has the highest prevalence of HIV, and the generalized nature of the epidemic results in a large proportion of the population at risk of HIV. However, geographical differences exist on a provincial and district level. Though the national average HIV prevalence (for those age 15-49) is 19%, the nine provinces range from 8% in the Western Cape province to 28% in KwaZulu Natal province. Gauteng province, the center of economic activity and the location of our study, has a prevalence of 18% [8]. Within the provinces, the HIV prevalence also varies based upon community type. Peri-urban areas and residential areas near major roads have been found to have higher HIV prevalence [11]. Within geographic boundaries, HIV risk and treatment outcomes vary by community type. Urban informal areas have higher HIV incidence and prevalence (30% prevalence for those aged 15-49), lower treatment proportion, and lower levels of HIV testing [8]. Additionally, rural areas are underserved for treatment access and when diseases progresses, treatment at tertiary hospitals is difficult to access.

2. Chronic disease

Chronic disease burden

Chronic diseases including diabetes, hypertension, and obesity are increasing in many developed countries. This trend is also beginning to occur in developing countries as residents adopt a western culture. Commonly, individuals have more than one chronic disease at the same time. The literature calls this comorbidity, multi-morbidity, or polymorbidity, with a range of chronic diseases included in their definitions. We define

chronic disease comorbidity as two or more chronic diseases including: 1) cardiovascular disease; 2) renal disease; 3) liver disorders; 4) osteopaenia; 5) endocrine and metabolic abnormalities including insulin resistance and diabetes; and 6) certain cancers.

In this study, we focus on the chronic diseases of diabetes, hypertension and obesity. Each of these diseases is on the pathway to adverse health outcomes such as coronary heart disease, heart failure, and stroke and the prevalence of these conditions is increasing throughout the world. Chronic diseases require ongoing clinical management, either through pharmaceutical intervention (for hypertension and diabetes), or continued medical appointments for obesity. The chronic disease burden on the health care system requires constant contact with the patient. Many of these issues are very difficult to completely resolve, so the many individuals have a drug burden from diagnosis until the end of life. Additionally, we choose to examine diabetes, hypertension, and obesity because the disease endpoints of coronary heart disease, heart failure, and stroke are rare and difficult to accurately measure, especially in low-resource environments.

South African burden of chronic disease

South Africa is a middle-income country with increasing prevalence of chronic disease. The prevalence of overweight or obesity was estimated to be 55% during the last Demographic and Health Survey in 2003 [12], with more recent studies indicating prevalence ranging from 24% to 25% [13, 14]. The estimated prevalence of hypertension is 50% [15]; and diabetes between 9% and 13% [16, 17]. In 2003, it was estimated that 7% of South Africans took chronic medication for hypertension, and two percent took medication for diabetes [12]. These chronic diseases often co-occur in individuals resulting in decreased quality of life and complex treatment regimens.

Individual-level risk factors for chronic disease

Individual-level risk factors for chronic disease include: genetics, tobacco use, unhealthy diet, lack of physical activity, and poor access to preventive care. These risk factors show a strong gender pattern, with the 2003 South Africa Demographic and Health Survey showing that only 24% of men and 14% of women were sufficiently active, with a decline with increasing age [12]. Additionally, the prevalence of inactivity is higher in those living in urban areas, with similar differences with regard to gender.

Increased age is a risk factor for chronic disease. A nationally representative study in South Africa found that while only 9% of those aged 18-49 had two or more chronic conditions, 30% of those aged 50 and above had 2 or more conditions [18]. This is a concern as the HIV positive population ages. Currently, 10% of all people living with HIV are above the age of 50 [1]. Another risk factor for chronic disease is socioeconomic status (SES). Lower SES results in higher risk of developing chronic disease in developed countries. Developing countries are increasingly seeing a similar trend, with some studies indicating SES influence differences by gender in developing countries [19].

One key issue to consider when examining chronic disease comorbidity is the prevalence of obesity, and whether obesity is considered a chronic condition. As women are more likely to be obese, when included in comorbidity measures, the difference in prevalence of obesity can often drive measures of comorbidity that include obesity as a chronic disease since these measures often sum the number of diseases.

Area-level studies

Some potential structural risk factors for chronic disease are: 1) availability of low cost highly refined foods that are high in fat and sugar resulting in a diet consisting of

refined grains, sugar sweetened carbonated beverages, and processed meats [20]; 2) unaffordable healthy diet [21, 22]; 3) affordable motorized transportation; 4) lack of safe and affordable exercise options [12]. Most African studies of chronic disease have not taken any area-level factors into account [13, 15]. If a study does measure an area-level factor, it is commonly urban vs. rural residential area. These studies have consistently found found that individuals living in urban areas more likely to be obese [12, 23].

3. HIV and chronic disease comorbidity burden

HIV and chronic disease comorbidity have potential for significant public health burden

Increased treatment access has increased the life expectancy of people living with HIV [24] and reduced the incidence of AIDS-defining opportunistic infections. Among people living with HIV and on treatment, conditions not directly linked to HIV infection have increasingly dominated as causes of morbidity and mortality.

There is evidence that HIV infection and treatment contribute to the risk of some chronic diseases. Current medical opinion indicates that chronic disease status in people living with HIV reflects a combination of factors: 1) the direct effect of HIV infection and associated inflammation; 2) toxicities resulting from use of certain cART regimens; 3) common behavioral risk factors (tobacco, diet, exercise), individual-level factors, and contextual factors [25]. Although some metabolic conditions can result from ART, ART also decreases inflammation and early and effective treatment can reduce the risk of some chronic conditions. Obesity it is now commonly seen at baseline instead of as an ART side-effect. A study in the US found that among HIV infected individuals on ART, 67% of men and 73% of women had at least two chronic conditions, and in those above the age of 60, this figure increased to nearly 90% [26].

South African burden of HIV and chronic disease comorbidity

An effect of the increased life expectancy of people living with HIV is the incidence of comorbidity of HIV and chronic disease. In South Africa, the literature on prevalence of HIV and chronic disease is predominantly done in small populations, but one nationally representative sample of South Africans over the age of 50 estimated the diabetes prevalence to be 10% regardless of HIV status and the prevalence of hypertension in HIV positive adults to be 76%, which was significantly higher than in the HIV-uninfected group [18]. This same study found that 29.6% of the population had two or more chronic conditions. In another study in rural KwaZulu-Natal, the prevalence of hypertension in a population with 24% HIV prevalence was 11.7% for Stage 1 and 7% for stage 2 and though the prevalence of overweight and obesity was lower in those with HIV, it was still high with 53% of HIV positive women having a BMI over 25 [27].

Gender, age, and low SES are individual-level factors associated with risk of HIV chronic disease comorbidity

In order to determine potential interventions to reduce the incidence of HIV and chronic disease comorbidity, it is important to determine factors associated with HIV and chronic disease in developing countries. However, most African chronic disease comorbidity studies have not taken HIV status into account [13, 15, 23].

Studies examining HIV and chronic disease include one population-based study in rural South Africa where measures of HIV status and chronic diseases allow us to examine the effect of HIV status on individual chronic diseases. The authors found that holding age, gender, education, household wealth, marital status, and place of residence (urban/rural) constant, subjects with positive HIV status had lower prevalence of overweight and hypertension. However, no adjustment was made for disease stage or

treatment status [28]. Another study focusing on urban black women in Johannesburg found lower BMI in HIV+ women compared to those who were HIV-, but those with CD4 counts greater than 345 showed no difference in median BMI from HIV negative women, and had a higher prevalence of obesity [20]. Lastly, a study in rural KZN in a population with 24% HIV prevalence examined chronic disease prevalence by HIV status and concluded that HIV+ individuals have lower BMI and lower prevalence of hypertension than HIV negative individuals, though no adjustment was made for disease stage or treatment duration [27].

Chronic Disease Comorbidity

No African studies have looked explicitly at prevalence of multiple chronic diseases by HIV status. However, a study pooling data from 10 study sites across the USA examined comorbidity in a cohort of HIV+ individuals on ART. This study found a high prevalence of comorbidity, so we can infer that there is likely significant overlap in the chronic diseases reported in other chronic disease prevalence studies [26].

In addition to HIV status, gender is associated with individual-level differences in chronic disease comorbidities. The study also reports that chronic disease comorbidity prevalence differed by gender, with 74% of women and 66% of men presenting with 2 or more chronic conditions, and 12.9 and 8.6% respectively presenting with 5 or more chronic conditions [26].

Lack of studies on area-level differences in HIV chronic disease comorbidity

There is currently insufficient information on area-level differences in studies of HIV and chronic disease in South Africa. This is an important gap in the research because chronic disease prevalence is increasing in South Africa and prevention strategies for this context are needed. One nationally representative study of South

African residents measured urban/rural differences, but did not present findings on HIV and chronic disease stratified by neighborhood type [18]. Studies examining BMI differences in those with HIV compared to those who are HIV negative are inconclusive. A study in a rural population found that regardless of treatment status, individuals with HIV had a lower BMI than those who were HIV negative [27]. Another study of urban black females found BMI only varied for women with low CD4 counts and in HIV positive women with CD4 counts above 345, there was no difference in BMI compared to HIV negative women [20]. One consistent finding in these studies is the high prevalence of obesity in women.

To our knowledge, only one study has examined spatial and neighborhood effects of HIV and chronic disease in South Africa. This study of a rural area in KZN province found a cluster of higher than expected obesity prevalence (85.1% prevalence of obesity compared to mean of 58.4%) in the only urban township in the surveillance area [28]. No hypertension clusters were reported. However, after adjusting for individual-level factors, including HIV status, no clustering of overweight individuals remained. Though this research focused primarily on a rural area, the obesity cluster in the urban township indicates different contextual factors may be occurring in urban areas.

4. Limitations of current HIV and chronic disease control in South Africa

In its current state, the South African public health care system will be unable to absorb the increased patient burden that will come from increased ART and chronic disease burden [29, 30]. The clinics often consist of largely vertical programs focused on HIV treatment but not integrated into other types of health care [31]. Currently, long wait time at clinics is a barrier to viral load suppression and the volume of patients at many clinics exceeds clinic capacity.

5. Neighborhoods and health theory

Structural factors are key to reduce disease burden from HIV in South Africa

HIV/AIDS was the top cause of disease burden in South Africa. Vaccine development has yet to bring a suitable candidate to market, and no cure for HIV is on the horizon. It is well documented that behavioral, biological, and structural factors are major factors in the spread of HIV and chronic disease [8, 32]. Many interventions have been implemented in order to modify individual-level behavior with inconsistent results. In order to maintain health of people living with HIV, it is necessary to consider the characteristics of the neighborhoods and contexts to which the individual belongs. Structural factors such as the safety of the neighborhood, the built environment, and quality of housing contribute to HIV incidence by affecting behavioral mediators and stress, which can increase negative health outcomes such as reduced ART adherence, chronic disease and high HIV risk behavior [33] (Figure 1.2). The recognition that structural factors contribute to HIV and chronic disease has led to a search for structural factors that may provide new options for health interventions.

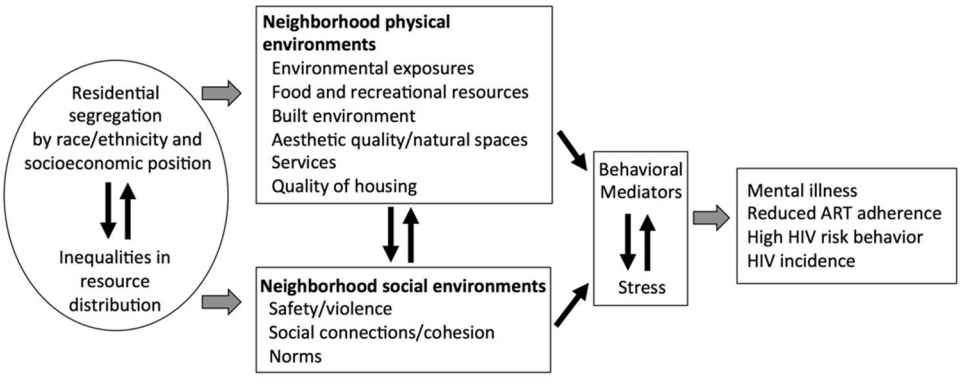


Figure 1.2 Schematic representation of the contributions of neighborhood environments to health inequalities (adapted from Diez Roux, 2010)

The urban environment has disproportionately high HIV prevalence

Currently 60% of South Africans live in urban areas, with urban growth across Africa increasing. As urbanization continues in South Africa, the number of informal settlements located on the edge of urban areas continues to increase [34]. South African residential areas are commonly broken down into three categories: urban, peri-urban, and rural. In addition to these definitions, the history of apartheid in South Africa has added another layer of terminology to the description of residential areas. Under apartheid, racial classes were systematically displaced into suburbs and townships. Black South Africans were relocated to areas referred to as ñtownshipsò or ñlocationsò. Soweto and Tembisa are examples of these all-black residential areas. In this paper, we refer to these areas as townships.

Urban growth promotes inequities through the expansion of deprived settlements and the inability of municipal authorities to respond to the growing demands of an increasing population for basic social and environmental amenities [35]. Contextual factors in South African urban areas include a history of segregation, high levels of unemployment, and a high proportion of national and international immigrants. Those residing in urban informal settlements are most likely to experience challenges in realizing their rights to basic services and access to health care. Residents of these neighborhoods are found to experience challenges in accessing water, sanitation, electricity and refuse collection. These factors have resulted in the urban environments of South Africa have high incidence of violent crime and HIV [8]. The compounding of multiple health determinants can lead to health disparities between urban dwellers and other South Africans.

Neighborhood context can impact the health and wellbeing of individuals

Neighborhood disorder and crime, which are common in urban areas, can result in psychosocial stress, decreased social connectedness and/or mental illness including depression and post-traumatic stress disorder. Furthermore, mental illness has been shown to increase HIV risk behavior [36] and decrease ART adherence [37]. Based upon this pathway, we hypothesize that there is a link between neighborhood context and health outcomes (HIV incidence, treatment outcomes, chronic disease) in African urban areas.

The built environment is one measure of the neighborhood context that could be key to health outcomes [38]. There is evidence from developed countries that the built environment impacts chronic diseases such as obesity [39] and diabetes [40], and infections diseases such as Gonhorrhea [41]. The one available study of the built environment and HIV in South Africa shows that the built environment can impact risk behavior [42].

Although neighborhood-level factors are not usually considered part of national health services infrastructure, evidence-led neighborhood-level interventions have been highlighted as a focus for South African health research. In order for neighborhood-level interventions to be created, it is key for our research to help determine structural level factors that are associated with poor health outcomes.

6. Spatial distribution of disease

Definition and overview of the study of spatial disease distribution

Disease risk and prevalence are not uniformly distributed across populations and instead tend to cluster. These clusters can occur at a variety of levels that can be conceptualized as nesting within one another. These levels range from the individual to the household, community, structural, and geographical level. In recent years,

improvements in Geographical Information Systems (GIS) and an increase in the availability of geographically referenced data have allowed for new methods to geographical disease variation.

Uses of spatial distribution findings

The spatial structure of a disease in a population can affect the persistence, disease dynamics, treatment success, and the cost effectiveness of interventions. With ever-present limits on public health resources, new strategies are essential to optimize interventions. GIS methods offer many benefits to public health research, including the ability to elucidate new associations between the physical environment and health events and to aid in detection of high-risk or underserved populations [43]. Another major advantage of GIS methods is that by mapping the spatial variability of a disease, GIS methods provide information to target limited public health resources, increase efficiency of interventions, and allow programs to create realistic targets in areas of high variability in risk factor or disease prevalence. Lastly, mapped results may speed the implementation of research findings, as policy makers prefer to visualize geographic distribution when deciding on interventions. Through these mechanisms, GIS methods are able to provide many advantages over non-spatial epidemiological approaches.

Current research in developing countries/sub-Saharan Africa/South Africa

Research on HIV treatment and adherence has primarily focused on individual-level determinants with less attention given to higher-level area or neighborhood-level factors. Country-wide HIV prevalence estimates are reported by province and district for South Africa [8] and GIS has effectively been used to examine HIV risk and prevalence by mapping the burden of disease and identifying geographic foci or hot spots [44-49]. Two rural South African research cites have reported the spatial distribution of HIV

prevalence and HIV-related mortality, Agincourt in Limpopo province and the Africa Centre in KwaZulu-Natal province [50, 51]. Studies conducted in rural areas of South Africa and Malawi have found hot spots of higher than expected HIV prevalence near national roads [11, 43]. GIS has also been used to estimate measures of proximity and access to health resources [52], distribution of behavioral risk factors [53], and distribution of stigma [54]. However, few studies have examined neighborhood-level factors with regard to HIV outcomes. A single national-level study conducted in Malawi examined neighborhood-level factors and found that they had influence on HIV prevalence [43].

As HIV transitions into a treatable chronic disease, few studies have examined factors associated with effective treatment or HIV and chronic disease comorbidity. With regard to treatment, a study in Philadelphia found that each level of the HIV treatment cascade had different spatial hot spots [55]. Additionally, a study in rural South Africa assessed ART coverage by SES and found that distance to the clinic was significant, even after adjusting for individual-level factors and urban/rural neighborhood [52]. The spatial and neighborhood-level factors associated with long-term health for urban, HIV positive individuals remain unknown. One clinic-based study assessed the treatment cascade in an urban setting in South Africa, but did not assess spatial variation [10].

7. Limitations of current research

Study population

Sub-Saharan Africa contains the greatest HIV and chronic disease burden in the world and all available information indicates that problem is growing. For this reason, research into geographic factors related to HIV and chronic disease in sub-Saharan Africa has potential for public health impact. However, few studies on this topic have been conducted in developing countries. Of the studies conducted in developing

countries, the majority derive from rural areas. A population-based research site called The Africa Centre has conducted most of the research into spatial determinants of disease in South Africa. However, this rural site cannot represent the urban South African population because there are different contextual factors. For example, findings from rural areas mainly report proximity to national roads as significant, but this finding does not translate to a well-connected urban environment [11, 43]. Though sub-Saharan Africa is rapidly urbanizing, no studies have conducted an in-depth analysis of the neighborhood-level effects of an urban township on HIV and chronic disease.

Study design and measures

Many of the studies conducted on this topic are cross-sectional studies, with a dearth of longitudinal studies, especially with regard to neighborhood-level factors. There is also limited information on how geographic factors relate to access to and retention in HIV care. Many treatment-focused studies are RCT or clinic-based research cohorts. The absence of a population-based recruitment strategy restricts the ability to analyze community-level factors and makes it impossible to measure barriers to health care in these populations, since they have both awareness and access to health services.

Spatial scale of data

When conducting spatial analysis, health outcomes are frequently aggregated to geographical scales that are too large to be used for detailed analysis of health determinants. This can be due to concerns about confidentiality, or lack of GIS coding of data during collection. These aggregated units do not allow for analysis at the scale of the process of interest and variability at the local level is lost when district, provincial, or national measures are averaged [44]. This is sometimes called the ñeverywhere is nowhereò problem, when the variation is so high that few local communities represent

the average at the aggregate level. When this is the case, no inferences can be made at a level below the aggregated scale, and factors operating at the local level will be overlooked.

Neighborhood-level analysis

The majority of studies only measure and adjust for individual-level exposures, covariates, and outcomes. If neighborhood-level data is analyzed, the variable is often an aggregate measure based on self-report from individual study respondents, instead of a neighborhood-level measure collected from community spaces by trained research staff. Additionally, few studies have a framework for the mechanism of the spatial factors on individual health, a gap that has been highlighted by field leaders [33].

Research on HIV treatment has focused primarily on the negative effects resulting from inadequate treatment with less attention to given to factors that shape adherence, both at the individual and community level. Most of the research on this topic has been out of one rural area with high HIV prevalence. This research will provide new evidence from a different highly mobile population that better represents the vulnerable highly mobile urban residents.

8. Conclusions

Urban areas now house more than 50% of total residents in developing countries, with this trend expected to continue for the foreseeable future. NCDs, HIV, and HIV/NCD comorbidity prevalence is higher in urban areas compared to rural areas. Neighborhood and contextual factors have been shown to impact individual health. There is a lack of granularity in most of this research, with place of residence only coded as either urban or rural, or no adjustment for any neighborhood-level factors. To

successfully reduce the rate of comorbidity, distribution and determinants in the urban population need to be described.

We have a unique opportunity to look at a diverse urban community with a variety of neighborhood- and individual-level indicators measured with a geographically randomized sampling method. We look within an urban township to measure factors that are associated with comorbidity in this high-risk increasingly common community type.

CHAPTER 2: RESEARCH DESIGN AND METHODS

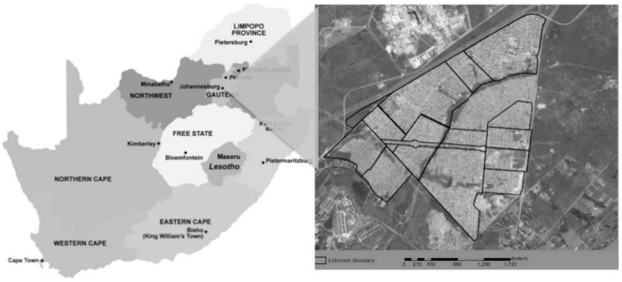
1. Overview of study design and populations

Study population

Diepsloot is a township on the northwestern periphery of Johannesburg, South Africa, with a population of over 500,000 residing in an area of approximately 12 km^2 (Figure 2.1). Housing varies between the 13 neighborhoods and is a mixture of corrugated iron shacks, Reconstruction and Development Programme (RDP) houses, and bonded houses. Access to municipal service varies, with some neighborhoods fully electrified and supplied with indoor plumbing, while others are highly informal with little access to electricity and water access at community taps. Access to health care within Diepsloot is limited to two overburdened public clinics and the nearest public tertiary hospital is 30 kilometers away.

The population is 61% female, 100% black race, and 29% of the population is youth between the age of 20 and 29 years [56]. Twenty two percent of the population is unemployed, and a further 61% are employed in informal or temporary employment. Diepsloot has high levels of crime and violence, with 87% of the population feeling unsafe or very unsafe at night [56].

Figure 2.1 Location of Diepsloot within South Africa.



South Africa Diepsloot, Gauteng Province, South Africa

Study design

The data derive from the Diepsloot Community Mapping Project (USAID Innovations Grant AID-674-A-12-00033) which took place from May 2013 to March 2014. The overall aim of the study was to quantify the disease burden and to develop a geographic risk profile for Diepsloot, South Africa. The study design was a cross-sectional community assessment of the prevalence of health factors in Diepsloot. At study initiation, the burden of HIV, TB, and other chronic diseases was not well understood for this population.

Using GIS software, 2000 GPS points were randomly placed within the residential area of Diepsloot. Study outreach teams drove into Diepsloot and approached an adult member of the household closest to the GPS point. If there was no household within 30 meters of the GPS point, this was noted and the point was not used. If the adult member of the household agreed to participate, all household members aged 15 and above were enumerated and one was randomly chosen to participate in the interview.

The enrollment criteria for the study were:

Inclusion criteria

- Consenting adult household members (Ó18 years)
- Adolescent and child household members aged 7-17 years from whom assent is obtained and for whom consent is given by a parent or legal guardian.
- Children <7 years in the household who are the children or legal ward of an adult participant for whom parental/guardian consent is given.

Exclusion criteria

- Individuals in any household declining initial enumeration
- Unable to understand consent document in English, Zulu or Sesotho.
- The randomly selected survey participant is unavailable after five visits by the survey team.
- The randomly selected survey participant declines participation in the study.
- Children under 18 years without parent or legal guardian consent.
- Households headed by a child. A child is defined as anyone aged less than 18 years.
- Adults or children who are psychologically or physically (e.g. drunk) unable to provide informed consent were excluded.

Informed consent was conducted and the participant was enrolled to participate in a once-off interview and health assessment. If the enumerated household member was female, had children and gave consent, a child health assessment was conducted on each child. The outreach teams, composed of a nurse and an HIV counselor, measured HIV status, urine glucose, blood pressure, BMI, and conducted a questionnaire including questions about demographic factors, socioeconomic status, health history, behavioral HIV risk factors, HIV care initiation for each study participant.

Once the data collection was complete, responses were entered into an MS Access database, checked for logical inconsistencies, and collapsed into categories for analysis. All HIV antibody test results were double checked for accuracy with the source documents before the database was closed.

2. Data collection and measurement

The following information was collected for consenting participants in the Diepsloot Community Mapping Project:

HIV status:

HIV status was measured using self-reported result of last HIV test and finger prick rapid HIV test using a Determine Rapid antibody test. Participants were able to choose one of four HIV testing options:

1) Receive HIV counselling and testing with the survey team and receive the result immediately;
2) Receive HIV counselling and testing with the survey team and receive the result at Witkoppen clinic;
3) Receive pre-test HIV counselling with the survey team and provide an anonymous sample for research purposes only- the participant was not able to later find out the result;
4) Refuse HIV testing.

Fourty-seven participants self-reported HIV positive status and refused HIV antibody testing. We include these participants in the HIV positive category, but do not include those who self-report HIV negative status but refuse HIV testing as being negative, they are considered to be of unknown HIV status.

HIV care initiation and ART adherence:

For participants self-reporting a HIV positive status, the following questions were asked during the interview: type of HIV treatment, date of ART initiation, last CD4 count, adherence to treatment, clinic where treatment occurs.

Body mass index (BMI):

We defined overweight or obese status based upon height and weight measurements conducted by study staff at the time of the interview. Study staff measured height and weight for all participants. BMI was then calculated as: weight (kg) / height $(m)^2$. BMI was categorized into the following categories [57]:

- Underweight: < 18.5
- Normal: 18.5ï 24.9
- Overweight: 25.0ï 29.9
- Obese: 30.0+

Urine glucose:

Diabetes status was measured by self-report and by urine glucose measured from a urine dipstick value. A urine dipstick value of of 2.8 mmol/L or greater was classified as ñabnormalò and an indicator of diabetic status. We defined participants as diabetic if they self-reported a diabetes diagnosis, self-reported taking diabetes medication, or had an abnormal urine glucose measure at the time of the interview.

Hypertension:

Hypertension was measured by self-report and blood pressure reading. Study staff measured resting blood pressure three times with an arm cuff. The mean of the three measures was calculated for systolic and diastolic measures. High blood pressure was defined as a mean systolic measure of 140 millimeters of mercury (mmHg) or greater and/or a mean diastolic measure greater or equal to 90 mmHg. We defined participants as hypertensive if they self-reported a hypertension diagnosis, self-reported taking

hypertension medication, or if the average of three consecutive blood pressure measures at time of interview were above 140/90.

Demographic information:

Demographics were measured by self-report during the interviewer-administered questionnaire which measured gender, age, country of origin, education, employment, relationship status, socioeconomic indicators, and health history. Age was measured in years and analyzed as either a continuous variable or categorized as: 15-29, 30-39, 40-49, or 50-94. Country of origin was collected and then collapsed into South Africa or Other. Level of education was categorized as: Primary or less, Some secondary/completed secondary, or Tertiary/Trade school. Employment status was categorized as: Formal employment, Informal/Self/Temp employment, or Unemployed. Relationship status was categorized as: Married, Not married but living with partner, Not living with partner, No partner. Socioeconomic indicators including household income, household assets, and food security were asked.

The following health history questions were asked for each chronic disease reported during the interview:

1. Has a health care worker ever told you that you have (chronic disease)?
2. Have you seen a doctor in the last 12 months for (chronic disease)?
3. Do you currently take any medications for (chronic disease)?

Behavioral HIV risk factors:

The following behavioral HIV risk factors were measured with an interviewer-administered questionnaire: 1) number of sexual partners in last 12 months; 2) concurrency of sexual partners (number of months of overlap in last 12 months); 3) HIV

status of sexual partner (HIV positive, HIV negative, don't know); 4) age of sexual partner (years); 5) condom use (average condom use and condom use at last sex act); 6) alcohol use before sex (yes/no).

Neighborhood aesthetic and built environment information:

Neighborhood aesthetic information was collected by trained staff for each visit point by a visual analysis by a trained staff member (Appendix 1). The staff member would stand in the road outside of the enumerated house and choose from predetermined categories to measure the number of trees, presence of wastewater, presence of streetlights, and the predominant housing type in the area. For this portion of data collection, participants did not give any information, it was only collected outside of the private residence by study staff. Additionally, the GPS point for all alcohol vendors, food vendors, and neighborhood facilities including clinics, schools, churches, police stations, and taxi ranks (Appendix 2).

3. Specific Aim One: To assess the built environment of an informal urban South African township.

Study design

There is a growing interest in the role of the built environment on health, but most built environment data collection tools are developed for use in the US or Europe. We compared the gain in insight in contextual factors using the newly developed tool to characterize the built environment of Diepsloot to the information available through census data as well as more traditional measures of contextual factors such as individual data on ownership of assets, employment, housing materials, access to water

and electricity. This information will guide the collection of neighborhood-level information for future epidemiological research in poor urban settings in Africa.

Assessment of variables

We compared three data sources for their ability to measure neighborhood characteristics (Table 2.1):

1) *Built Environment Measurement Tool*- Data collected from a data collection tool specifically created to measure the built environment in an urban South African township
2) *Individual-level information from Diepsloot Mapping Study*- Data collected from individuals consenting to the Diepsloot Community Mapping Project
3) *South African Census data*- Data on 177 Enumeration Areas (the smallest geographical area (piece of land) into which the country is divided for census) within Diepsloot collected during the 2011 South African census

Table 2.1 Overview of neighborhood characteristics collected from three data sources.

	Data collection method 1	**Data collection method 2**	**Data collection method 3**
	Data collected with Built Environment Measurement Tool	**Individual-level information from Diepsloot Mapping Study**	**Data available at Census Enumeration Area level for Diepsloot (n=122) from South African Census**
Housing type/material	Predominant housing type	Type of main dwelling and construction material	Type of main dwelling and construction material Estimated value of property
Water	Presence of waste water	Main source of drinking water	Access and reliability of piped water
Sewage	Presence of waste water	Shared toilet facilities	Toilet facilities
Refuse	Presence of trash on streets	Refuse disposal	Refuse disposal
Lighting	Presence of street lights	Household electricity	Household electricity
Additional information	Presence of trees		

Analysis

Digital geographic data from the City of Johannesburgôs Geographic Information Systems (GIS) department was used to define community boundaries. The Transverse Mercator Hartebeesthoek projection was used to ensure distance measurements were accurate. We used the 13 extensions (Diepslootôs neighborhoods) as the unit of analysis for the spatial analysis of neighborhood aesthetics.

Principal Components Analysis

To determine if the information obtained by the newly developed data collection tool corroborates or provides additional information not measured by aggregating individual-level information that obtained by individual-level questionnaires and individual-level South African Census data, we first aligned the information spatially to the neighborhood and then compared the prevalence of each neighborhood characteristic of interest. Because the neighborhood aesthetics information collected by the three data sources were not directly comparable, we conducted a principal components analysis for each of the three data sources to obtain a meaningful and comparable index. For the principal components analysis, we first rank ordered each item of each data source from ñlowerò to ñhigherò aesthetic. For example, no streetlights and overflowing piles of rubbish in a neighborhood were scored lower, and having streetlights and little rubbish in the streets were scored higher. Next, the data structure for each data source required adjustment to the covariance matrix to ensure the assumptions were met in the principal components analysis. We used a polychoric covariance matrix for the binomial and categorical information obtained by the Built Environment Measurement Tool and the Diepsloot Mapping Study individual-level survey data. No adjustments to the covariance matrix were needed for the South African

Census data as the information was continuous. We then used the principal axis method to extract the components, followed by varimax (orthogonal) rotation. We determined the number of meaningful components in several ways. First, the eigenvalue-one criterion was applied in order to retain and interpret any component with an eigenvalue greater than 1.00. We next conducted a scree test to identify components that group above breaks in the plot. We examined the common variance and assessed whether any of the components identified by the eigenvalue of the scree test method accounted for less than 5% of the variance. To ensure we had meaningful components, we assessed the overlap and interpretability of the solutions found by the different methods applied. We next removed any factors that loaded on multiple neighborhood variables and reviewed the remaining components with loadings greater than 0.40. Finally, we computed the variability-weighted component score and computed the average index score for each neighborhood for each of the three data sources. We then compared the neighborhood ranking for each of the three data sources using the Spearman's rank correlation coefficient to assess whether neighborhoods were ranked similarly by the three data collection methods.

4. Specific Aim Two: Explore the spatial distribution and role of contextual factors in HIV prevalence in an urban informal settlement in South Africa

Study design

Using cross-sectional data collected in 2013-2014 from a GIS randomized community survey, we estimates the distribution of HIV-seropositive individuals across Diepsloot using the Spatial Scan Statistic. Based on these data, we are able to identify hotspots of HIV infectiousness. This information provides an estimate of the level of HIV clustering across areas of Diepsloot. We also performed an exploratory analysis of the

spatial distribution at three phases of the HIV treatment cascade: diagnosis, retention, and treatment. Based on these results, we are able to assess the possible role of contextual factors on the HIV care cascade.

Assessment of variables:

Outcomes

The main outcomes of interest were neighborhood HIV prevalence, neighborhood HIV infectiousness, and neighborhood coverage of the steps of the HIV care cascade.

HIV status

All participants who did not self-report a known positive HIV status were offered an HIV test. Participants who agreed to test were given three options: home-based test with immediate test results, home-based test with disclosure of results at clinic on the following day, or anonymous testing for research purposes. Participants were categorized as HIV positive if they self-reported to be HIV positive or had a positive rapid HIV antibody test; HIV negative if they had a negative rapid HIV antibody test; or HIV status unknown if they self-reported a HIV negative or unknown status but refused the rapid HIV antibody test.

HIV infectious

We classified a participant as infectious if they were: a) newly diagnosed as HIV positive at the time of the interview; b) self-reported being HIV positive and not on ART; or c) self-reported being HIV positive and not adherent to ART.

HIV care cascade levels

We categorized a participant as being in care if they self-reported that they were receiving regular care for HIV. HIV positive participants were considered eligible for ART if their most recent self-reported CD4 count was Ò350 cells/ε l. We categorized participants as being on treatment if they self-reported being on ART. We categorized participants as adherent on ART if they self-reported that they followed their treatment schedule over the previous four days.

Exposure

Our exposure variable was the 13 neighborhood (called extensions) within Diepsloot. Digital geographic data from the City of Johannesburgôs GIS department were used to define community boundaries. The 13 neighborhoods vary with regard to service delivery (some receive electrical power while others do not) and housing material (some are predominantly informal while others are made of concrete blocks). Because neighborhoods of a similar size allow for better estimation of the variation in HIV outcomes, we divided the five largest, most populous neighborhoods (Extensions 1, 2, 4, 6, and 7) into smaller sub-extensions.

Missing data on HIV status

We report the proportion of study participants who refused the HIV antibody test and compare those consenting to the HIV antibody and those refusing the HIV antibody test on demographic factors including: age, gender, education status, employment status, country of origin, and marital status by using a chi-squared test. We explored imputing HIV status for those refusing the HIV antibody test with multiple imputation.

Analysis

We used chi-square tests to compare age, gender, education status, employment status, country of origin, and marital status between those with a known HIV status and unknown HIV status.

We assessed the spatial distribution of HIV outcomes using the ArcGIS geographic information system (GIS). We used the spatial clustering analysis in SaTScanÊ (Martin Kulldorff, National Cancer Institute) [58, 59] to identify clusters of higher than expected prevalence by creating a circular window of various sizes to scan the study area. For each window, the number with the HIV outcome inside the window was compared to those outside of the window and a likelihood ratio test was used to evaluate the statistical significance of each potential hotspot. We used a spatial-only design with discrete Poisson distribution, maximum cluster size of 50% of the population at risk, and limited the clusters to those with no geographical overlap.

We used a log binomial model to examine whether age, gender, level of education, employment status, currently living with partner, alternative care in last 12 months, alcohol consumption, country of origin were associated with residing in a hotspot of HIV infectiousness. All covariates that were significant at a p-value of Ò0.10 when examining their relationship with the outcome were entered into the adjusted model. These variables were age, gender, level of education, employment status, currently living with partner, alcohol consumption. Covariates not significantly associated with the outcome at p-value < 0.05 were eliminated from the model one at a time, creating the final, adjusted model. An alpha level of 0.05 was selected as the level of statistical significance to make final inferences from the adjusted model.

5. Specific Aim Three: Explore the spatial distribution and role of contextual factors in co-morbidity of HIV and chronic disease in Diepsloot, South Africa

Study design

Using the same 2013-2014 cross-sectional dataset from a GIS randomized community survey, we examined the distribution of HIV, hypertension and obesity, three highly prevalent chronic diseases in urban South Africa. We first mapped the distribution of each chronic disease, both individually and as co-morbidities, using the Spatial Scan Statistic to identify hotspot areas. We then estimated the magnitude of individual and contextual factors on chronic disease comorbidity using multilevel models by assessing the association between density and distribution of healthy food vendors and chronic disease comorbidity.

Assessment of variables

Outcome

The main outcome of interest was HIV and chronic disease comorbidity, which was defined as having HIV and one or more of the following conditions: diabetes, hypertension, or a BMI (body mass index) greater than 25.

We defined participants as HIV positive if there was a positive result on the HIV antibody test conducted during the interview or if the participant self-reported a positive HIV status. HIV negative was defined as a negative result on the HIV antibody test. Those who self-reported an unknown or negative HIV status and refused the HIV antibody test were considered to be of unknown HIV status. We defined participants as diabetic if they self-reported a diabetes diagnosis, were taking diabetes medication, or had an abnormal urine glucose measure at the time of the interview. We defined overweight or obese status based upon height and weight measurements conducted by

study staff at the time of the interview. BMI was calculated (weight(kg)/height^2(cm)) and used to categorize participants into the following categories: underweight- BMI > 18.5; normal- BMI 18.5 to <25; overweight- BMI 25.0 to <30; obese- BMI Ó30 [60]. We defined participants as hypertensive if they self-reported a hypertension diagnosis, were taking hypertension medication, or if the average of three consecutive blood pressure measures at time of interview were above 140/90.

We were interested in looking at predictors of chronic disease comorbidity in those living with HIV and those not living with HIV so we stratified our analysis by HIV status. This resulted in two models and a total of four exclusive groups in which a participant could be categorized. The first model assessed factors associated with chronic disease in those who were living with HIV. The second model assessed factors associated with chronic disease in those who were not living with HIV. In total, a participant could fall into one of the following categories: HIV+ and chronic disease, HIV only, chronic disease only, or neither HIV+ nor chronic disease positive

Exposure

The main exposure for this analysis was the distance from the individualôs residence to the nearest supermarket. In the Diepsloot context, a supermarket is either a chain or a locally run store that sells frozen meat (often chicken portions, cuts of beef, and sausages), refrigerated goods including margarine, milk products and cold sodas, a variety of bread (whole grain and white), some fresh produce, eggs, non-perishable foods, and home goods. There is one large national-chain grocery store within Diepsloot that sells bulk items at a reduced cost with the remainder of the stores are significantly smaller and often locally run. The exposure was categorized into two categories: residence less than 300 meters from nearest supermarket, or residence 300 meters or greater from nearest supermarket.

Covariates

We adjusted the analysis for the following individual-level covariates: age, gender, employment status, marital status, socioeconomic status and country of origin.

Missing data

Missing data on HIV status was explained in the Aim 2 methods section. Missing data on chronic disease outcomes is sparse with only 17 individuals missing blood pressure measures and 26 missing BMI. Due to the low prevalence of missing data for these measures, we conducted a complete case analysis for blood pressure and BMI.

Data analysis

We assessed whether the neighborhood context of Diepsloot, South Africa was associated with chronic disease comorbidity. All food vendors in Diepsloot were mapped and the map was then restricted to include only supermarket locations. The distance to the nearest supermarket was calculated using the ArcGIS distance function. Core areas where outcomes were disproportionately high or low were identified using spatial clustering analysis in SaTScanÊ (Martin Kulldorff, National Cancer Institute). We used a spatial-only design with discrete Poisson distribution, maximum cluster size of 50% of the population at risk, and limited the clusters to those with no geographical overlap.

We then conducted a log binomial regression analysis to assess whether a priori factors (distance to nearest supermarket, age, gender, level of education, employment status, food insecurity, and country of origin) were associated with prevalent chronic disease among those living with HIV, and among those who were HIV negative. All covariates that were significant at a p-value of Ò0.10 when examining their relationship with the outcome were entered into the model. These variables were distance to nearest

supermarket, age, gender and country of origin. Covariates not significantly associated with the outcome at p-value < 0.05 were eliminated from the model one at a time, creating the final, adjusted model. An alpha level of 0.05 was selected as the level of statistical significance to make final inferences from the adjusted model. The statistical software package SAS (v. 10, Cary, NC, USA) was used for this analysis.

CHAPTER 3: AIM 1 RESULTS

1. Introduction

Over the past two decades, numerous studies in North America, Europe, and Australia have demonstrated associations between neighborhood characteristics and health outcomes including chronic diseases, mental health, and infectious diseases [39-41, 61-65]. Aspects of the built environment that may positively influence health are access to physical activity, public open spaces, presence of supermarkets, and neighborhood walkability, while those that may negatively influence health include access to unhealthy food outlets and a degraded built environment [40, 62, 63, 66, 67]. These factors can influence situational opportunities and exposures that lead to detrimental changes in behavior and increased stress, which can in turn result in negative health outcomes [33].

While great advances have been made in the measurement of neighborhood characteristics in the past decade, many issues remain. For example, the measurement of neighborhoods should correspond to the study hypothesis, which can either require an individual assessment, neighborhood-level assessment, or both [68]. This issue of model specification commonly arises when studies hypothesize effects at neighborhood level but only measure and adjust for individual-level factors. Furthermore, when neighborhood-level data is used, the variable is often an aggregate of individual data instead of a true neighborhood-level measure purposefully collected by assessment of community spaces [69]. This is important because the perceived measure at the

individual level and objective measure at the neighborhood level are not always correlated, [70, 71] and may have different implications for health [68].

Little is known about the effect of the neighborhood context on health in communities in low and middle income countries. The few studies published have demonstrated associations between degraded external built environment and mental illness in Kenya [67], neighborhood context and youth risk behavior in Cape Town [42], and the effect of local food environment on body mass index in Ghana [72]. Since few studies have been conducted in the developing world, there is a dearth of built environment data collection tools, particularly in the urban context. The methodological issues experienced when measuring built environment in the US or Europe are thus magnified in resource poor areas as most built environment data collection tools have been developed for use in the US or Europe and then applied to other contexts without adaptation to appropriately measure the differing structural factors [73, 74]. Exceptions are studies in India and seven African countries (including South Africa) that adapted the Neighborhood Environment Walkability Scale to the local context [73-75]. Unfortunately, this tool requires a comprehensive, in-depth measurement of the built environment which is not feasible for most studies [76].

Understanding the impact of urban environments on health is of growing importance given the rural-urban migration trend occurring in the developing world [38, 77-79]. In order to increase the quality of epidemiological studies assessing the effect of the built environment on the health of the population in resource-limited settings, low-cost simple data collection tools are needed. We created a tool to characterize the built environment of Diepsloot, South Africa, a peri-urban township. We described the neighborhood contextual factors using this tool, and compared the findings to information obtained by collection of individual level and Census Enumeration Area data for the same community.

2. Methods

Study site and study population

The study was nested within the Diepsloot Community Mapping Project, a cross-sectional community-based survey which took place between May 2013 and March 2014. The parent study aimed to evaluate the geographic disease risk profile of Diepsloot, South Africa. Diepsloot is a low-income, densely populated, urban township located on the northwestern periphery of Johannesburg. Within the approximately 12 km2 area of Diepsloot, the population is estimated to be over 500,000. The houses are a mixture of corrugated iron shacks, Reconstruction and Development Programme (RDP) houses (government subsidized housing), and cement block/brick houses. Access to municipal service varies, with some fully electrified and supplied with indoor plumbing, while others are highly informal without electricity and water access limited to community taps. Access to health care within Diepsloot is limited to three primary care clinics. The nearest public hospital is 30 kilometers away.

Using shape files of administrative units in Diepsloot obtained from the municipal government, 2000 random global positioning system (GPS) points were placed in the residential areas of Diepsloot, called extensions, using ArcGIS software (ESRI 2011. ArcGIS Desktop: Release 10. Redlands, CA: Environmental Systems Research Institute). Study staff approached an adult member of the household closest to the selected GPS point. If there was no household within 30 meters of the GPS point, the point was not used. If the adult member of the household agreed to enumeration, all household members aged 15 and above were enumerated and one was randomly chosen and offered participation in the survey.

Data source 1: Neighborhood aesthetic and built environment information

We created the Built Environment Measurement Tool to collect data on neighborhood characteristics in approximately 5 minutes by a lay person (HIV counselor). We used the Nigeria-adapted Neighborhood Environment Walkability Scale as a starting point and selected elements that were considered valid for the Diepsloot environment given our visual assessment of the different neighborhoods and based on feedback from Diepsloot residents [73]. Staff members were trained to collect neighborhood aesthetic information by conducting a visual analysis of the surroundings of selected GPS points to measure the number of trees, presence of trash and wastewater, presence of streetlights, and the predominant housing type in the area (Table 3.1, Table 3.2).

Data source 2: Individual-level information

As part of the parent study, staff members collected individual-level clinical and demographic data as well as information about the type of main dwelling and its construction material, main source of drinking water, shared toilet facilities, refuse disposal, and access to electricity for lighting were collected (Table 3.2). We limited the analysis to 1184 of the 1231 individuals who completed the interviewer-administered individual-level questionnaire because the remaining had missing data for the analysis variables.

Data source 3: Census Enumeration Area information

The South African Census is conducted every 10 years and collects information on individuals living in South Africa [80]. We obtained information about residents of Diepsloot from the 2011 South African Census conducted by the South African government (data available through Statistics South Africa). Information was collected

on an individual level and aggregated into 177 enumeration areas in order to preserve confidentiality. We analyzed 120 Census Enumeration Areas for this study because the remaining 57 had missing data for the analysis variables. Data collected included main dwelling type, construction material, tenure status, estimated property value, access and reliability of piped water, toilet facilities, refuse disposal, and access to electricity for lighting (Table 3.2).

3. Data analysis

Digital geographic data from the City of Johannesburgôs Geographic Information Systems (GIS) department was used to define community boundaries. The Transverse Mercator Hartebeesthoek projection was used to ensure distance measurements were accurate. We used the 13 extensions (Diepslootôs neighborhoods) as the unit of analysis for the spatial analysis of neighborhood aesthetics.

Principal Components Analysis

To determine if the information obtained by the newly developed data collection tool corroborates or provides additional information not measured by aggregating individual-level information that obtained by individual-level questionnaires and individual-level South African Census data, we first aligned the information spatially to the neighborhood and then compared the prevalence of each neighborhood characteristic of interest. Because the neighborhood aesthetics information collected by the three data sources were not directly comparable, we conducted a principal components analysis for each of the three data sources to obtain a meaningful and comparable index. For the principal components analysis, we first rank ordered each item of each data source from ñlowerò to ñhigherò aesthetic. For example, no streetlights and overflowing piles of rubbish in a neighborhood were scored lower, and having

streetlights and little rubbish in the streets were scored higher. Next, the data structure for each data source required adjustment to the covariance matrix to ensure the assumptions were met in the principal components analysis. We used a polychoric covariance matrix for the binomial and categorical information obtained by the Built Environment Measurement Tool and the Diepsloot Mapping Study individual-level survey data. No adjustments to the covariance matrix were needed for the South African Census data as the information was continuous. We then used the principal axis method to extract the components, followed by varimax (orthogonal) rotation. We determined the number of meaningful components in several ways. First, the eigenvalue-one criterion was applied in order to retain and interpret any component with an eigenvalue greater than 1.00. We next conducted a scree test to identify components that group above breaks in the plot. We examined the common variance and assessed whether any of the components identified by the eigenvalue of the scree test method accounted for less than 5% of the variance. To ensure we had meaningful components, we assessed the overlap and interpretability of the solutions found by the different methods applied. We next removed any factors that loaded on multiple neighborhood variables and reviewed the remaining components with loadings greater than 0.40. Finally, we computed the variability-weighted component score and computed the average index score for each neighborhood for each of the three data sources. We then compared the neighborhood ranking for each of the three data sources using the Spearmanõs rank correlation coefficient to assess whether neighborhoods were ranked similarly by the three data collection methods.

4. Ethics statement

This study was approved by the Human Research Ethics Committee of the University of the Witwatersrand and by the Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill.

5. Results

Built environment data collection tool findings

The findings of the Built Environment Measurement Tool indicated clear diversity of neighborhood characteristics, with substantial differences between the 13 neighborhoods (ó extentionsô) of Diepsloot, South Africa (Figure 3.1). Extensions 1, 12, and 13 had the fewest streetlights and trees, and highest amount of trash and wastewater, whereas extensions 3, 4, and 9 had more streetlights and trees, and less trash and wastewater.

Principal components analysis

The average principal components analysis index score for each of the 13 neighborhoods obtained using each of the three data sources separately is shown in Figure 3.2. The ranking of the neighborhoods was similar for the three data sources, with extensions 1, 12, and 13 ranking lowest by all 3 methods and extensions 3, 5, 6, 9 and 10 ranking highest. The Spearmanôs rank correlation coefficients indicated very strong correlations between the built environment tool and aggregated individual-level survey data (correlation coefficient 0.97) and between the built environment tool and aggregated South African census data (correlation coefficient 0.80) (Table 3.3).

6. Discussion

Using a newly created, simple data collection tool, we were able to identify areas of higher and lower built environment characteristics within a single 12 km^2 urban informal settlement in South Africa. Using principal component analysis, we could quantify the built environment into a single index that could be used as a quantitative exposure variable in epidemiological studies aimed at determining the association between built environment and health outcomes. Different neighborhoods characteristics showed collinearity, with areas with a lower score for one measure (e.g. presence of wastewater) also having lower scores for other built environment characteristics (e.g. lack of streetlights).

We assessed whether the tool would rank the aesthetic of the neighborhoods in a similar order to rankings from different sources. We found that a 5 minute tool developed to directly and visually assess the built environment ranked neighborhoods similarly compared to information obtained through aggregation of individual-level survey data or South African census data. Direct visual assessment of neighborhood characteristics is faster (5 minutes per data point), requires less training and is less costly than interviewing individuals, which is often resource intensive, time-consuming, and may be subject to biases due to non-response or recall. However, if data collection is not possible, use of census is a valid option as the correlation between information obtained through the Built Environment Measurement Tool and the census data was high (Correlation Coefficient Ó0.80).

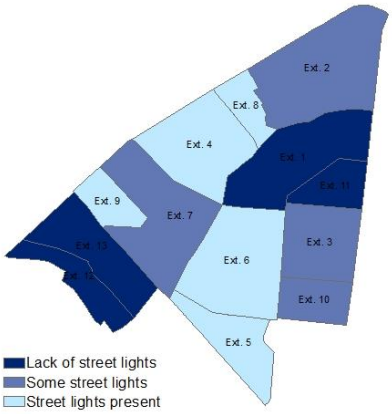
Our findings from an urban informal area of South Africa concluded that our Built Environment Data Collection Tool findings were comparable to publically available census data. Though a similar comparison in the data could not be identified, our results reinforce the diversity of applications for which publically available data can be used. For example, when racial composition information from the United States census was

compared to individual-level self-report of perceived racial composition of a neighborhood, the researchers found only 51% concordance between the two data sources [81]. Additionally, the United States census data on house ownership was compared individual-level socio-economic position indicators and these studies found a correlation between census-level measures such as percentage of housing units that were owner occupied and the individual-level measures of income, education and occupation [82, 83]. In order to determine which level of data to use, the data source must reflect the research question and ideally, a combination of individual and neighborhood-level factors should be included in the analyses [84].

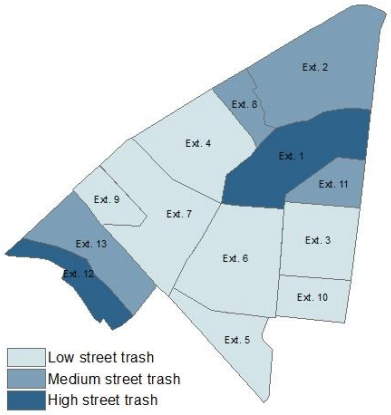
This study was not without limitations. The neighborhood context information is based on a visual assessment on a single day, whereas survey or census data can address the ñaverageò situation. As such, observations may be influenced by factors outside the control of the researcher, such as changes in trash pick-up dates and the amount of rain the area has received. Furthermore, there may be information relevant to the built environment that was not included in our Built Environment Measurement Tool. Further research should determine whether addition of other factors, including context specific factors, further improve the validity of the tool in characterizing neighborhoods in low and middle income settings. Future research should also be performed to assess whether direct measurement of the built environment and aggregation of individual-level data results in the same strength of association with health outcomes Using a simple built environment data collection tool, we were able to create a summary index that was highly correlated to both individual-level survey data and the South African census data. To advocate for and plan interventions, more high quality evidence on the association between built environment and health in low and middle income countries is needed.

Figure 3.1 Distribution of findings from data collection tool

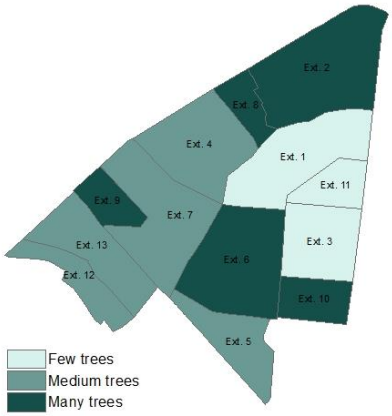
a) Street lights



b) Trash



c) Trees or shrubs



d) Waste water

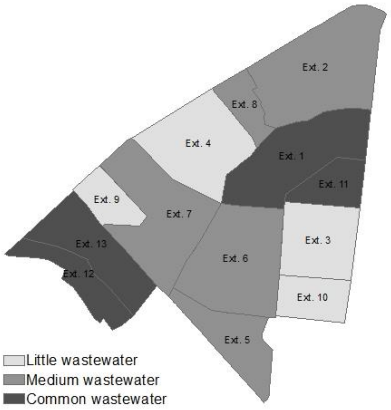
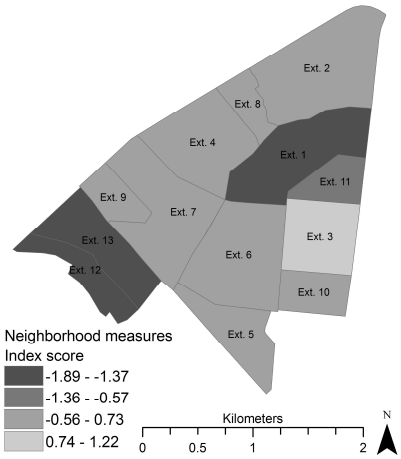
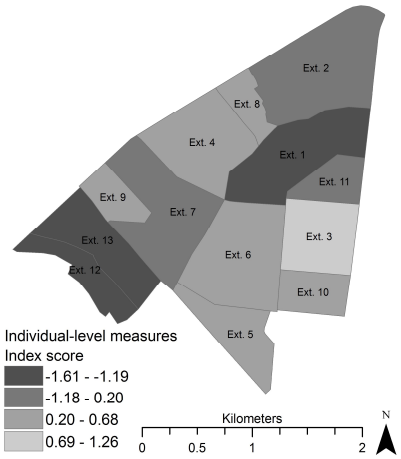


Figure 3.2 Average component for each individual by neighborhood from three data sources.

a) Built Environment Measurement Tool



b) Individual-level information from Diepsloot Mapping Study



c) South African Census

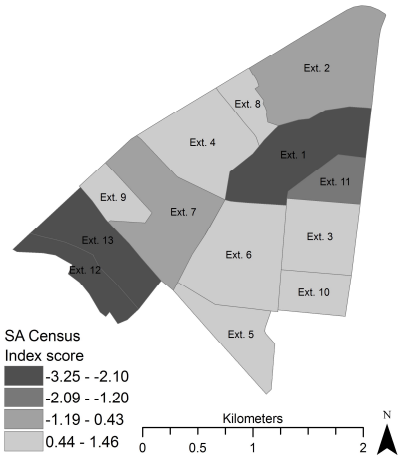


Table 3.1 Fields present in the Neighborhood aesthetic data collection tool

Item	Question	Response
Trees	Are there trees visible on the street in which the selected dwelling is located (including trees in peopleõs backyards?	1. Little to no trees (0-4) 2. Some trees (5-19) 3. Many trees (20+)
Trash	Is trash present?	1. Little to no trash (0-20 pieces, trash mainly in receptacles, small amount of loose trash on street) 2. Some trash (greater than 20 pieces, or 1-2 small piles) 3. Piles of trash (3 or greater large piles of trash)
Wastewater	Is open wastewater visible?	1. No wastewater visible 2. Wastewater from dishes, bath water, car wash is visible (no foul smell) 3. Wastewater containing human excrement or with a foul smell is visible
Street lights	Are there street lights visible on the street in which the selected dwelling is located?	1. No street lights visible 2. 1-5 street lights 3. 6 or more street lights
Housing	Counting the selected dwelling and the closest 19 households (20 total), how many of the following housing types are visible from the street? (write number in space)	1. Standalone house non-RDP 1-2 rooms (brick) 2. Standalone house non-RDP 3 or more rooms (brick) 3. Standalone house RDP (brick) 4. Townhouse/cluster house/semi-detached house (brick) 5. Flat in a block of flats (brick) 6. House/flat/room in backyard (brick) 7. Informal dwelling/shack in backyard (corrugated iron, wood, other) 8. Informal dwelling/shack NOT in backyard (corrugated iron, wood, other)

Table 3.2. Overview of neighborhood characteristics collected from three data sources.

	Built Environment Measurement Tool (n=1496)	**Individual-level information from Diepsloot Mapping Study (n= 1184)**	**South African Census (n-120 Enumeration Areas)**
Housing type/material	Predominant housing type	Type of main dwelling and construction material	Type of main dwelling and construction material Tenure status Estimated value of property
Water	Presence of waste water	Main source of drinking water	Access and reliability of piped water
Sewage	Presence of waste water	Shared toilet facilities	Toilet facilities
Refuse	Presence of trash on streets	Refuse disposal	Refuse disposal
Lighting	Presence of street lights	Household electricity	Household electricity
Trees	Presence of trees	--	--

Table 3.3 Spearman's rank correlation coefficient results comparing the principal component index from three data sources.

Comparison	**Correlation coefficient**	**p-value**
Built Environment Measurement Tool vs. Individual- level information	0.97	p< 0.0001
Built Environment Measurement Tool vs. SA Census	0.80	p=0.0010
Individual- level information vs. SA Census	0.86	p= 0.0002

CHAPTER 4: AIM 2 RESULTS

1. Introduction

The HIV care cascade is used across the globe and has been incorporated into the UNAIDS 90-90-90 strategy for the year 2020 [85]. The definition of the HIV care cascade has varied in past research, [86, 87] but most studies [88] include some combination of the following six stages: 1) HIV infected; 2) HIV diagnosed; 3) linked to HIV care; 4) retained in care; 5) on ART; 6) suppressed viral load. The cascade has been shown to provide a conceptual framework to identify gaps in achieving population viral suppression [10] and help treatment providers identify and focus resources on the stages where HIV positive individuals are in the greatest need of interventions to meet the goal of viral suppression [87]. Few studies have examined and mapped the extent to which communities meet the HIV treatment care cascade. Such information could help to inform targeted health care delivery to efficiently use health resources at the local level.

Currently 60% of South Africans live in urban areas [79]. Urban growth promotes health inequities through the expansion of informal settlements (unplanned residential areas) where municipal authorities struggle to respond to rising demands for basic municipal services, social programs, and health care provision [35, 38, 89]. As urbanization increases across the country ï and the continent ï the number of informal settlements located on the edge of Africaõs urban areas is expected to continue to grow [34]. Neighborhood disorder and crime, which are common in urban informal areas, can result in psychosocial stress, decreased social connectedness and/or mental illness

including depression and post-traumatic stress disorder [90-93]. Stressors and poor psychological health has been shown to increase HIV risk behavior [36] and decrease ART adherence [37]. The exposure to stressors caused by living in the urban informal areas of South Africa may contribute to the higher HIV incidence and prevalence (30% among urban residents aged 15-49), lower levels of HIV testing, and the lower proportion of individuals on HIV treatment seen in this population [94]. The lower performance of the urban informal population at achieving each level of the HIV care cascade can further increase health disparities between urban informal dwellers and other South Africans, producing a gap that warrants further study.

Global Information Systems (GIS) have effectively been used to examine HIV risk and prevalence by mapping the burden of disease and identifying geographic foci or hot spots [44-49]. Studies conducted in rural areas of South Africa and Malawi have found hotspots of higher than expected HIV prevalence near national roads [11, 43]. GIS has also been used to estimate measures of proximity and access to health resources [52], distribution of behavioral risk factors [53], and distribution of stigma [54]. A single national-level study conducted in Malawi found that neighborhood-level factors influenced HIV prevalence [43]. No studies have used GIS to examine whether neighborhood-level factors are related to the spatial distribution of the HIV care cascade or infectiousness in a low or middle-income country.

Utilizing geospatial mapping and the HIV care cascade framework, we aimed to assess geographic hotspots of HIV prevalence, HIV infectiousness, engagement in care and treatment within a densely populated urban township. We hypothesized that the geographic hotspots for these HIV outcomes would not differ for different levels of the HIV care cascade.

2. Methods

Study population and data collection

Study Setting and Population

In 2013-2014, we conducted a cross-sectional household community survey of 1231 randomly selected residents of Diepsloot, a poor, largely informal residential community on the northern periphery of Johannesburg, South Africa. 2000 GPS points were randomly assigned across the residential areas in the 13 neighborhoods of Diepsloot. Study teams located the household closest to the randomly assigned point using hand-held global positioning system receivers. Members of participating households were enumerated and one adult was randomly selected for study participation. Following consent, the study team conducted a questionnaire to collect socio-demographic information, medical history, health-seeking behavior, and performed a health assessment that included an HIV test.

Study variables

Outcomes

The main outcomes of interest were neighborhood HIV prevalence, neighborhood HIV infectiousness, and neighborhood coverage of the steps of the HIV care cascade.

HIV status

All participants who did not self-report a known positive HIV status were offered an HIV test. Participants who agreed to test were given three options: home-based test with immediate test results, home-based test with disclosure of results at clinic on the following day, or anonymous testing for research purposes. Participants were categorized as HIV positive if they self-reported to be HIV positive or had a positive rapid HIV antibody test; HIV negative if they had a negative rapid HIV antibody test; or HIV

status unknown if they self-reported a HIV negative or unknown status but refused the rapid HIV antibody test.

HIV infectious

We classified a participant as infectious if they were: a) newly diagnosed as HIV positive at the time of the interview; b) self-reported being HIV positive and not on ART; or c) self-reported being HIV positive and not adherent to ART.

HIV care cascade levels

We categorized a participant as being in care if they self-reported that they were receiving regular care for HIV. HIV positive participants were considered eligible for ART if their most recent self-reported CD4 count was Ò350 cells/ε l. We categorized participants as being on treatment if they self-reported being on ART. We categorized participants as adherent on ART if they self-reported that they followed their treatment schedule over the previous four days.

Exposure

Our exposure variable was the 13 neighborhood (called extensions) within Diepsloot. Digital geographic data from the City of Johannesburgôs GIS department were used to define community boundaries. The 13 neighborhoods vary with regard to service delivery (some receive electrical power while others do not) and housing material (some are predominantly informal while others are made of concrete blocks). Because neighborhoods of a similar size allow for better estimation of the variation in HIV outcomes, we divided the five largest, most populous neighborhoods (Extensions 1, 2, 4, 6, and 7) into smaller sub-extensions.

3. Data Analysis

We used chi-square tests to compare age, gender, education status, employment status, country of origin, and marital status between those with a known HIV status and unknown HIV status.

We assessed the spatial distribution of HIV outcomes using the ArcGIS geographic information system (GIS). We used the spatial clustering analysis in SaTScanÊ (Martin Kulldorff, National Cancer Institute) [58, 59] to identify clusters of higher than expected prevalence by creating a circular window of various sizes to scan the study area. For each window, the number with the HIV outcome inside the window was compared to those outside of the window and a likelihood ratio test was used to evaluate the statistical significance of each potential hotspot. We used a spatial-only design with discrete Poisson distribution, maximum cluster size of 50% of the population at risk, and limited the clusters to those with no geographical overlap.

We used a log binomial model to examine whether age, gender, level of education, employment status, currently living with partner, alternative care in last 12 months, alcohol consumption, country of origin were associated with residing in a hotspot of HIV infectiousness. All covariates that were significant at a p-value of Ò0.10 when examining their relationship with the outcome were entered into the adjusted model. These variables were age, gender, level of education, employment status, currently living with partner, alcohol consumption. Covariates not significantly associated with the outcome at p-value < 0.05 were eliminated from the model one at a time, creating the final, adjusted model. An alpha level of 0.05 was selected as the level of statistical significance to make final inferences from the adjusted model.

4. Ethics statement

This study was approved by the Human Research Ethics Committee of the University of the Witwatersrand and by the Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill.

5. Results

Study participant demographics

Of the houses identified by the 2000 GPS points, 1,628 households were enumerated and 1,231 adults consented to study participation (Figure 4.1). The median age was 32 years (range of 15-95 years), the majority completed some or all secondary school (68%), one quarter were unemployed (27%) with five times as many women as men receiving government grants (15% vs. 3%), 75% were in a relationship, and one in five (21%) were born outside of South Africa (Table 4.2).

HIV prevalence and cascade outcomes

Among the 1,231 participants, HIV status could be determined in 78% (22% refused testing), among whom 196 were HIV positive, corresponding to an HIV prevalence of 16% (Table 4.3). Two-thirds (64%, n=125) self-reported a known positive HIV status, and 71 (36%) were newly diagnosed with HIV. Of those who were known HIV positive, two-thirds (68%, n=85) were in care. Based on the 2013 South African ART eligibility guidelines (CD4 count Ò850 cells/εl), 69 of 92 (74%) participants eligible for ART were on treatment. Of those who reported taking ART, 63 (91%) said that they followed their schedule over the previous four days.

HIV prevalence was higher in women (21% among women vs. 10% among men, $p<0.001$). Women were more likely to be aware of their positive HIV status at the time of the interview (69% vs. 52%, $p = 0.03$). Proportions of participants in care (79% vs. 65%,

p=0.14), on treatment (72% vs. 50%, p=0.10), and adherent (95% vs. 98%, p=0.91) did not differ significantly between men and women, though a higher proportion of men reported being in care.

Of the 196 participants living with HIV (PLWH), 130 (66%) were considered infectious: 71 (54%) were unaware of their HIV infection at the time of the interview, 33 (25%) were known HIV positive but not yet eligible for ART, 23 (18%) were ART eligible but not on treatment, and 2 (1%) were on ART but not adherent. The proportion classified as infectious did not differ between men and women living with HIV (p=0.70).

HIV prevalence varied between neighborhoods, from 6% in Extension 3 to 24% in Extension 7. Extensions 1, 2, 7, 9, 12, and 13 were hotspots for HIV prevalence (Figure 4.3a). Hotspots for HIV infectiousness were found in extensions 4, 7, 9, and 13 (Figure 4.3b). Clusters were also identified for each step of the care cascade with little geographic overlap between diagnosis and care. Extensions 1, 2, 4, 7, 8, and 9 were hotspots for not being aware of HIV status, extensions 5 and 6 were a hotspot for not being in care and extensions 5, 6, and 13 for not being on ART (Figure 4.3c-e).

Multivariable log binomial regression

Multivariable log binomial regression associations for demographic and behavioral with HIV infectiousness are shown in Table 4.4 Compared with individuals not residing in an HIV infectious hotspot, individuals residing in an HIV infectious hotspot were more likely to be educated at secondary school or higher (adjusted Risk Ratio=1.43, 95%CI: 1.14-1.78) and unemployed without government grant assistance (aRR=1.21, 95%CI: 1.00-1.46) (Table 4.4).

6. Discussion

The neighborhood environment, which is made up of the man-made physical environment in which people live, work, and participate in recreation on a day-to-day basis [33], has been shown to be important for health. Pathways by which neighborhood may influence health are theorized to be mediated by behavioral modifications and stress [33]. In a poor urban informal settlement in South Africa, we observed geographical variation in engagement in the HIV prevalence, engagement in HIV care, ART treatment, ART adherence, and level of HIV infectiousness. These findings suggest that there may be different neighborhood-level drivers at the different stages of the care cascade. We were able to pinpoint areas where individuals are in greater need of HIV testing or ART, and areas where individuals are at higher risk of transmitting HIV, suggesting that targeted interventions may effective in reaching high levels of community viral suppression.

To date, limited is known on how geographic factors relate to access to and retention in HIV care as most studies of the HIV care cascade have been clinic-based research cohorts [86]. The absence of a population-based recruitment strategy in these studies restricts the assessment of community-level factors. The importance of a community-based study design was recently highlighted in a study that found that the population viral load based on a respondent-driven sample of community members without regard to engagement in care was correlated with HIV incidence whereas the population viral load in the subset of individuals engaged in care was not correlated with HIV incidence [95].

The informal settlement studied, which is a typical urban informal settlement, was not close to meeting the 90-90-90 UNAIDS targets: only 32% of PLWH were on treatment and adherent, compared to the target of 72% of the population with an unsuppressed viral load [85]. This proportion matches the 32% global average for viral

suppression in PLWH [88]. Failing to achieve the targets has important consequences. It has been estimated that if the target of 81% of people living with HIV on ART by 2020 is met, more than 2 million HIV-associated deaths in South Africa could be averted [96].

Prevalence of infectiousness among PLWH ranged from 3% to 23%, suggesting that the infectious pressure and likelihood of HIV transmission differs even within neighborhoods of a single community and supports targeted interventions for decreasing new HIV infections. Our findings indicate that, in order to reduce HIV transmission in this urban population, the primary intervention should focus on HIV testing both men and women since 54% of the infectious PLWH were unaware of their HIV status. Though a higher proportion of men were not aware of their HIV status (48% vs. 31%), the HIV prevalence was higher in women, resulting in more women in our sample with undiagnosed HIV than men (44 vs. 27). The roll-out of Universal Test and Treat Strategy, where all PLWH are ART eligible independent of CD4 cell count [97],could decrease the number of HIV-infectious PLWH in the population [98-102].

Factors associated with living in a HIV infectious hotspot were higher education level and unemployed without government grant assistance. Though these findings seem to be contradictory, Diepsloot often serves as the first residence of economic migrants who travel to Johannesburg in search of work. We hypothesize that these individuals may be educated, in search of work, and not eligible for government grants. No other studies of community factors associated with HIV infectiousness are available from an African setting. In Philadelphia, USA, living in a hotspot of low viral suppression was associated with economic deprivation, female gender, and a shorter distance to a pharmacy, indicating the potential for different drivers in different contexts [103] and highlighting the importance role that context plays in shaping social risk factors for HIV.

There are limitations to this study. The inferences were made using cross sectional data and self-reported treatment and adherence measures. Of the selected GPS points, only 1231 participated and there was a 22% HIV test refusal proportion. The adult participants were however randomly distributed as attempted a priori, and those who refused were/were not different from those who did. Furthermore, the dynamic nature of HIV testing and treatment makes the care cascade a difficult pathway to assess with cross-sectional data [104]. Cross checking self-report with clinic records, blood draws to measure viral load and ARV blood levels could improve the validity of estimates in future studies. Though there was a 22% HIV test refusal proportion for this study, we were conservative in our analysis and used the entire population as denominator for HIV prevalence estimates. Therefore, so our estimates are likely underestimates of the population HIV prevalence.

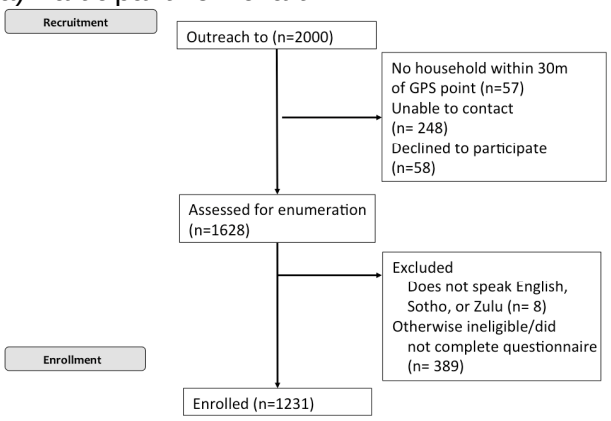
This geospatial analysis allowed us to identify areas of high HIV prevalence, high HIV infectiousness and poor coverage of the care cascade. This information could be used to target interventions such as to mobile HIV testing units and patient support by community health workers to population needs, in order to more effectively reach the 90-90-90 targets. Our findings are also a starting point for examining pathways for disease incidence that are related to contextual factors. Future research should explore neighborhood drivers of HIV outcomes and assess the impact of geographically targeted interventions in high HIV burden settings.

7. Conclusion

In a poor urban informal settlement in South Africa, we observed geographical variation in engagement in the HIV care cascade and level of HIV infectiousness, suggesting different drivers for each level of the care cascade. Our findings support the potential for targeted interventions at the neighborhood level.

Figure 4.1 Participant flow chart and refusal proportion by neighborhood

a) Participant flow chart



b) Refusal proportion

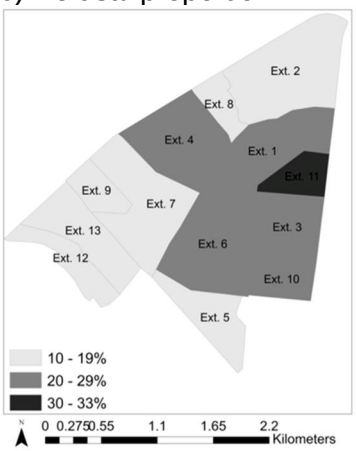


Figure 4.2 The HIV care cascade compared to the UNAIDS 90-90-90 targets for Diepsloot, South Africa, 2013-2014

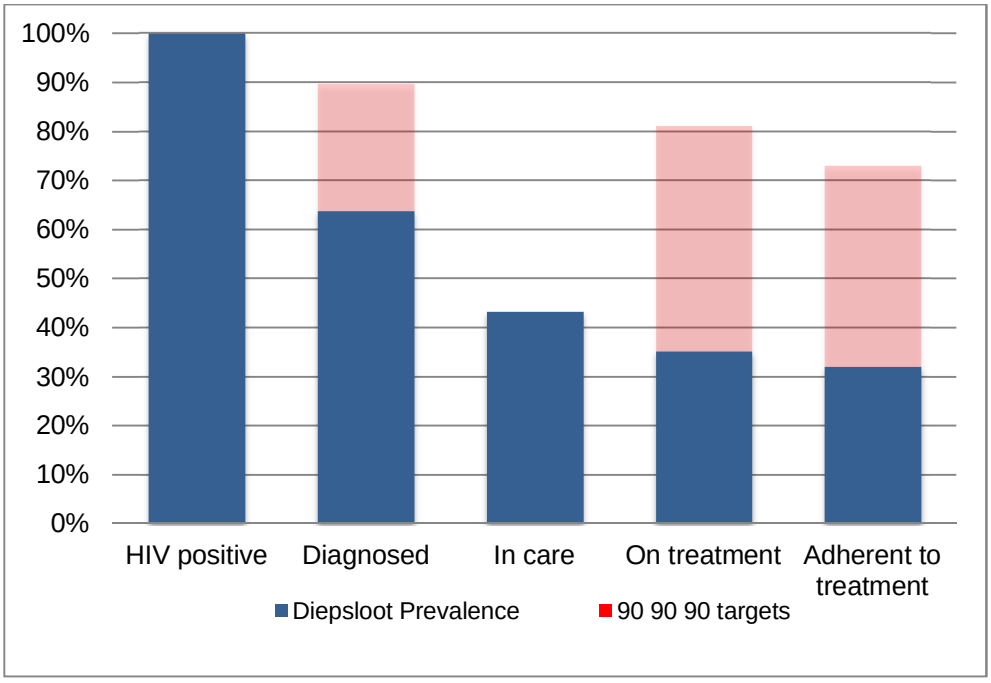
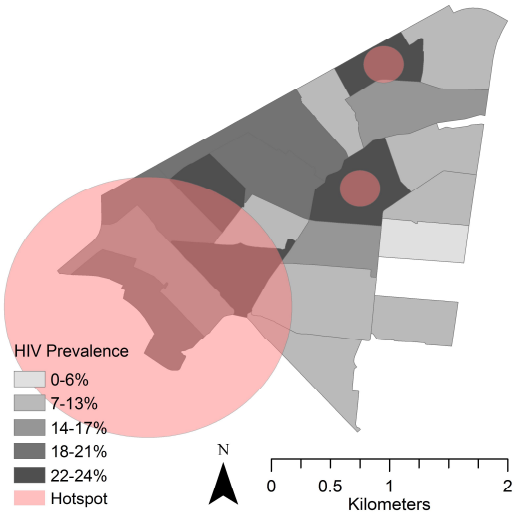
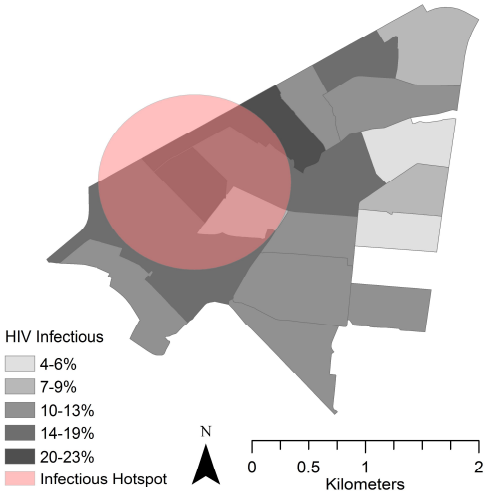


Figure 4.3 Prevalence of HIV (a), evidence of HIV infectiousness (b), and levels of the HIV care cascade (c, d, and e), by neighborhood in Diepsloot, South Africa 2013-2014

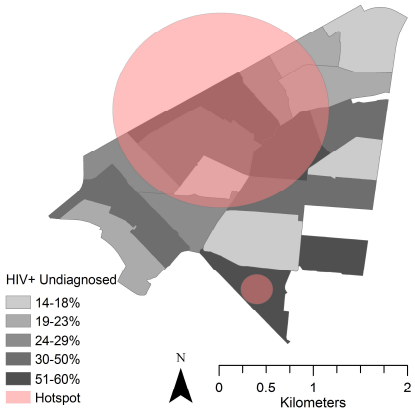
a) HIV prevalence



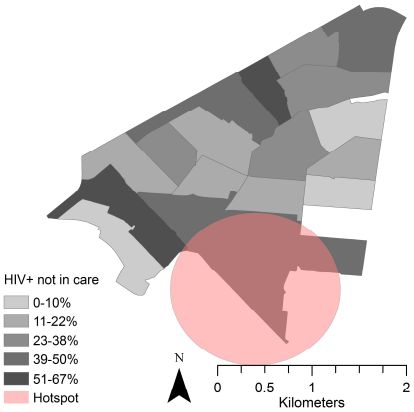
b) Evidence of HIV infectiousness



c) HIV+ undiagnosed



d) HIV+ not in care



e) HIV+ not on ART

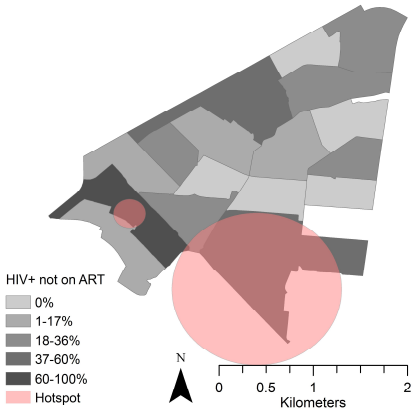


Table 4.1 Summary of measures for HIV outcomes

HIV outcome	Self-report	Biomarker
HIV status	Ever tested for HIV Result of most recent HIV test	Rapid HIV antibody test
Proportion infectious		
On ART and adherent	Ever tested for HIV Result of most recent HIV test Currently taking ARVs Adherence to ARVs	Rapid HIV antibody test
Cascade level		
Diagnosed	Ever tested for HIV Result of most recent HIV test	Rapid HIV antibody test
In care	Currently attending a clinic or seeing a doctor on a regular basis to treat HIV	
On ART	Currently taking ARVs CD4 count in the last year Main reason not currently taking ARVs	

Table 4.2 Sociodemographic profile of cohort participants in Diepsloot, South Africa 2013-2014

Characteristic	Total *N*= 1231 *n* (%)	Male *N*= 560 *n* (%)	Female *N*= 671 *n* (%)
Age			
15-29	499 (41%)	222 (40%)	277 (41%)
30-39	365 (30%)	161 (29%)	204 (30%)
40-49	195 (16%)	90 (16%)	105 (16%)
50-94	172 (14%)	87 (16%)	85 (13%)
Level of Education			
Primary or less	306 (25%)	144 (26%)	162 (24%)
Some secondary/completed secondary	833 (68%)	374 (67%)	459 (69%)
Tertiary/Trade school	89 (7%)	42 (8%)	47 (7%)
Employment status			
Employed	883 (73%)	435 (79%)	448 (68%)
Unemployed with grant	114 (9%)	15 (3%)	99 (15%)
Unemployed no grant	215 (18%)	101 (18%)	114 (17%)
Relationship status			
Married	228 (19%)	128 (23%)	100 (15%)
Not married but living with partner	287 (24%)	127 (23%)	160 (24%)
Not living with partner	401 (33%)	174 (31%)	227 (34%)
No partner	301 (25%)	126 (23%)	175 (26%)
Country of origin			
South African	975 (79%)	442 (79%)	533 (80%)
Other	254 (21%)	118 (21%)	136 (20%)

Table 4.3 Prevalence of HIV outcomes in participants in Diepsloot, South Africa 2013-2014

Characteristic	Total *n* (%)	Male *n* (%)	Female *n* (%)
HIV status (n=1231)			
Self-report or Antibody Positive	196 (16%)	56 (10%)	140 (21%)
Negative	767 (62%)	353 (63%)	414 (62%)
Refused/Unknown	268 (22%)	151 (27%)	117 (17%)
Level of HIV infectiousness (n=196)			
Less infectious-Adherent to ART	66 (34%)	20 (36%)	46 (33%)
Infectious- Not on treatment or not adherent	130 (66%)	36 (64%)	94 (67%)
HIV Care Cascade			
Diagnosed HIV positive (n=196)			
Diagnosed HIV+	125 (64%)	29 (52%)	96 (69%)
Undiagnosed HIV+	71 (36%)	27 (48%)	44 (31%)
HIV care status (n=125)			
In HIV care	85 (68%)	23 (79%)	62 (65%)
Not in HIV care	40 (32%)	6 (21%)	34 (35%)
Treatment status (n=125)			
On ART	69 (55%)	21 (72%)	48 (50%)
ART eligible- not on ART	23 (18%)	3 (10%)	20 (21%)
Not eligible for ART	33 (26%)	5 (17%)	28 (29%)
Self-reported ART adherence (n=69)			
Half of the time or less	2 (3%)	1 (5%)	1 (2%)
Most or all of the time	67 (97%)	20 (95%)	47 (98%)

Table 4.4 Log binomial regression analysis of factors associated with living within a cluster of HIV infectiousness in Diepsloot, South Africa 2013-2014

Characteristic	Residence within HIV infectious hotspot N=436	Residence not within HIV infectious hotspot N=795	Unadjusted Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI)
Age			1.00 (0.99-1.00)	1.00 (0.99-1.01)
Gender				
Female	236	435	1	1
Male	200	360	1.02 (0.87-1.18)	0.95 (0.81-1.13)
Level of Education				
Primary or less	85	221	1	1
Secondary or higher	349	573	1.36 (1.12-1.66)	1.43 (1.14-1.78)
Employment status				
Employed	305	578	1	1
Unemployed with grant	39	75	0.99 (0.76-1.30)	1.08 (0.81-1.44)
Unemployed no grant	86	129	1.16 (0.96-1.40)	1.21 (1.00-1.46)
Currently living with partner				
No	185	330	1	1
Yes	245	457	1.03 (0.88-1.20)	1.03 (0.87-1.21)
Alternative care in last 12 mos				
No	354	654	1	
Yes	82	141	1.05 (0.86-1.27)	
Alcohol consumption				
None	287	507	1	1
Any	147	286	0.94 (0.80-1.10)	0.94 (0.79-1.12)
Country of origin				
South African	345	630	1	
Other	91	163	1.01 (0.84-1.21)	

CHAPTER 5: AIM 3 RESULTS

1. Introduction

The combination of HIV and other chronic disease comorbidities, such as hypertension, diabetes, and obesity, pose a significant public health burden. Expanded treatment access has increased the life expectancy of people living with HIV and reduced the incidence of AIDS-defining opportunistic infections [24]. Among people living with HIV who are on treatment, chronic conditions have increasingly dominated as major causes of morbidity and mortality which can result in more complicated care, an increased pill burden and medical complications.. A study in the US found that among HIV-infected individuals on antiretroviral therapy (ART), 67% of men and 73% of women had at least two chronic conditions, and in those above the age of 60, this figure increased to nearly 90% [26]. This trend is also occurring in South Africa, with an estimated 30% of South Africans over the age of 50 presenting with two or more chronic conditions [18]. In order to determine potential interventions to reduce the incidence of HIV and chronic disease comorbidity, it is important to determine factors associated with HIV and chronic disease in developing countries.

Current medical opinion indicates that chronic disease status in people living with HIV reflects a combination of factors [105]. First, there may be a direct effect of HIV infection and associated inflammation- HIV infected individuals have been found to have higher levels of a variety of inflammatory cytokines including interleukin-6, which is associated with higher all-cause mortality [25, 106, 107]. Second, toxicities resulting from use of certain ART regimens may influence risk- for example, tenofovir and some

protease inhibitors have been found to be associated with renal impairment [108, 109]. Although some metabolic conditions can result from ART, this medication also decreases inflammation. Therefore, early and effective HIV treatment can reduce the risk of chronic conditions associated with long term inflammation and may therefore be protective for inflammatory mediated chronic diseases, such as cardiovascular and atherosclerotic diseases. A third factor is behavioral risk factors (tobacco, diet, exercise) that are common to all persons, regardless of HIV status. Finally, some have posited that contextual factors, including the neighborhood in which one lives may influence chronic disease among those with HIV. Clinic or hospital based studies have estimated chronic disease prevalence [110-112], and one representative study has examined prevalence in Tanzania and Uganda [113]. However, no urban African studies have looked explicitly at prevalence of multiple chronic diseases by HIV status in a representative community sample.

Chronic disease prevention interventions have been implemented in order to modify individual-level behavior with inconsistent results. In order to maintain the health of people living with HIV, it is necessary to move beyond the individual level and consider the characteristics of the neighborhoods and contexts to which the individual belongs. Structural factors such as the safety of the neighborhood, the built environment, and quality of housing can affect behavioral mediators and stress, which can result in negative health outcomes such as chronic disease status or reduced ART adherence [33]. The recognition that structural factors contribute to HIV and chronic disease has led to a search for specific contextual factors that may provide new options for health interventions. To our knowledge, only one study has examined the association between spatial and neighborhood factors on HIV and chronic disease prevalence in South Africa. This study of a rural area in KwaZulu-Natal province found a cluster of higher than expected obesity prevalence (85.1% prevalence of obesity compared to mean of 58.4%)

in the only urban township in the surveillance area [28]. Though this research focused primarily on a rural area, the obesity cluster in the urban township indicates different contextual factors may be contributing to chronic disease prevalence in urban areas. One important factor is the presence of healthy food vendors. Living in close proximity to outlets that sell healthy food has been shown to impact diet and weight in the developed world [39, 114, 115], but there is little information on this relationship in lesser-developed countries.

Using a cross-sectional dataset from a GIS randomized community survey conducted in Diepsloot, South Africa, we aimed to examine the distribution of HIV, hypertension, diabetes and obesity, four highly prevalent chronic diseases in urban South Africa and assessed the association between distance to supermarket and chronic disease comorbidity. We hypothesized that the distribution of HIV and chronic diseases would differ and that closer proximity to a supermarket would be associated with decreased prevalence of chronic disease.

2. Methods

Study population and data collection

The data was derived from the Diepsloot Community Mapping Project, which took place from May 2013 to March 2014. The overall aim of the study was to quantify the disease burden and to develop a geographic risk profile for Diepsloot, South Africa, a densely-populated low-income urban township north west of Johannesburg. The study design was a cross-sectional community assessment of the prevalence of health factors in Diepsloot, and at study initiation, the burden of HIV, TB, and other chronic diseases was not well understood for this population.

The study team obtained shape files of Diepsloot from the municipal government and used ArcGIS software (ESRI 2011. ArcGIS Desktop: Release 10. Redlands, CA:

Environmental Systems Research Institute) to randomly place 2000 global positioning system (GPS) points within the residential areas of Diepsloot. Study outreach teams then drove into Diepsloot and approached an adult member of the household closest to the selected GPS point. If there was no household within 30 meters of the GPS point, this was noted and the point was not used. If the adult member of the household agreed to participate, all household members aged 15 and above were enumerated and one was randomly chosen to participate in the interview.

In addition to information from the individuals within the households, the location for all food vendors in Diepsloot was measured by driving through every street of the neighborhood and documenting the GPS point, vendor type (categorized as: supermarket, tuk shop/spaza shop, market stall, restaurant/take-away, or butcher/live animal vendor), and the number of each of the following food types sold: fresh fruit, fresh vegetables, protein (meat, eggs), dairy (milk/yogurt), starch (bread, rice, pap), and high-fat /high-sugar for each food vendor.

Study variables

Outcome

The main outcome of interest was HIV and chronic disease comorbidity, which was defined as having HIV and one or more of the following conditions: diabetes, hypertension, or a BMI (body mass index) greater than 25.

We defined participants as HIV positive if there was a positive result on the HIV antibody test conducted during the interview or if the participant self-reported a positive HIV status. HIV negative was defined as a negative result on the HIV antibody test. Those who self-reported an unknown or negative HIV status and refused the HIV antibody test were considered to be of unknown HIV status. We defined participants as diabetic if they self-reported a diabetes diagnosis, were taking diabetes medication, or

had an abnormal urine glucose measure at the time of the interview. We defined overweight or obese status based upon height and weight measurements conducted by study staff at the time of the interview. BMI was calculated (weight(kg)/height^2(cm)) and used to categorize participants into the following categories: underweight- BMI > 18.5; normal- BMI 18.5 to <25; overweight- BMI 25.0 to <30; obese- BMI Ó30 [60]. We defined participants as hypertensive if they self-reported a hypertension diagnosis, were taking hypertension medication, or if the average of three consecutive blood pressure measures at time of interview were above 140/90.

We were interested in looking at predictors of chronic disease comorbidity in those living with HIV and those not living with HIV so we stratified our analysis by HIV status. This resulted in two models and a total of four exclusive groups in which a participant could be categorized. The first model assessed factors associated with chronic disease in those who were living with HIV. The second model assessed factors associated with chronic disease in those who were not living with HIV. In total, a participant could fall into one of the following categories: HIV+ and chronic disease, HIV only, chronic disease only, or neither HIV+ nor chronic disease positive

Exposure

The main exposure for this analysis was the distance from the individualôs residence to the nearest supermarket. In the Diepsloot context, a supermarket is either a chain or a locally run store that sells frozen meat (often chicken portions, cuts of beef, and sausages), refrigerated goods including margarine, milk products and cold sodas, a variety of bread (whole grain and white), some fresh produce, eggs, non-perishable foods, and home goods. There is one large national-chain grocery store within Diepsloot that sells bulk items at a reduced cost with the remainder of the stores are significantly smaller and often locally run. The exposure was categorized into two categories:

residence less than 300 meters from nearest supermarket, or residence 300 meters or greater from nearest supermarket.

3. Data analysis

We assessed whether the neighborhood context of Diepsloot, South Africa was associated with chronic disease comorbidity. All food vendors in Diepsloot were mapped and the map was then restricted to include only supermarket locations. The distance to the nearest supermarket was calculated using the ArcGIS distance function. Core areas where outcomes were disproportionately high or low were identified using spatial clustering analysis in SaTScanÊ (Martin Kulldorff, National Cancer Institute). We used a spatial-only design with discrete Poisson distribution, maximum cluster size of 50% of the population at risk, and limited the clusters to those with no geographical overlap.

We then conducted a log binomial regression analysis to assess whether a priori factors (distance to nearest supermarket, age, gender, level of education, employment status, food insecurity, and country of origin) were associated with prevalent chronic disease among those living with HIV, and among those who were HIV negative. All covariates that were significant at a p-value of Ò0.10 when examining their relationship with the outcome were entered into the model. These variables were distance to nearest supermarket, age, gender and country of origin. Covariates not significantly associated with the outcome at p-value < 0.05 were eliminated from the model one at a time, creating the final, adjusted model. An alpha level of 0.05 was selected as the level of statistical significance to make final inferences from the adjusted model. The statistical software package SAS (v. 10, Cary, NC, USA) was used for this analysis.

4. Ethics statement

This study was approved by the Human Research Ethics Committee of the University of the Witwatersrand and by the Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill.

5. Results

Study participant demographics

Of the 2000 GPS points randomized for screening, 1231 consented to participate in the study. The majority of the study population was female (n=671, 55%) and under the age of 30 years (n=499, 41%) (Table 5.1). Sixty-eight percent had completed at least some secondary school (n=833) and few were formally employed (n=231, 19%), with a higher proportion of males in formal employment (n=151, 27%) compared to females (n=80, 12%). Those living with HIV were more likely to be female (71% vs. 29%), age 30-39 (39% vs. 27%), and unemployed (57% vs. 76%).

Food vendors

We were able to identify a total of 64 supermarkets within Diepsloot. These supermarkets tended to be located along major roads and were not evenly distributed throughout the area: the supermarkets tended to be found along major roads and were less likely to be found in neighborhoods without access to electricity (Figure 5.1). The supermarkets had an average of 4.2 types of fruit and vegetables, 3.7 types of protein, and 4.6 types of salty/fatty foods, representing a variety of healthy and less healthy options for shoppers.

Chronic disease prevalence

Three percent (n=42) of the study population were classified as diabetic, 29% (n=359) were hypertensive, and nearly 50% (n= 576) of the population was either overweight or obese, with women having a higher prevalence than men (66% vs. 26%) (Table 5.2). Thirty percent (n=195) of women were categorized as overweight (BMI 25-29) and an additional 36% (n=238) were obese (BMI 30 or above), for a total of 66% (n=433) of women classified as either overweight or obese. Those living with HIV were less likely to have diabetes (1% vs. 4%) or to have a BMI that categorized them as obese (18% vs. 23%),

When assessing the conditions geographically, high blood pressure prevalence varied by neighborhood, with a prevalence of 15-19% in Extensions 6, 9, 12 and 13, and a prevalence of 25-30% in Extensions 2, 3, 7 and 11 (Figure 5.2a). Similar patterns were found for high BMI, with Extension 12 and 13 measured as the lowest overweight/obese prevalence and Extensions 2, 6, 10, and 11 containing the highest prevalence (Figure 5.2b) and diabetes (Figure 5.2c). In the hotspot analysis, one large cluster was identified as having higher chronic disease prevalence than expected (extensions 1, 2, 4, and 8) (Figure 5.2d). Furthermore, HIV prevalence was greater than expected in different extensions (extensions 1, 2, 12, and 13) (Figure 5.2e) than the chronic diseases, and when mapping the HIV and chronic disease comorbidity, two hotspots were found (extensions 1, 2, 7, 8, 9, 12, and 13), one overlapping with the chronic disease hotspot and the other overlapping with the HIV prevalence hotspot (Figure 5.2f).

Multivariable log binomial regression

Among individuals living with HIV who were not comorbid with another chronic condition, those with a chronic condition were more likely to live less than 300 meters from the nearest supermarket (Prevalence Ratio(PR)=1.21, 95% Confidence

Interval(CI): 0.97-1.51), and were less likely to be male (PR=0.65, 95%CI: 0.47-0.89) or originate from a country other than South Africa (PR=0.50, 95%CI: 0.32-0.78) (Table 5.3a). In comparison, among those not living with HIV, those who had a chronic condition were less likely to be male (PR=0.95, 95%CI: 0.91-0.98), but distance to the nearest supermarket (PR=1.00, 95%CI: 0.95-1.06) or originating from a country other than South Africa (PR=1.00, 95%CI: 0.95-1.06) were not significantly associated with living with a prevalent chronic condition (Table 5.3b).

6. Discussion

Our findings highlight the high prevalence of chronic conditions in an urban South African informal area. In our sample, 24% of the population had high blood pressure, and nearly half had a BMI that was classified as overweight or obese. Females had higher prevalence of HIV and overweight/obese status while males had higher prevalence of hypertension. Overall, nine percent of this representative sample was living with HIV and at least one other chronic disease (hypertension, diabetes, or overweight/obese status). These findings are more similar to the clinic-based studies conducted in Malawi (hypertension: 24%, diabetes: 4%, comorbidity 26%) [111] and higher than those in Zimbabwe (hypertension: 10%, diabetes 2%, comorbidity: 15%) [110] and though these studies did not measure overweight/obesity status and were not representative.

We found overlapping hotspots of hypertension, diabetes, and obesity prevalence that differed from the areas of high HIV prevalence. When examining the prevalence of HIV and chronic disease comorbidity- there were two main hotspots- one overlapping with the high HIV prevalence and one overlapping with the high chronic disease prevalence. Assessing HIV and chronic disease comorbidity allows for a more complete picture of the health status in this neighborhood and provides a target for

community health interventions. In an effort to identify a target for interventions, we assessed whether distance to supermarket was associated with chronic disease. In those living with HIV, residing in a home that was more than 300 meters was associated with greater prevalence of chronic disease comorbidity. This neighborhood factor mirrors studies that were conducted in developed countries examining the association between supermarket distance and food intake [116, 117] and provide new evidence of the generalizability of this association across different contexts. One factor that might mediate this relationship is the perception of safety in Diepsloot. Diepsloot is an area that has a reputation for violence and a recent study found that 25% of residents feel unsafe in the area during the day and the majority feel unsafe (59%) or very unsafe (28%) in the area at night [56]. This fear could result in shopping occurring closer to the house as to avoid walking through unfamiliar areas of Diepsloot. Another factor related to access to healthy food in Diepsloot may be access to electricity. There are some extensions of Diepsloot that were not electrified at the time of the study (Extensions 1, 12, and 13), some areas that were electrified experienced service delivery interruptions in the municipal power during the time of the study. This may account for some of the neighborhood-level disparity in chronic disease comorbidity. Residents with consistent household electricity are able to buy perishable foods such as vegetables and meat in bulk at a discount from the area supermarkets. This provides cost savings and the opportunity to consume healthier foods. Residents who do not have access consistent access to electricity are forced to buy in smaller quantities and likely rely on more non-perishable food items that have higher salt and fat content.

The strength of the study is the way in which the outcomes were measured. A trained nurse conducted biometric measures of BMI, blood pressure, urine glucose, and HIV antibody status for all consenting participants. The representative nature of the sampling allows for inference of the prevalence of these conditions for the

neighborhoods as a whole, without the limitation of access to care, which is commonly a constraint in research studies. Limitations are present in this analysis- the study was a cross-sectional study design so we are not able to confirm that disease onset occurred at the current residential location. We also did not collect information on the locations of other places the participants frequented, such as their employment location. Understanding pathway from place of residence to place of employment is important to fully understand the healthy food exposure that an individual has on a daily basis. Additionally, we did not measure food intake for the sample, which would have clarified the relationship between distance to the nearest supermarket and chronic conditions.

Future research into the mechanisms that relate distance to supermarkets and health in this population is crucial. We did not measure food intake, but other research conducted in a South African township found that in general, the diets of low-income South African women consisted of high fat, sugar, and refined food items [20] and low dietary diversity [21]. It is important to next step to see if there is a difference in the quality of food intake for those who live closer to supermarkets. Further research into interventions that could increase access to healthy food at the neighborhood level is also needed. Studies have found that neighborhood walkability and food environment predicts obesity [39, 115], and it is important to determine if these relationships apply to the urban informal context of South Africa.

7. Conclusion

Our results have public health potential because increasing healthy food options in low-income areas could prevent new cases of HIV and chronic disease comorbidity. Preventing the dual burden of HIV and chronic disease comorbidity from occurring may increase long term adherence. Further research into other neighborhood factors such as

walkability and density of healthy food vendors may deepen our understanding of this relationship and provide further options for interventions.

Figure 5.1 Supermarket locations in Diepsloot, South Africa 2013-2014

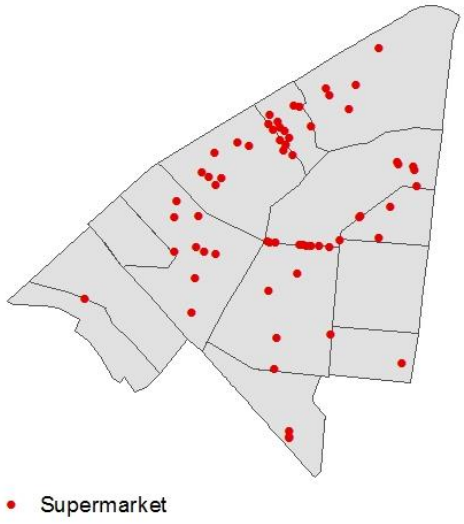
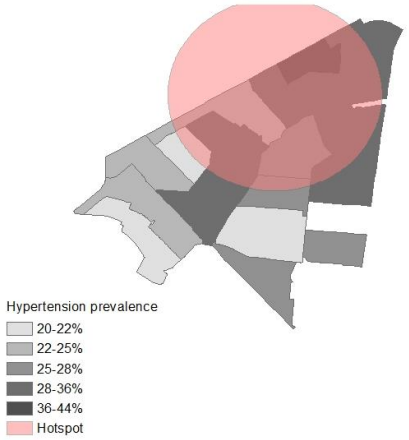
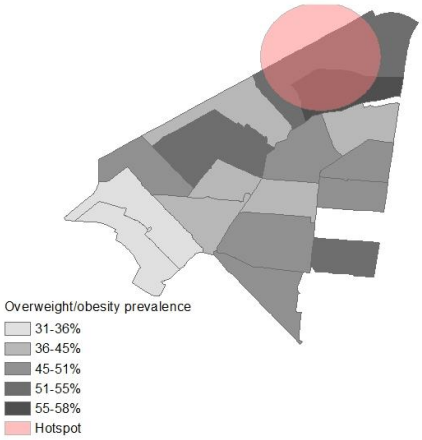


Figure 5.2 Prevalence of hypertension (a), overweight or obesity (b), diabetes (c), any chronic disease (d), HIV (e), and HIV and chronic disease comorbidity (f) by neighborhood in Diepsloot, South Africa 2013-2014

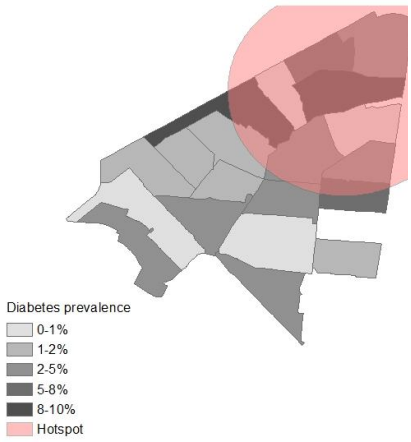
a) Hypertension



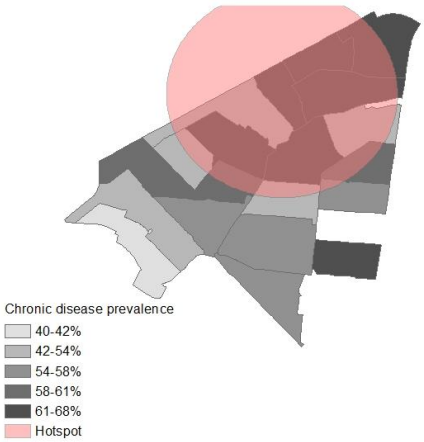
b) Overweight or obese



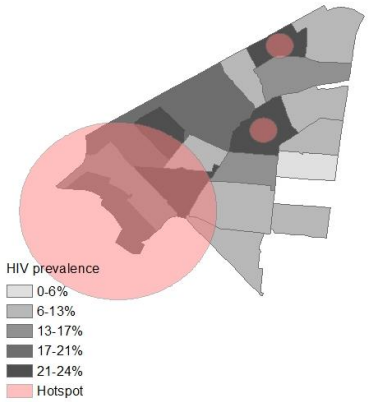
c) Diabetes



d) Chronic disease prevalence



e) HIV prevalence



f) HIV and chronic disease comorbidity

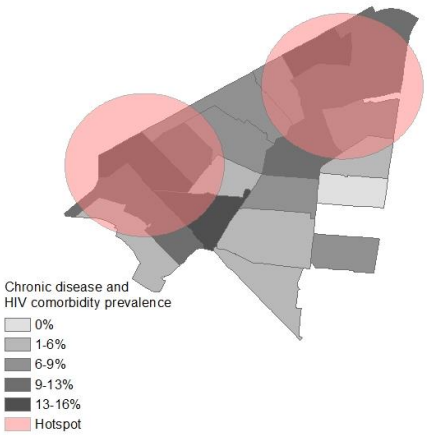


Table 5.1 Sociodemographic profile of cohort participants in Diepsloot, South Africa 2013-2014

Characteristic	Total *N*= 1231 *n* (%)	HIV positive *N*= 196 *n* (%)	HIV negative *N*= 767 *n* (%)	Unknown HIV status *N*= 268 *n*
Gender				
Male	560 (45%)	56 (29%)	353 (46%)	151 (56%)
Female	671 (55%)	140 (71%)	414 (54%)	117 (44%)
Age				
15-29	499 (41%)	53 (27%)	344 (45%)	102 (38%)
30-39	365 (30%)	76 (39%)	205 (27%)	84 (31%)
40-49	195 (16%)	43 (22%)	109 (14%)	43 (16%)
50-94	172 (14%)	24 (12%)	109 (14%)	39 (15%)
Level of Education				
Primary or less	306 (25%)	53 (27%)	200 (26%)	53 (20%)
Some secondary/completed secondary	833 (68%)	134 (69%)	510 (67%)	189 (71%)
Tertiary/Trade school	89 (7%)	8 (4%)	55 (7%)	26 (10%)
Employment status				
Employed	883 (73%)	110 (57%)	577 (76%)	196 (74%)
Unemployed with grant	114 (9%)	34 (18%)	60 (8%)	20 (8%)
Unemployed no grant	215 (18%)	49 (25%)	118 (16%)	48 (18%)
Relationship status				
Married	228 (19%)	24 (12%)	139 (18%)	65 (25%)
Not married but living with partner	287 (24%)	43 (22%)	179 (24%)	65 (25%)
Not living with partner	401 (33%)	76 (39%)	245 (32%)	80 (30%)
No partner	301 (25%)	52 (27%)	194 (26%)	55 (21%)
Country of origin				
South African	975 (79%)	144 (74%)	613 (80%)	218 (82%)
Other	254 (21%)	51 (26%)	154 (20%)	49 (18%)

Table 5.2 Prevalence of chronic disease by HIV status in participants in Diepsloot, South Africa 2013-2014

Characteristic	**Total** *N*= 1231 *n* (%)	**HIV positive** *N*= 196 *n* (%)	**HIV negative** *N*= 767 *n* (%)	**Unknown HIV status** *N*= 268 *n* (%)
Diabetes				
Yes	42 (3%)	1 (1%)	28 (4%)	13 (5%)
No	1189 (97%)	195 (99%)	739 (96%)	255 (95%)
Hypertension				
Yes	359 (29%)	51 (26%)	228 (30%)	80 (30%)
No	872 (71%)	145 (74%)	539 (70%)	188 (70%)
Overweight/obese (n=1205)				
Underweight/normal (BMI > 25)	629 (52%)	111 (57%)	389 (51%)	129 (51%)
Overweight (BMI 25-29)	300 (25%)	49 (25%)	192 (25%)	59 (23%)
Obese (BMI Ó30)	276 (23%)	34 (18%)	176 (23%)	66 (26%)
HIV and chronic disease comorbidity				
No chronic disease	721 (59%)	109 (56%)	465 (61%)	147 (55%)
Any chronic disease	510 (41%)	87 (44%)	302 (39%)	121 (45%)

Table 5.3a Log binomial regression analysis of factors associated with prevalent chronic disease among those living with HIV in Diepsloot, South Africa 2013-2014

Characteristic	HIV and any chronic disease N=109	HIV with no chronic disease N=87	Unadjusted Prevalence Ratio (95% CI)	Adjusted Prevalence Ratio (95% CI)
Distance to nearest supermarket				
Less than 300m	83	72	1	1
300m or greater	26	15	1.18 (0.90-1.56)	1.21 (0.97-1.51)
Age			1.02 (1.01-1.02)	1.01 (1.00-1.02)
Gender				
Female	86	54	1	1
Male	23	33	0.67 (0.48-0.94)	0.65 (0.47-0.89)
Level of Education				
Primary or less	30	32	1	
Secondary or higher	78	64	0.97 (0.73-1.28)	
Employment status				
Employed	64	46	1	
Unemployed with grant	19	15	0.96 (0.68-1.35)	
Unemployed no grant	26	26	0.91 (0.67-1.24)	
Food insecurity				
No	82	59	1	
Yes	27	27	0.86 (0.64-1.16)	
Country of origin				
South African	93	51	1	1
Other	15	36	0.45 (0.29-0.71)	0.50 (0.32-0.78)

Table 5.3b Log binomial regression analysis of factors associated with prevalent chronic disease among those who are HIV negative in Diepsloot, South Africa 2013-2014

Characteristic	HIV negative with any chronic disease N=463	HIV negative with no chronic disease N=302	Unadjusted Prevalence Ratio (95% CI)	Adjusted Prevalence Ratio (95% CI)
Distance to nearest supermarket				
Less than 300m	370	250	1	1
300m or greater	95	52	1.08 (0.95-1.24)	1.00 (0.95-1.06)
Age			1.00 (1.00-1.00)	1.00 (1.00-1.00)
Gender				
Female	305	109	1	1
Male	160	193	0.62 (0.54-0.70)	0.95 (0.91-0.98)
Level of Education				
Primary or less	143	57	1	
Secondary or higher	320	245	0.79 (0.71-0.89)	
Employment status				
Employed	342	235	0.71 (0.62-0.81)	
Unemployed with grant	50	10	1	
Unemployed no grant	64	54	0.65 (0.53-0.80)	
Food insecurity				
No	366	253	1	
Yes	95	49	1.12 (0.98-1.28)	
Country of origin				
South African	387	226	1	1
Other	78	76	0.80 (0.68-0.95)	1.00 (0.95-1.06)

CHAPTER 6: DISCUSSION

1. Introduction

We used data from a community health survey that collected GIS information to identify a population-based sample of individuals living in Diepsloot, South Africa, an urban township with a population of 500,000. In this area, there was sufficient variation between neighborhoods to study how context influences HIV and comorbidities. In this analysis, we explored the association between place and HIV prevalence to help describe the HIV epidemic on a local level and to explore the relationship between place and individual health on an urban South African population. Specifically, we assessed the built environment of an informal urban South African township using a novel Built Environment Data Collection Tool and compared the findings to information obtained by collection of individual level and Census Enumeration Area data for the same community (Aim 1). We further assessed the spatial distribution of HIV prevalence, HIV infectiousness, and levels of the HIV care cascade in this population and examined factors (e.g. age, gender, education and alcohol consumption) associated with living in an area of higher than expected HIV infectiousness (Aim 2). We hypothesized that the geographic hotspots would vary for the different levels of the HIV care cascade and HIV infectiousness. The final aim of the study was to explore the spatial distribution and role of contextual factors in co-morbidity of HIV and chronic disease in this population (Aim 3). We hypothesized that the distribution of HIV and chronic diseases would differ and that closer proximity to a supermarket would be associated with decreased prevalence of chronic disease.

2. Summary of findings

For Aim 1, our Built Environment Measurement Tool helped differentiate neighborhoods by several characteristics (e.g. presence of wastewater, refuse and streetlights) of the neighborhood (ñextensionsò) in Diepsloot township. The ranking of neighborhoods was similar for the three data sources (Built Environment Measurement Tool, Individual-level information, and South African Census information), with three extensions ranking lowest by all three methods and five extensions ranking highest based upon measures of housing material, sewage, refuse, and neighborhood lighting. The Spearmanôs rank correlation coefficients indicated strong correlations between neighborhood-level characteristics as measured by the Built Environment Measurement Tool and individual-level questionnaire data (0.97) and between the Built Environment Measurement Tool and census data (0.80). Therefore, using a simple built environment data collection tool, we were able to create a summary index that was highly correlated to both individual-level survey data and the South African census data. To advocate for and plan interventions, more high quality evidence on the association between built environment and health in low and middle income countries is needed. By using the Built Environment Measurement Tool, researchers could incorporate a built environment measure into their research plans in order to explore these relationships.

For Aim 2, we observed an HIV prevalence of 16%, of which two-thirds (64%, n=125) self-reported a known positive HIV status and 71 (36%) were newly diagnosed with HIV. Of those known to be HIV positive, two-thirds (68%, n=85) were in care. Of the 92 participants eligible for ART (CD4 count Ò350 cells/εl), 69 (75%) were on treatment. Sixty-six percent (n=130/196) of HIV positive individuals were classified as infectious. HIV prevalence varied between neighborhoods (median 16%, range 6-24%) and significant clusters were identified for each step of the care cascade with little overlap between clusters of diagnosis and care. Contrary to our hypothesis and research in

more developed areas, we observed that individuals residing in a HIV infectiousness hotspot (defined as those who were HIV positive and not on ART or not adherent to ART) were more likely to be of higher education level (at least secondary school) (Risk Ratio=1.43, 95%CI: 1.14-1.78) and unemployed without government grant assistance (RR=1.21, 95%CI: 1.00-1.46).

For Aim 3, we observed that sixteen percent of the study population were living with HIV, 3% (n=42) were diabetic, 29% (n=359) were hypertensive, and nearly 50% (n= 576) of the population was either overweight or obese, with women having a higher prevalence than men (66% vs. 26%). Overall, 9% of the sample was living with HIV and at least one other chronic disease (hypertension, diabetes, or overweight/obese status). Overlapping hotspots of hypertension, diabetes, and obesity prevalence were present and differed from the areas of high HIV prevalence. There were two hotspots of HIV and chronic disease comorbidity- one overlapped with the HIV prevalence hotspot and one overlapped with the chronic disease prevalence hotspot. HIV positive participants with a chronic condition were more likely to live more than 300 meters from the nearest supermarket (Prevalence Ratio(PR)=1.21, 95% Confidence Interval(CI): 0.97-1.51), and were less likely to be male (PR=0.65, 95%CI: 0.47-0.89) or originate from a country other than South Africa (PR=0.50, 95%CI: 0.32-0.78) compared to those living with HIV without any comorbidities. Our findings demonstrate a high prevalence of chronic conditions in an urban South African informal area. The results also suggest a significant association between further distance from residence to a supermarket and higher prevalence of at least one chronic condition in those living with HIV.

3. Interpretation of findings

We measured the built environment, alcohol vendors, food vendors, municipal services, chronic disease, HIV status, and HIV infectiousness for the densely-populated

urban township of Diepsloot, South Africa. The findings from our analysis indicate that the built environment differs between neighborhoods, that hotspots of HIV infectiousness and HIV and chronic disease comorbidity differ, and that distance from a supermarket is associated with chronic disease comorbidity in those who are living with HIV. In order to understand these results, it is important to discuss each extension specifically to examine the context that may have shaped the results that we observed in this dissertation.

We found that the neighborhoods within Diepsloot could be grouped based upon similarities in built environment, HIV prevalence/infectiousness, and chronic disease prevalence. The first set of neighborhoods were Extensions 1, 11, 12, 13. These were the most informal of the neighborhoods of Diepsloot. They had high neighbourhood degradation according to the Built Environment Measurement tool (no electricity access, presence of wastewater, few trees and the highest amount of rubbish) and there were only eight supermarkets in these neighborhoods. The lack of supermarkets is likely due to the lack of electricity which would require a generator to keep the frozen and fresh food at the required temperatures. There was a hotspot of HIV prevalence in one section of Extension 1 and over Extensions 12 and 13. The prevalence of hypertension and obesity was low in Extensions 12 and 13, but high in Extension 1. Both Extensions 1 and 12 were found to be hotspots for HIV and chronic disease comorbidity.

The second set of neighborhoods were Extensions 3, 5, 6, 10. These were the most formal of Diepsloot's neighborhoods. They had low neighbourhood degradation according to the Built Environment Measurement Tool (electricity access with the resulting streetlights, little wastewater and street trash). There were 8 supermarkets, within the extension, including the one large, chain grocery store that sells the largest variety of food at the lowest prices. There was a hotspot of undiagnosed HIV in Extension 5, and a hotspot of those living with HIV but not in care or on ART in

extensions 5 and 6. There were no hotspots of chronic disease or chronic disease and HIV comorbidity in these neighborhoods.

The third set of neighborhoods were Extensions 2, 4, 7, 8, 9. These areas were generally in the middle of the grading of the Built Environment Measurement Tool. They were all electrified, with the resulting streetlights, had moderate to little wastewater in the streets and low to medium street trash. There was a small hotspot of HIV prevalence in Extension 2. There was a hotspot of HIV infectiousness in Extensions 4, 7, and 9 and a hotspot of undiagnosed HIV in 2, 4, 7, 8, and 9 (likely due to the contribution of undiagnosed HIV in the HIV infectiousness). These extensions had high chronic disease prevalence (hypertension, obesity, and diabetes) and also had HIV and chronic disease comorbidity.

By looking at many different neighborhood factors, we see that access to electricity, sanitation, health care, and healthy foods vary within the township of Diepsloot. We did not look at distance to clinic, but it is an interesting question for future research. There is currently a plan to develop the land directly across the street from Diepsloot, including RDP houses and a tertiary hospital. This will change the health care landscape of the area and will hopefully improve health access and outcomes.

In each of our models, citizenship was an important factor. Diepsloot is often the first place in Gauteng for many economic migrants who move from Zimbabwe and Limpopo and Eastern Cape provinces of South Africa. Any economic migrant is vulnerable, but non-South African without permanent residency or refugee status are not eligible for the social grants that keep many South Africans afloat financially until formal employment can be secured. These grants include: child support grants (R 350/month), elderly grants (R 1,510/month), and disability grants (R 1,510 /month). 21% of our study population reported being born in a country other than South Africa. This is similar to another survey conducted in 2006 which found that 18% of Diepsloot residents reported

being non-South African [56]. Though our proportion is higher than the previous study, we believe that this number may still be under-reported due to the stigma associated with being non-legal residents of South Africa. This under-reporting may be from those who refused to participate in the study, or from those who did not disclose that they were born outside of South Africa. South Africa is not accepting additional asylum seekers and is actively decreasing the number of work permits it grants to Zimbabweans. This may be a cause of additional stress which can have negative health outcomes for those already vulnerable individuals.

4. Strengths and limitations

The goal of the research was to examine the effect of neighborhood factors on HIV and chronic disease in Diepsloot, South Africa. Though the study was conducted in South Africa, urban townships similar to those in South Africa exist in developing countries around the world. Information gained from this study can be applied to many other developing countries.

The study developed a more efficient (e.g. easier to implement and less time) instrument for evaluating neighborhood characteristics. The neighborhood environment is made up of the human-made space in which people live, work, and participate in recreation on a day-to-day basis. Neighborhoods have been shown to be incredibly important for health, including presence of food and recreational resources, aesthetic quality, presence of violence, and availability of services. Pathways by which neighborhood may influence health are theorized to be mediated by behavioral modifications and stress [33]. Although there is a growing body of research on the built environment and health in Africa, there are few studies examining how and what measures may be important for health in the context of HIV and HIV related chronic

diseases. Our study addressed this critical gap, by examining a novel built environment data collection tool specifically created for an urban informal township.

This was the first study to assess the association between neighborhood factors and chronic disease in an urban township in South Africa. Structural factors on the neighborhood level are key determinants of the health of individuals in the neighborhood. However, many of the studies of structural factors are conducted at a national level, limited to rural areas, or simply dichotomize residential area as urban or rural. This is an important limitation because few conclusions can be drawn by examining differences at such a broad level of aggregation. The study is innovative because it analyzed in detail the neighborhood level determinants of health in an urban African environment.

The spatial methods used in this research allow for novel analysis of influence of contextual factors on chronic disease prevalence. The research question posed here lends itself to a spatial analysis, due to the geographic nature of the neighborhood-based chronic disease risk factors including access to unhealthy food outlets and a degraded built environment [40, 62, 63, 66, 67]. By analyzing the spatial distribution of HIV and chronic disease, we were able to determine areas where individuals were at higher risk for these conditions, and where the health needs are greatest. Previously, there was no rigorous spatial analysis of neighborhood factors and health for an urban South African township. Coordinate data on the built environment of Diepsloot allowed the research team to determine if density, distance, and coverage of the neighborhood factors are related to health outcomes. This allowed us to explore additional pathways for disease incidence that are related to contextual factors in the urban African context.

The study collected a variety of neighborhood- and individual-level data for a poorly understood context. We were able to characterize the built environment of the different neighborhoods within Diepsloot and determine the location and quality of foods

at different types of food vendors in Diepsloot. The built environment measurements were compared against public data from the SA census and from individual-level data collected from the mapping study interview. We were also able to measure the presence of food vendors by driving through the streets of Diepsloot. Additionally, the health outcomes were measured by a trained nurse who conducted biometric measures of BMI, blood pressure, urine glucose, and HIV antibody status for all consenting participants. The representative nature of the sampling allows for inference of the prevalence of these conditions for the neighborhoods as a whole, without the limitation of access to care, which is commonly a constraint in research studies.

Limitations are present in this analysis. The study was a cross-sectional study design so we are not able to confirm that disease onset occurred at the current residential location. Furthermore, the dynamic nature of HIV testing and treatment makes the care cascade a difficult pathway to assess with cross-sectional data [104]. The neighborhood context information is based on a visual assessment on a single day, whereas survey or census data can address the ñaverageò situation. As such, observations may be influenced by factors outside the control of the researcher, such as changes in trash pick-up dates and the amount of rain the area has received.

There were a large number of study participants who refused the HIV test, even though anonymous testing was offered. Of the selected GPS points, only 1231 participated and there was a 22% HIV test refusal proportion. Though we believe our measurement of biometric data was a strength, we were limited in our conclusions because we lacked some key information. We did not collect dried blood spots during the HIV testing so we were not able to conduct any viral load measure and hypertension and diabetes status were self-reported. Cross checking self-report with clinic records, blood draws to measure viral load and ARV blood levels could improve the validity of estimates in future studies because these self-reported measures may have been

skewed toward responses that were perceived to be socially acceptable due to social desirability bias (potentially overestimating adherence measures) or an under-reporting of chronic conditions due to recall bias (potentially underestimating the prevalence of hypertension).

We did not collect information on the locations of other places the participants frequented, such as their employment location. Understanding pathway from place of residence to place of employment is important to fully understand the exposures that an individual has on a daily basis. Additionally, we did not measure food intake for the sample, which would have clarified the relationship between distance to the nearest supermarket and chronic conditions and would have provided insight into the extent to which the distance to a supermarket affects food intake. The lack of food intake information could bias our findings toward the null for those who own cars because the distance to a supermarket would have less of an impact if a person is able to transport groceries using an automobile or for those who work near a supermarket and purchase their groceries on their way home from their employment location.

5. Public health implications

There are a number of new initiatives to improve treatment access and outcomes for HIV and chronic disease that are being implemented by the South African National Department of Health. These policy changes could affect the results that were observed in the study and are important to take into consideration as new interventions are implemented. Universal Test and Treat was implemented in September 2016 in order to initiate those testing positive for HIV onto treatment regardless of CD4 count. This initiative has the potential to result in a reduction in the number of infectious individuals who are aware of their status but have not initiated treatment because they are awaiting their CD4 count to meet the previous threshold (<500 cells/εl) for ART initiation. This

could shift the infectious hotspots to areas where there is a high prevalence undiagnosed or nonadherent individuals. A second national initiative, the South African National Department of Health Adherence Guidelines have been implemented to provide a framework to intervene on all steps of the care cascade to reach the 90-90-90 targets for viral suppression and the Ideal Clinic program has been implemented to bring a sub-set of clinics up to a higher standard to increase patient satisfaction and clinical outcomes in the public sector. These adherence interventions allow for stable patients to collect chronic medication (including ARVs) at Adherence Clubs, provide structure for enhanced adherence counselling for unstable patients and encourage early tracing after a missed medication collection visit. These interventions have the potential to reduce the number of nonadherent individuals. Finally, Pre-exposure Prophylaxis (PREP) is now available and has been targeted to MSM (men who have sex with men) and young women. The implementation of PREP has the potential to reduce new infections in vulnerable populations and also reduce the impact of a high community viral load for individuals who are taking PREP. Though these initiatives focus on vulnerable populations and specific levels of the treatment cascade, there is no explicit geographic targeting component. The findings from our study provide evidence for the importance of focusing on the geographic distribution of HIV and chronic disease and provide areas for targeted interventions during the roll-out of these new programs in South Africa.

APPENIDX 1. AESTHETICS ASSESSMENT TOOL

Date: __ __ / __ __ / __ __ __ __	Time: __ __:__ __	Study ID:
GPS Coordinates:	Latitude:	Longitude:
First and surname of person completing form:		
Directions: From the street in front of the selected dwelling, scan 360 degrees to determine the amount of the following items.		
A. Are there trees visible on the street in which the selected dwelling is located (including trees in peoplê s backyards? ☐ Little to no trees (0-4) ☐ Some trees (5-19) ☐ Lots of trees (20+)		
B. Is trash present? ☐ Little to no trash (0-20 pieces, trash mainly in receptacles, small amount of loose trash on street) ☐ Some trash (greater than 20 pieces, or 1-2 small piles) ☐ Piles of trash (3 or greater large piles of trash)		
C. Is open wastewater visible? ☐ No wastewater visible ☐ Wastewater from dishes, bath water, car wash is visible (no foul smell) ☐ Wastewater containing human excrement or with a foul smell is visible		
D. Are there street lights visible on the street in which the selected dwelling is located? ☐ No street lights visible ☐ 1-5 street lights ☐ 6 or more street lights		
E. Counting the selected dwelling and the closest 19 households (20 total), how many of the following housing types are visible from the street? (write number in space) __ Stand alone house non-RDP 1-2 rooms (brick) __ Stand alone house non-RDP 3 or more rooms (brick) __ Stand alone house RDP (brick) __ Townhouse/cluster house/semi-detached house (brick) __ Flat in a block of flats (brick) __ House/flat/room in backyard (brick) __ Informal dwelling/shack in backyard (corrugated iron, wood, other) __ Informal dwelling/shack NOT in backyard (corrugated iron, wood, other) __ Other _____		
Notes:		

APPENDIX 2. FOOD AND ALCOHOL VENDOR ASSESSMENT TOOL

Date:	Extension #:	Page: ___ of ___
Name and surname of person collecting data:		

Start time	End time	Food Vendor Type (**tick one**)					Vendor Approval **(tick)**		Variety of Food/Stock (write **number** of each type)								Alcohol Vendor Type (**tick one**)		
Lat	Long	Supermarket	Tuk shop/Spaza shop	Market stall	Restaurant/take-away	Butcher/live animals	Yes	No	Fresh fruit	Fresh Vegetables	Protein (meat, eggs)	Dairy (milk/yogurt)	Starch (bread, rice, pap)	High-fat / High-sugar	Cigarettes	Condoms	Liquor store	Bar/Tavern/Shebeen	Restaurant
1		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
2		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
3		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
4		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
5		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
6		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
7		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
8		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
9		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
10		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
11		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
12		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
13		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
14		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
15		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
16		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
17		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
18		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
19		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐
20		☐	☐	☐	☐	☐	☐	☐									☐	☐	☐

REFERENCES

1. UNAIDS. *AIDS by the numbers*. 2013 http://www.unaids.org/sites/default/files/media_asset/JC2571_AIDS_by_the_numbers_en_1.pdf (accessed Jan 10, 2015)].

2. UNAIDS. *Regional fact sheet, sub-Saharan Africa*. 2012 http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/2012_FS_regional_ssa_en.pdf (accessed Jan 10, 2015)].

3. UNAIDS. *Terminology guidelines* 2011 http://www.unaids.org/sites/default/files/media_asset/JC2118_terminology-guidelines_en_0.pdf (accessed Jan 10, 2015)].

4. Fisher, J.C., H. Bang, and S.H. Kapiga, *The association between HIV infection and alcohol use: a systematic review and meta-analysis of African studies.* Sex Transm Dis, 2007. **34**(11): p. 856-63.

5. Luke, N., *Age and economic asymmetries in the sexual relationships of adolescent girls in sub-Saharan Africa.* Stud Fam Plann, 2003. **34**(2): p. 67-86.

6. Freeman, E.E., et al., *Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies.* Aids, 2006. **20**(1): p. 73-83.

7. UNAIDS. *Global Report* 2013 http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf (accessed Jan 28, 2015)].

8. Simbayi LC, O.S., T.Rehle, D.Onoya, S.Jooste, N.Zungu, D.Labadarios, K.Zuma, *South African National HIV Prevalence, Incidence and Behaviour Survey, 2012.* HSRC Press, Cape Town, South Africa, 2014.

9. Yudkin, P.L., et al., *Deaths caused by HIV disease under-reported in South Africa.* Aids, 2009. **23**(12): p. 1600-2.

10. Fox, M.P., et al., *Attrition through multiple stages of pre-treatment and ART HIV care in South Africa.* PLoS One, 2014. **9**(10): p. e110252.

11. Tanser, F., et al., *Localized spatial clustering of HIV infections in a widely disseminated rural South African epidemic.* Int J Epidemiol, 2009. **38**(4): p. 1008-16.

12. Department of Health, M.R.C., OrcMacro, *South Africa Demographic and Health Survey.* Pretoria: Department of Health, 2007.

13. Alaba, O. and L. Chola, *Socioeconomic inequalities in adult obesity prevalence in South Africa: a decomposition analysis.* Int J Environ Res Public Health, 2014. **11**(3): p. 3387-406.

14. Mkhonto, S.S., D. Labadarios, and M.L. Mabaso, *Association of body weight and physical activity with blood pressure in a rural population in the Dikgale village of Limpopo Province in South Africa.* BMC Res Notes, 2012. **5**: p. 118.

15. Basu, S. and C. Millett, *Social epidemiology of hypertension in middle-income countries: determinants of prevalence, diagnosis, treatment, and control in the WHO SAGE study.* Hypertension, 2013. **62**(1): p. 18-26.

16. Bertram, M.Y., et al., *The non-fatal disease burden caused by type 2 diabetes in South Africa, 2009.* Glob Health Action, 2013. **6**: p. 19244.

17. Peer, N., et al., *Rising diabetes prevalence among urban-dwelling black South Africans.* PLoS One, 2012. **7**(9): p. e43336.

18. Negin, J., et al., *Prevalence of HIV and chronic comorbidities among older adults.* Aids, 2012. **26 Suppl 1**: p. S55-63.

19. Micklesfield, L.K., et al., *Socio-cultural, environmental and behavioural determinants of obesity in black South African women.* Cardiovasc J Afr, 2013. **24**(9-10): p. 369-75.

20. Wrottesley, S.V., et al., *Dietary intake and body composition in HIV-positive and -negative South African women.* Public Health Nutr, 2014. **17**(7): p. 1603-13.

21. Oldewage-Theron, W. and R. Kruger, *Dietary diversity and adequacy of women caregivers in a peri-urban informal settlement in South Africa.* Nutrition, 2011. **27**(4): p. 420-7.

22. Temple, N.J. and N.P. Steyn, *The cost of a healthy diet: a South African perspective.* Nutrition, 2011. **27**(5): p. 505-8.

23. Phaswana-Mafuya, N., et al., *Sociodemographic predictors of multiple non-communicable disease risk factors among older adults in South Africa.* Glob Health Action, 2013. **6**: p. 20680.

24. Bor, J., et al., *Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment.* Science, 2013. **339**(6122): p. 961-5.

25. Deeks, S.G., S.R. Lewin, and D.V. Havlir, *The end of AIDS: HIV infection as a chronic disease.* Lancet, 2013. **382**(9903): p. 1525-33.

26. Buchacz, K., et al., *Disparities in prevalence of key chronic diseases by gender and race/ethnicity among antiretroviral-treated HIV-infected adults in the US.* Antivir Ther, 2013. **18**(1): p. 65-75.

27. Malaza, A., et al., *Hypertension and obesity in adults living in a high HIV prevalence rural area in South Africa.* PLoS One, 2012. **7**(10): p. e47761.

28. Zhou, J., et al., *Determinants and spatial patterns of adult overweight and hypertension in a high HIV prevalence rural South African population.* Health Place, 2012. **18**(6): p. 1300-6.

29. Reynolds, L., *HIV as a chronic disease considerations for service planning in resource-poor settings.* Global Health, 2011. **7**: p. 35.

30. Levitt, N.S., et al., *Chronic noncommunicable diseases and HIV-AIDS on a collision course: relevance for health care delivery, particularly in low-resource settings--insights from South Africa.* Am J Clin Nutr, 2011. **94**(6): p. 1690s-1696s.

31. Abdool Karim, S.S., et al., *HIV infection and tuberculosis in South Africa: an urgent need to escalate the public health response.* Lancet, 2009. **374**(9693): p. 921-33.

32. Shetty, A.K., *Epidemiology of HIV infection in women and children: a global perspective.* Curr HIV Res, 2013. **11**(2): p. 81-92.

33. Diez Roux, A.V. and C. Mair, *Neighborhoods and health.* Ann N Y Acad Sci, 2010. **1186**: p. 125-45.

34. Bocquier, P., *Urbanisation in developing countries: is the 'Cities Without Slums' target attainable? .* Int. Dev. Plann. Rev, 2008. **30**.

35. Konteh, F.H., *Urban sanitation and health in the developing world: reminiscing the nineteenth century industrial nations.* Health Place, 2009. **15**(1): p. 69-78.

36. Maman, S., et al., *The intersections of HIV and violence: directions for future research and interventions.* Soc Sci Med, 2000. **50**(4): p. 459-78.

37. Gonzalez, J.S., et al., *Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis.* J Acquir Immune Defic Syndr, 2011. **58**(2): p. 181-7.

38. Vearey, J., et al., *Urban health in Johannesburg: the importance of place in understanding intra-urban inequalities in a context of migration and HIV.* Health Place, 2010. **16**(4): p. 694-702.

39. Lopez, R.P., *Neighborhood risk factors for obesity.* Obesity (Silver Spring), 2007. **15**(8): p. 2111-9.

40. Pasala, S.K., A.A. Rao, and G.R. Sridhar, *Built environment and diabetes.* Int J Diabetes Dev Ctries, 2010. **30**(2): p. 63-8.

41. Cohen, D., et al., *"Broken windows" and the risk of gonorrhea.* Am J Public Health, 2000. **90**(2): p. 230-6.

42. Burns, P.A. and R.C. Snow, *The built environment & the impact of neighborhood characteristics on youth sexual risk behavior in Cape Town, South Africa.* Health Place, 2012. **18**(5): p. 1088-100.

43. Feldacker, C., M. Emch, and S. Ennett, *The who and where of HIV in rural Malawi: Exploring the effects of person and place on individual HIV status.* Health Place, 2010. **16**(5): p. 996-1006.

44. Cuadros, D.F. and L.J. Abu-Raddad, *Spatial variability in HIV prevalence declines in several countries in sub-Saharan Africa.* Health Place, 2014. **28**: p. 45-9.

45. Grabowski, M.K., et al., *The role of viral introductions in sustaining community-based HIV epidemics in rural Uganda: evidence from spatial clustering, phylogenetics, and egocentric transmission models.* PLoS Med, 2014. **11**(3): p. e1001610.

46. Hixson, B.A., et al., *Spatial clustering of HIV prevalence in Atlanta, Georgia and population characteristics associated with case concentrations.* J Urban Health, 2011. **88**(1): p. 129-41.

47. Kandala, N.B., et al., *The geography of HIV/AIDS prevalence rates in Botswana.* HIV AIDS (Auckl), 2012. **4**: p. 95-102.

48. Madise, N.J., et al., *Are slum dwellers at heightened risk of HIV infection than other urban residents? Evidence from population-based HIV prevalence surveys in Kenya.* Health Place, 2012. **18**(5): p. 1144-52.

49. Qian, S., et al., *Diversity of HIV/AIDS epidemic in China: a result from hierarchical clustering analysis and spatial autocorrelation analysis.* Aids, 2014. **28**(12): p. 1805-13.

50. Mee, P., et al., *Evidence for localised HIV related micro-epidemics associated with the decentralised provision of antiretroviral treatment in rural South Africa: a spatio-temporal analysis of changing mortality patterns (2007-2010).* J Glob Health, 2014. **4**(1): p. 010403.

51. Namosha, E., B. Sartorius, and F. Tanser, *Spatial clustering of all-cause and HIV-related mortality in a rural South African population (2000-2006).* PLoS One, 2013. **8**(7): p. e69279.

52. Cooke, G.S., et al., *Population uptake of antiretroviral treatment through primary care in rural South Africa.* BMC Public Health, 2010. **10**: p. 585.

53. Kruse, G.R., et al., *Drug choice, spatial distribution, HIV risk, and HIV prevalence among injection drug users in St. Petersburg, Russia.* Harm Reduct J, 2009. **6**: p. 22.

54. Akullian, A., et al., *Geographic distribution of HIV stigma among women of childbearing age in rural Kenya.* Aids, 2014. **28**(11): p. 1665-72.

55. Eberhart, M.G., et al., *Behind the cascade: analyzing spatial patterns along the HIV care continuum.* J Acquir Immune Defic Syndr, 2013. **64 Suppl 1**: p. S42-51.

56. De Wet T, P.L., Korth M, Forrester C, *Johannesburg Poverty and Livelihoods Study.* Centre for Social Development in Africa, 2006.

57. Organization, W.H. *Overweight and Obesity Fact sheet N°311*. 2015 http://www.who.int/mediacentre/factsheets/fs311/en/ accessed on May 3, 2015].

58. Jennings, J.M., et al., *Geographic identification of high gonorrhea transmission areas in Baltimore, Maryland.* Am J Epidemiol, 2005. **161**(1): p. 73-80.

59. Jung, I., M. Kulldorff, and O.J. Richard, *A spatial scan statistic for multinomial data.* Stat Med, 2010. **29**(18): p. 1910-8.

60. Garrow, J.S. and J. Webster, *Quetelet's index (W/H2) as a measure of fatness.* Int J Obes, 1985. **9**(2): p. 147-53.

61. Lawrence, L.M., et al., *Environments Associated with Moderate-to-Vigorous Physical Activity and Sedentary Behavior of Colorectal Cancer Survivors.* Int J Behav Med, 2016.

62. Mezuk, B., et al., *Beyond Access: Characteristics of the Food Environment and Risk of Diabetes.* Am J Epidemiol, 2016. **183**(12): p. 1129-37.

63. Paquet, C., et al., *Food environment, walkability, and public open spaces are associated with incident development of cardio-metabolic risk factors in a biomedical cohort.* Health Place, 2014. **28**: p. 173-6.

64. Jongeneel-Grimen, B., et al., *Impact of a Dutch urban regeneration programme on mental health trends: a quasi-experimental study.* J Epidemiol Community Health, 2016.

65. Melis, G., et al., *The Effects of the Urban Built Environment on Mental Health: A Cohort Study in a Large Northern Italian City.* Int J Environ Res Public Health, 2015. **12**(11): p. 14898-915.

66. Kolbe-Alexander, T.L., et al., *The relationship between the built environment and habitual levels of physical activity in South African older adults: a pilot study.* BMC Public Health, 2015. **15**: p. 518.

67. Ochodo, C., et al., *External built residential environment characteristics that affect mental health of adults.* J Urban Health, 2014. **91**(5): p. 908-27.

68. Jack, E. and G.R. McCormack, *The associations between objectively-determined and self-reported urban form characteristics and neighborhood-based walking in adults.* Int J Behav Nutr Phys Act, 2014. **11**: p. 71.

69. Brownson, R.C., et al., *Measuring the built environment for physical activity: state of the science.* Am J Prev Med, 2009. **36**(4 Suppl): p. S99-123.e12.

70. McGinn, A.P., et al., *Exploring associations between physical activity and perceived and objective measures of the built environment.* J Urban Health, 2007. **84**(2): p. 162-84.

71. Ball, K., et al., *Mismatch between perceived and objective measures of physical activity environments.* Prev Med, 2008. **47**(3): p. 294-8.

72. Dake, F.A., et al., *The Local Food Environment and Body Mass Index among the Urban Poor in Accra, Ghana.* J Urban Health, 2016. **93**(3): p. 438-55.

73. Oyeyemi, A.L., et al., *Evaluation of the neighborhood environment walkability scale in Nigeria.* Int J Health Geogr, 2013. **12**: p. 16.

74. Adlakha, D., J.A. Hipp, and R.C. Brownson, *Adaptation and Evaluation of the Neighborhood Environment Walkability Scale in India (NEWS-India).* Int J Environ Res Public Health, 2016. **13**(4).

75. Oyeyemi, A.L., et al., *NEWS for Africa: adaptation and reliability of a built environment questionnaire for physical activity in seven African countries.* Int J Behav Nutr Phys Act, 2016. **13**: p. 33.

76. Glanz, K., J.F. Sallis, and B.E. Saelens, *Advances in physical activity and nutrition environment assessment tools and applications: recommendations.* Am J Prev Med, 2015. **48**(5): p. 615-9.

77. Prasad, A., et al., *Metrics in Urban Health: Current Developments and Future Prospects.* Annu Rev Public Health, 2016. **37**: p. 113-33.

78. Ebrahim, S., et al., *Tackling non-communicable diseases in low- and middle-income countries: is the evidence from high-income countries all we need?* PLoS Med, 2013. **10**(1): p. e1001377.

79. United Nations, D.o.E.a.S.A., Population Division *World Urbanization Prospects: The 2014 Revision, Highlights (ST/ESA/SER.A/352).* 2014.

80. Africa, S.S., *South African Census 2011 Statistical release – P0301.4. 2012.* 2012.

81. Hidalgo, B., et al., *Diagnostic accuracy of self-reported racial composition of residential neighborhood.* Ann Epidemiol, 2015. **25**(8): p. 597-604.

82. Diez-Roux, A.V., et al., *Area characteristics and individual-level socioeconomic position indicators in three population-based epidemiologic studies.* Ann Epidemiol, 2001. **11**(6): p. 395-405.

83. Fiscella, K. and P. Franks, *Impact of patient socioeconomic status on physician profiles: a comparison of census-derived and individual measures.* Med Care, 2001. **39**(1): p. 8-14.

84. Sanchez, B.N., et al., *Combining data from primary and ancillary surveys to assess the association between neighborhood-level characteristics and health outcomes: the Multi-Ethnic Study of Artherosclerosis.* Stat Med, 2008. **27**(27): p. 5745-63.

85. (UNAIDS), J.U.N.P.o.H.A. *90-90-90 An ambitious treatment target to help end the AIDS epidemic*. 2014.

86. Kranzer, K., et al., *Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic review.* J Int AIDS Soc, 2012. **15**(2): p. 17383.

87. Haber, N., et al., *Constructing the cascade of HIV care: methods for measurement.* Curr Opin HIV AIDS, 2016. **11**(1): p. 102-8.

88. Levi, J.R., A; Pozniak, A; Vernazza, P; Kohler, P; Hill A, *Can the UNAIDS 90-90-90 target be achieved? A systematic analysis of national HIV treatment cascades.* BMJ Global Health, 2016. **1**: p. e000010.

89. Makoni, F.S., et al., *Impact of waste disposal on health of a poor urban community in Zimbambwe.* East Afr Med J, 2004. **81**(8): p. 422-6.

90. Ross, C.E. and S.J. Jang, *Neighborhood disorder, fear, and mistrust: the buffering role of social ties with neighbors.* Am J Community Psychol, 2000. **28**(4): p. 401-20.

91. Atwoli, L., et al., *Trauma and posttraumatic stress disorder in South Africa: analysis from the South African Stress and Health Study.* BMC Psychiatry, 2013. **13**: p. 182.

92. Lemanski, C., *A new apartheid? The spatial implications of fear of crime in Cape Town, South Africa.* Environment and Urbanization, 2004. **16**(2): p. 101-111.

93. Stafford, M., T. Chandola, and M. Marmot, *Association between fear of crime and mental health and physical functioning.* Am J Public Health, 2007. **97**(11): p. 2076-81.

94. Simbayi LC, O.S., T.Rehle, D.Onoya, S.Jooste, N.Zungu, D.Labadarios, K.Zuma, *South African National HIV Prevalence, Incidence and Behaviour Survey, 2012*. 2014: Cape Town, South Africa.

95. Solomon, S.S., et al., *Community viral load, antiretroviral therapy coverage, and HIV incidence in India: a cross-sectional, comparative study.* Lancet HIV, 2016. **3**(4): p. e183-90.

96. Granich, R., et al., *Trends in AIDS Deaths, New Infections and ART Coverage in the Top 30 Countries with the Highest AIDS Mortality Burden; 1990-2013.* PLoS One, 2015. **10**(7): p. e0131353.

97. Pillay Y, P.A., *Implementation of the Universal Test and Treat Strategy for HIV positive patients and differentiated care for stable patients*. 2016: South Africa. p. 1-2.

98. Eaton, J.W., et al., *Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a*

combined analysis of 12 mathematical models. Lancet Glob Health, 2014. **2**(1): p. e23-34.

99. Cohen, M.S., et al., *Acute HIV-1 Infection.* N Engl J Med, 2011. **364**(20): p. 1943-54.

100. Cohen, M.S., et al., *Antiretroviral Therapy for the Prevention of HIV-1 Transmission.* N Engl J Med, 2016. **375**(9): p. 830-9.

101. Granich, R.M., et al., *Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model.* Lancet, 2009. **373**(9657): p. 48-57.

102. Tanser, F., et al., *High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa.* Science, 2013. **339**(6122): p. 966-71.

103. Eberhart, M.G., et al., *Individual and community factors associated with geographic clusters of poor HIV care retention and poor viral suppression.* J Acquir Immune Defic Syndr, 2015. **69 Suppl 1**: p. S37-43.

104. Powers, K.A. and W.C. Miller, *Critical Review: Building on the HIV Cascade: A Complementary "HIV States and Transitions" Framework for Describing HIV Diagnosis, Care, and Treatment at the Population Level.* J Acquir Immune Defic Syndr, 2015. **69**(3): p. 341-7.

105. Mayne, E.S. and J.A. George, *Mortal allies: human immunodeficiency virus and noncommunicable diseases.* Curr Opin HIV AIDS, 2017. **12**(2): p. 148-156.

106. Neuhaus J, J.D.J., Baker JV, Calmy A, Duprez D, La Rosa A, Kuller LH, Pett SL, Ristola M, Ross MJ, Shlipak MG, Tracy R, Neaton JD, *Markers of inflammation, coagulation, and renal function are elevated in adults with HIV infection.* J Infect Dis, 2010(201): p. 1788ï 95.

107. Kuller LH, T.R., Belloso W, De Wit S, Drummond F, Lane HC, Ledergerber B, Lundgren J, Neuhaus J, Nixon D, Paton NI, Neaton JD, *Inflammatory and coagulation biomarkers and mortality in patients with HIV infection.* PLoS Med, 2008(5): p. e203.

108. Ryom L, M.A., Kirk O, Worm SW, Kamara DA, Reiss P, Ross M, Fux CA, Morlat P, Moranne O, Smith C, Lundgren JD, *Association between antiretroviral exposure and renal impairment among HIV-positive persons with normal baseline renal function: the D:A:D study.* The Journal of infectious diseases, 2013. **207**: p. 1359ï 69.

109. Scherzer R, E.M., Li Y, Choi AI, Deeks SG, Grunfeld C, Shlipak MG, *Association of tenofovir exposure with kidney disease risk in HIV infection.* Aids, 2012. **26**: p. 867ï 75.

110. Magodoro, I.M., T.M. Esterhuizen, and T. Chivese, *A cross-sectional, facility based study of comorbid non-communicable diseases among adults living with HIV infection in Zimbabwe.* BMC Res Notes, 2016. **9**: p. 379.

111. Divala, O.H., et al., *The burden of hypertension, diabetes mellitus, and cardiovascular risk factors among adult Malawians in HIV care: consequences for integrated services.* BMC Public Health, 2016. **16**(1): p. 1243.

112. Rabkin, M., et al., *Missed Opportunities to Address Cardiovascular Disease Risk Factors amongst Adults Attending an Urban HIV Clinic in South Africa.* PLoS One, 2015. **10**(10): p. e0140298.

113. Kavishe, B., et al., *High prevalence of hypertension and of risk factors for non-communicable diseases (NCDs): a population based cross-sectional survey of NCDS and HIV infection in Northwestern Tanzania and Southern Uganda.* BMC Med, 2015. **13**: p. 126.

114. Boone-Heinonen, J., et al., *Fast food restaurants and food stores: longitudinal associations with diet in young to middle-aged adults: the CARDIA study.* Arch Intern Med, 2011. **171**(13): p. 1162-70.

115. Rundle, A., et al., *Neighborhood food environment and walkability predict obesity in New York City.* Environ Health Perspect, 2009. **117**(3): p. 442-7.

116. Laraia, B.A., et al., *Proximity of supermarkets is positively associated with diet quality index for pregnancy.* Prev Med, 2004. **39**(5): p. 869-75.

117. Moore, L.V., et al., *Associations of the local food environment with diet quality--a comparison of assessments based on surveys and geographic information systems: the multi-ethnic study of atherosclerosis.* Am J Epidemiol, 2008. **167**(8): p. 917-24.