Racial and Ethnic Disparities in Type-2 Diabetes: A Multilevel Perspective

Rebecca Shackelton Piccolo

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Research group affiliation(s): New England Research Institutes, Inc.

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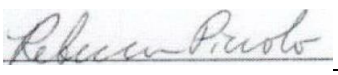
Signed: _  _____ Date: _21/July/2015_____

Rebecca Shackelton Piccolo

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ABSTRACT

In the United States (US), diabetes affects an estimated 13% of adults (25.8 million people).[2, 3] A disproportionate burden of the disease is borne by US minority populations.[4] Black and Hispanic Americans have higher prevalence of type 2 diabetes mellitus (T2DM),[5] achieve poorer disease control,[6, 7] and have more T2DM complications than their White counterparts.[8, 9] Efforts to reduce these disparities are hindered by the fact that patients typically have T2DM for 4-7 years prior to diagnosis.[10] There is a confluence of disadvantages: behavioural risk factors, genetic predisposition, lack of access to adequate health care, and local environmental disadvantages, all are likely to contribute to these increased burdens in a synergistic fashion. A comprehensive understanding of "upstream" factors contributing to racial/ethnic differences in T2DM therefore offers the greatest potential to reduce the "downstream" costs of T2DM faced by disadvantaged populations.[11]

This research investigated the roles of certain risk factors in racial/ethnic variation in T2DM using the Boston Area Community Health (BACH) Survey. The BACH Survey is a community-based, stratified random sample, epidemiologic cohort of 5,502 Boston, Massachusetts residents. Follow-up surveys were conducted approximately five (BACH II, 2008-2010, N=4,144) and seven (BACH III, 2010-2012, N=3,155) years later. The BACH III survey was designed to assess the relative contributions of (1) genetic, (2) lifestyle/behavioural, (3) psychosocial, (4) biophysiologic, (5) contextual/neighbourhood, and (6) social/economic determinants to racial/ethnic disparities in diabetes. Therefore, my analyses focused on the 3,155 participants of the third wave of the BACH survey.

First, I examined the role of biogeographic ancestry (BGA) versus socioeconomic factors in racial/ethnic disparities in the incidence of T2DM over roughly seven years of follow-up. I used the excess relative risk method, the risk difference method, and g-computation to examine the direct and indirect effects of race/ethnicity on T2DM incidence. Using the g-computation

method, I found that socioeconomic factors accounted for 44.7% of the excess risk of T2DM among Blacks and 54.9% among Hispanics. The findings indicated that BGA had almost no direct association with T2DM and was almost entirely mediated by self-identified race/ethnicity and socioeconomic factors.

Second, I examined the role of neighbourhood contextual factors in racial/ethnic disparities. Two-level random intercepts logistic regression was applied to assess the associations between race/ethnicity, neighbourhood characteristics (census tract socioeconomic status, racial composition, property and violent crime, open space, geographic proximity to grocery stores, convenience stores, and fast food, and neighbourhood disorder) and prevalent T2DM (BACH III diabetes status). Multilevel models indicated a significant between-neighbourhood variance estimate of 0.943, providing evidence of neighbourhood variation. Individual-level demographic factors (race/ethnicity, age and gender) explained 22.3% of the neighbourhood variability in T2DM. However, the addition of neighbourhood-level variables to the model had very little effect on the magnitude of the racial/ethnic disparities and on the between-neighbourhood variability.

Finally, I assessed the relative contributions of six domains of influence to racial/ethnic disparities in T2DM: (1) socioeconomic, (2), local environmental, (3) psychosocial, (4) lifestyle/behavioural, (5) biophysiologic, and (6) genetic/ancestral. I constructed risk scores for each domain of influence and used structural equation models (SEM) to evaluate the direct effects of each conceptual domain of influence on T2DM prevalence as well as the indirect effect of each conceptual domain on the magnitude of the racial/ethnic disparities in T2DM. The final models indicated that 38.9% of the total effect of Black race on T2DM prevalence was mediated by the socioeconomic, environmental, psychosocial, lifestyle/behavioural risk scores with 21.8% of the total effect of Black race being explained by socioeconomic risk. 45.7% of total effect of Hispanic ethnicity was mediated. Again, the largest mediator was the socioeconomic risk score with 26.2% of the total association explained.

My analyses consistently demonstrated that social determinants contributed to racial/ethnic disparities in T2DM. My results suggest that socioeconomic factors are the largest contributors to the causation and/or amplification of these disparities. Biogeographic ancestry (an individual's genetic race/ethnicity) had no direct effect on T2DM prevalence or incidence. Neighbourhood factors did not contribute to racial/ethnic disparities once individual socioeconomic factors were taken into account. Finally, while lifestyle/behavioural and biophysiologic characteristics had significant direct effects on T2DM prevalence, they did not appear to substantially contribute to disparities in T2DM once socioeconomic factors were taken into account.

These results have national and local policy implications as they suggest that in order to reduce disparities, either wide-scale social and economic policy shifts need to occur, or interventions need to be targeted toward racial/ethnic minorities and the socially and economically disadvantaged.

Contents

Tables

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Acronyms and abbreviations

AIMS = Ancestry Informative Markers

ARIC = Atherosclerosis Risk in Communities

AusDiab = Australian Diabetes, Obesity, and Lifestyle Study

BACH = Boston Area Community Health

BAS = Bi-dimensional Acculturation Scale

BGA= Biogeographic ancestry

BMI = Body mass index

CDC = Centers for Disease Control

CFA = Confirmatory factor analysis

CFI = Comparative fit index

CI = Confidence interval

CRP = C-reactive protein

DAG = Directed Acyclic Graph

ERR = Excess relative risk

FFQ = Food frequency questionnaire

FG = Fasting glucose

GAP = Genetic Analysis Platform

GIS = Geographic information systems

HbA1c = Glycated haemoglobin

HIA = Health impact assessment

HPA = Hypothalamic-pituitary-adrenal

ICC = Intra class correlation coefficient

KNN = k nearest neighbour

MCAR = Missing completely at random

MICE = Multivariate Imputation by Chained Equations

MTO = Moving to Opportunity

NEFA = Non-esterified fatty acid

NHANES = National Health and Nutrition Examination Survey

NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases

NIH = National Institutes of Health

RMSEA = Root mean square error of approximation

RR = Risk ratio

SE = Standard error

SEM = Structural equation modelling

SES = Socioeconomic status

SNP = Single nucleotide polymorphism

T2DM = Type 2 Diabetes Mellitus

WC = Waist circumference

WHI = Women's Health Initiative

WHR = Waist to hip ratio

1 Introduction

1.1 Introduction

Achieving health equity, eliminating disparities, and improving the health of all population groups has been identified as a national priority in the United States (US)[12] and worldwide.[13] The term 'disparities' refers to group differences in the burden of mortality and morbidity that are distributed inequitably by: race/ethnicity, gender, sexual identity, age, disability, or socioeconomic status. Effectively combating disparities requires addressing multiple potential influences on the health status of specific populations.[11] These include variations in individual/proximate causes (lifestyles and behaviours and biological influences), as well as population/upstream causes (socio-demographic influences and/or local environment).[14] Complex factors—genetic, physiological, psychological, familial, cultural, social, political and economic may coalesce to determine these disparities.[15]

The burden of type 2 diabetes mellitus (T2DM) disproportionately affects US minority populations. Black and Hispanic Americans have a higher T2DM prevalence,[2] greater diabetes risk factors, poorer control of their diabetes,[6, 7] and a greater number of diabetes-related complications than White Americans.[8, 9, 16] Diabetes is the seventh and fourth leading cause of death among White and Black Americans, respectively[17] and diabetes accounts for a loss of 0.332 years of life among Black versus White Americans.[18]

Many factors have been identified as contributing to these disparities, including variations in lifestyles and behaviours,[19-21] biophysiological, [22-25, 26] psychosocial,[27-29] sociodemographic,[30-32] environmental factors,[33-35] and underlying genetic/ancestral factors,[36, 37] and events occurring during foetal life including maternal physiology and life context. Several studies have attempted to evaluate whether racial/ethnic disparities can be attributed to factors other than race/ethnicity.[30, 38-43] However, research to date has largely focussed on individual risk factors in

isolation and the relative contribution of these multiple competing factors has not been identified.

1.2 Overall Aim and Objectives

This research aimed to explore racial/ethnic disparities in T2DM using a novel multilevel, multisystem conceptual model of the creation and/or amplification of racial/ethnic disparities in T2DM. I tested this conceptual model using data from the Boston Area Community Health (BACH) Survey which was specifically designed with the goal of understanding racial/ethnic differences in the prevalence and incidence of diabetic illness. The specific objectives of the research papers are:

1. to quantify the contribution of genetic biogeographic ancestry versus socioeconomic factors to racial/ethnic disparities in T2DM incidence,
2. to identify and estimate the contribution of specific aspects of contextual environments/neighbourhoods to racial/ethnic disparities in T2DM prevalence, and
3. to quantify the relative contribution of (1) social and economic, (2) contextual/neighbourhood, (3) psychosocial, (4) lifestyle/behavioural, (5) biophysiologic, and (6) genetic/ancestral factors to racial/ethnic disparities in prevalent T2DM.

1.3 Structure of the Thesis

This thesis incorporates four published papers as chapters; three of which have been submitted and published in peer-reviewed journals. These papers comprise Chapters 5-8. These chapters are prefaced by the required cover sheet and evidence of copyright retention. The accepted, un-copyedited text of the manuscripts is presented. However, for consistency the journal submission formatting has not been used (e.g. tables and figures are in-line with text). Additional

analyses and details that could not be included due the journal's word limits are included following the reproduced paper.

This initial chapter provides a framework for the thesis including my role in the research, collaborating institutions, ethical clearances and funding. The second chapter is a literature review that focuses on genetic/ancestral, lifestyle/behavioural, psychosocial, biophysiologic, contextual/neighbourhood, and socioeconomic determinants of T2DM as well as their potential roles in creating and/or amplifying racial/ethnic disparities in T2DM. This literature review is not intended to be comprehensive; rather it is intended to identify and categorize the major determinants of T2DM that are potential contributors to disparities. The third chapter provides a description of the methodologies used in the study and the study's conceptual framework.

The first paper is a cohort profile of the Boston Area Community Health (BACH) Survey. This constitutes **Chapter 0** and provides details on the BACH study which was used to address this thesis's main objectives.

There are three main chapters addressing the study's objectives analysing the BACH study data. **Chapter 5** focuses on the contribution of biogeographic ancestry to racial/ethnic disparities in T2DM. **Chapter 6** examines the contributions of neighbourhood characteristics to racial/ethnic disparities. **Chapter 7** examines the relative contributions of socioeconomic, neighbourhood, psychosocial, lifestyle/behavioural, biophysiologic, and biogeographic ancestral factors to racial/ethnic disparities in T2DM.

Chapter 8 is a discussion section that synthesizes the findings from each of the chapters including discussion of the strengths and limitations of this work. Chapter 0 discusses the implications of the study findings for policy and practice.

The appendices provide additional material relevant to this work including ethics approval, data collection instruments, and publications and presentations relevant to this work.

1.4 Role of the Candidate

The BACH III study was conceptualised, proposed, and awarded to the Principal Investigator of the BACH study, John B. McKinlay. I served as the project manager, lead scientist, and lead statistician on the project. I designed the study questionnaires, secured the necessary ethics approval, assisted with the development of the data management system, assisted with the recruitment and training of staff, and managed all day-to-day aspects of the study.

I conceptualized the papers for publication included in the body of this thesis, conducted all statistical analyses, and wrote the initial draft of all four papers. I then incorporated feedback from co-authors in an iterative process.

1.5 Collaborating Institutions

The institutions collaborating on this research were New England Research Institutes, Inc. (Watertown, MA), Massachusetts General Hospital (Boston, MA), and the London School of Hygiene and Tropical Medicine (London, UK).

1.6 Ethical Clearance

Ethical approval for this work was provided by the New England Research Institutes Institutional Review Board and the London School of Hygiene and Tropical Medicine Ethics Committee (see Appendix A).

1.7 Funding

Funding to support this research was received from the National Institute of Diabetes and Digestive and Kidney Diseases, U.S. Department of Health and Human Services Grant Number DK080786.

2 Background

National survey data from National Health and Nutrition Examination Survey (NHANES) estimate that approximately 40% of the US population has some hyperglycaemic condition.[2] It is estimated that 12.9% of US adults have diabetes and another 29.5% have prediabetes.[3] According to a fact sheet released in 2014 by the CDC, T2DM is a growing public health problem that affects 29.1 million US adults.[2] Diabetes is implicated in kidney failure, lower-limb amputations, blindness, heart disease, and stroke, and is the seventh leading cause of death in the US.[2] A disproportionate burden of T2DM is experienced by minorities in the US. US national survey data indicate that 12.8% of Hispanics, and 13.2% of non-Hispanic Blacks have diagnosed diabetes compared to 7.6% of non-Hispanic Whites.[2] When including both undiagnosed and diagnosed diabetes in these estimates, 18.7% of all Blacks have diabetes compared to only 10.2% of Whites.[2] The incidence of diabetes is estimated to be 66% higher among Hispanics and 77% higher among Black adults than among White adults.[2] Further research shows that Black and Hispanic Americans have poorer control of their diabetes[6, 7] and a greater number of diabetes-related complications than Whites.[8, 9, 16]

The contributors to racial/ethnic disparities in T2DM are complex. Individual characteristics and behaviours are often the focus of epidemiologic studies.[15] However, these ubiquitous risk factors do not appear to explain the widespread racial/ethnic disparities in population health which are produced by multiple reinforcing risk factors.[15] Underlying the problem are a complex interplay of factors including: (i) social, political and economic structure and policy, (ii) contextual/neighbourhood environments, (iii) psychosocial stressors, (iv) lifestyle/behavioural factors and their driving forces (e.g. cultural, familial), (v) biophysiologic factors, and (vi) genetics, ancestry, and foetal programming. While many risk factors for T2DM have been identified and implicated in the aetiology of racial/ethnic disparities in T2DM, most research has viewed these risk factors in isolation or explored one particular category of explanation (i.e.

lifestyle characteristics associated with T2DM). The relative contributions of these identified risk factors to T2DM overall, and to racial/ethnic disparities in T2DM, are unknown.

The purpose of the following review of the literature is two-fold: (1) identify and categorize the major determinants of T2DM to ensure that the measures included in this thesis research are as inclusive as possible, (2) elucidate how these independent risk factors for T2DM may contribute to racial/ethnic disparities. Furthermore, this literature review helps to identify and quantify the major measured and unmeasured influences in the models considered in this research.

Given these aims, this literature review places an emphasis on large, multi-ethnic or multi-racial, observational research projects conducted among adults. The strengths and limitations of some of the research projects mentioned frequently in this background are described below.

The National Health and Nutrition Examination Survey (NHANES) is the largest program of studies designed to assess health in the US. The survey combines data from individual interviews and physical examinations. Nearly 5,000 individual participants, representative of the US population, participate each year. Despite the strengths in sample size, survey design, breadth of measures, and representativeness, there are nonetheless limitations to the NHANES data. Specifically, each yearly instalment is cross-sectional in nature and there are small numbers of participants within certain racial/ethnic subgroups, including non-Mexican Hispanic adults.

The Atherosclerosis Risk in Communities (ARIC) study is a prospective population study initiated in 1987.[44] Conducted in four cities in the US, 15,792 subjects were enrolled and followed three times through 1995. The strengths of the ARIC study, particularly to informing this research, are the extensive measures collected (including social, lifestyle/behavioural, and extensive genetic markers), the large sample size, the varied study locations (both rural and urban with differing social, economic, and geographic profiles), the prospective design, and the large sample of Black and White participants. Limitations relevant to evaluating potential determinants in this

research are that the study lacks adequate numbers of Hispanic participants to evaluate determinants relevant to Hispanic populations.

The Multiethnic Study of Atherosclerosis (MESA) study is a prospective cohort study initiated in 2000.[45] Conducted in six geographically and compositionally diverse areas in the US, the study enrolled 6,814 racially/ethnically diverse participants (White, Black, and Hispanic). Five follow-up examinations have occurred through 2012. The strengths of the MESA study are the prospective design, the varied study locations, the racially/ethnically diverse participants, and the inclusion of markers identifying pre- and undiagnosed- diabetes. While both the ARIC and the MESA studies provide a wealth of prospectively captured data elements from racially/ethnically diverse cohorts, there is an emphasis in both of these studies' publications on biophysiologic and genetic determinants. Although there are several publications from both that focus on neighbourhood determinants of disease.

The Whitehall II study, in contrast, was specifically designed to investigate social and economic influences on health. Initiated in 1985 (N=10,308), the prospective cohort study's sample base was all civil servants working in London – Whitehall departments. The Whitehall II study provides an excellent opportunity to examine long-term exposures including childhood and life-course measures. However, there are limitations in generalizing information gathered from the UK based sample to the US. Notably, the socioeconomic diversity of individuals employed as civil servants cannot be extrapolated to the full spectrum of socioeconomic diversity in the US. Additionally, there is limited racial/ethnic diversity in the sample.

2.1 Genetic/Ancestral Factors

2.1.1 Family History

First-degree relatives of individuals with T2DM are at increased risk of developing hyperglycaemic conditions including insulin resistance,[46-49] decreased beta cell function,[50, 51]

metabolic syndrome,[51, 52] and have a 4-to 5- fold higher risk of developing this disease than those without a family history.[53] This association is consistent across generations of research studies, across cultures,[54] and across study designs from classical experimental designs[55, 56] to population studies. In addition to the genetic risk associated with a family history of T2DM, it has been suggested that genetic predisposition to T2DM is related to ethnicity.[47,48,57] For example, Jensen *et al* state that "it is apparent that genetic predisposition related to ethnicity is a major determinant of diabetes risk."[57] However, the authors' findings suggest that that the pathogenesis of T2DM is similar among racial/ethnic groups.

2.1.2 Biogeographic Ancestry

Despite considerable discussion of the roles of genetics versus environmental factors in health disparities,[58-60] considerable uncertainty remains regarding the importance of genetic variation. The concepts of genetics, race, and ethnicity are often confused.[61-63] The term 'race' is commonly defined in terms of biological differences between groups assumed to have different biogeographical ancestries.[64] However, the genes associated with 'race' represent only a small fraction of the estimated 30,000 total genes in our genomes.[65, 66] It is important to note that there is substantially less genetic variation between than within commonly defined racial/ethnic groups.[67] Analysis of variance of genetic variation has indicated that approximately 75% of genetic variance is found 'within' racial/ethnic groups, while 10% of the variance is found 'between' races.[64] Furthermore, the US Census categorizations (White, Black, Asian, etc.) are largely social constructs, as is the concept of biological race itself.[63, 68] In contrast, ethnicity is a complex multidimensional construct that reflects biological factors, geographical origins, historical influences, as well as social, cultural, economic factors.[69]

A genetic basis for racial/ethnic differences in diabetes risk, the 'thrifty gene' hypothesis, was first proposed over 40 years ago.[70] The thrifty gene hypothesis proposed that the high prevalence of obesity and T2DM in African Americans, Native Americans and admixed Hispanics was due to a metabolic efficiency rendered detrimental by Western society's abundance

coupled with a shift towards a sedentary lifestyle in both occupation and leisure activities.[70-72] The hypothesis has been heavily criticized from several different perspectives,[61] but has nevertheless been revived in recent years as the rapid evolution of science and technologies have facilitated an expansion in genetic research.

Since T2DM has a complex genetic aetiology, it may be important to account for the substantial heterogeneity in genetic heritage that exists in admixed populations.[73-76] Individual proportions of European, African, and Native American ancestry can vary substantially among the commonly-used categories of Black [73], Hispanic [75], and White.[77] Several studies have suggested that the biologic mechanisms leading to increased T2DM risk in Black and Hispanic Americans may be related to genes associated with BGA[47,4857] since certain genetic markers tend to cluster by BGA.[78] Although these genes constitute only a very small portion of genetic variation, their presence suggests that genetic differences across racial/ethnic groups could have some implications for racial/ethnic disparities.

Ancestry Informative Markers (AIMs) are a method of genotyping an individual's genetic race/ethnicity. Several studies have examined the role of BGA in T2DM by utilizing these markers. These studies have produced mixed results to date. Cross-sectional analysis from ARIC Study found that BGA was not associated with HbA1c among African Americans and found that the contributions of demographic and metabolic factors outweighed the contributions of BGA.[79] However, an analysis of ARIC/Jackson Heart data, found that BGA was associated with T2DM among African Americans, a finding that changed little after adjustment for lifestyle and socioeconomic factors.[80] The latter study was also cross-section in nature, which may overestimate the contribution of genetic (immutable) factors and underestimate the contribution of socioeconomic and/or lifestyle behavioural (mutable) factors.

Studies among Hispanic populations have also produced mixed results. In a study of Columbian and Mexican participants, the association between ancestry and T2DM was attenuated when socioeconomic factors were taken to account.[36] However, SES was measured based on

residential location, rather than individually reported. In a study of Puerto Rican participants living in the continental US demonstrated a negative association between West African BGA and T2DM, meaning participants with a greater percentage of West African ancestry actually had a lower prevalence of T2DM.[81] While this study was cross-sectional, on the spot diabetes testing (fasting glucose $\geq$ 126 mg/dl), allowed for both diagnosed and undiagnosed disease to be captured.

Prior to BACH, only one study had examined the effects of ancestry among both African and Hispanic Americans. The Women's Health Initiative (WHI) found that ancestry was significantly associated with diabetes risk, but that socioeconomic factors attenuated the effects among Hispanic but not African American women.[37] The WHI is a prospective clinical trial/cohort study and included 16,476 in this analysis using time-to-diabetes diagnosis. However, the WHI used geocoded addresses to obtain individual-level socioeconomic information which may attenuate diabetes risk attributable to SES due to measurement error. The BACH III study examined the effect of West African and Native American ancestry on fasting glucose and HbA1c among non-diabetic individuals. In these analyses we found that West African but not Native American ancestry had a small, but significant, effect on fasting glucose and HbA1c. These findings were not affected by adjustment for socioeconomic factors.[82]

These studies highlight the complexity of the relationship between biogeographic ancestry and socioeconomic status. Specifically, in several studies among admixed Hispanic populations, country of origin, individual genetic ancestry, and socioeconomic status were intertwined. Martinez-Marignac *et al* suggest among Hispanic populations, individual genetic ancestry may be, in part, affected by socioeconomic stratification (segregation) and country of origin.[36, 83] At the very least, these arguments underscore the need for comprehensive measures of socio-demographic factors when examining the role of genetic determinants in T2DM.

2.1.3 Other Genetic Factors

Genetic studies have identified and confirmed approximately 70 loci that are associated with T2DM risk and over 30 loci associated with variations in fasting glucose.[84-87] Early studies focused primarily on people of European descent. However, recent studies have extended this research to Black and Hispanic populations.[88-90] The findings from these studies indicate substantial overlap in the T2DM susceptibility loci across racial/ethnic groups. This indicates that genetic variants contribute similarly to diabetes risk across races/ethnicities,[80, 85, 90-93] meaning that it is unlikely that these identified loci explain racial/ethnic differences in diabetes risk. A recent study which recruited a large sample of African Americans and European Americans found that African Americans have a greater overall T2DM risk allele load. However, they found that cumulative risk allele load was associated with risk of T2DM in European Americans, but only marginally in African Americans.[94] This result suggests that total risk allele load may differentially affect people of different race/ethnicities.

2.2 Lifestyle/Behavioural Determinants

2.2.1 Physical Activity

Physical activity is an important risk factor for the development of diabetes.[19] Individuals who participate in regular physical activity demonstrate a reduced risk of developing T2DM.[19] Subjectively[95] (self-report) and objectively[96] (accelerometry) measured physical activity data demonstrate that light to moderate physical activity is beneficial to glucose tolerance whereas sedentary time is detrimental glucose tolerance. Research has repeatedly suggested that substituting light-intensity activity for television viewing or other sedentary time may be a practical and achievable preventive strategy to reduce the risk of T2DM. This observation evidence is further bolstered by data from a randomized study of overweight/obese adults. This trial indicated that interrupting sitting time with short bouts of light- or moderate-intensity walking lowers post meal glucose and insulin levels thereby improving glucose metabolism.[97]

According to self-report data, White Americans have significantly more leisure-time physical activity than Black and Hispanic Americans.[98] However, accelerometry data, which may be less prone to self-report measurement and recall error, indicate that Hispanics may have overall higher physical activity levels than Blacks and Whites. This may be due, in part, to physically demanding occupational or domestic activities.[99]

Indirectly, physical activity affects T2DM risk through its effect on BMI/obesity. Regular physical activity, in addition to helping to maintain a healthy weight, is associated with short-term up-regulation and long-term down-regulation of inflammatory markers, a key biophysiologic pathway to insulin resistance, pre-diabetes, and T2DM.[100, 101] Clinical studies have shown that exercise improves skeletal muscle glucose uptake and increases insulin sensitivity.[102] Physical activity affects several components in the insulin signalling pathway simultaneously, which facilitate glucose uptake into skeletal muscle.[103]

2.2.2 Dietary Patterns

Like physical activity, healthy dietary patterns have been linked to a reduced risk of developing diabetes in a number of research studies.[20] Long-term data from NHANES have indicated differences in dietary patterns between White and Black participants (1971-2002).[104] These data indicated that Black participants tend to consume foods higher in energy density (i.e. fat and sugar) and consume fewer vegetables than their White counterparts.[104] In particular, diets that are high in refined sugars, high in saturated fat, and low in fibre are associated with pro-inflammatory responses that may be in the causal pathway towards T2DM. For example, a diet high in refined sugars (e.g. sugar sweetened beverages, candy, white bread) is associated with increased levels of pro-inflammatory markers like C-reactive protein (CRP).[105] The consumption of saturated fatty acids is associated with deficient insulin signalling through several molecular pathways,[106-108] and also with pro-inflammatory responses.[109, 110]

2.2.3 Alcohol Consumption

Alcohol abuse is considered as a risk factor for several adverse public health outcomes. A systematic review of the literature[111] indicated that low-to-moderate alcohol intake (1-3 drinks/day) may result in a lower incidence of T2DM versus teetotallers (33% to 56% lower incidence) whereas heavy alcohol consumption (> 3 drinks/day) may increase the risk for incident T2DM (43% increased incidence of diabetes). Moderate alcohol consumption appears to augment insulin sensitivity and may decrease the incidence of non-alcoholic fatty liver disease, which is closely related to metabolic diseases including insulin resistance and obesity.[112-114] Most research indicates a J- or U-shaped relationship between alcohol consumption and the development of T2DM,[111, 115] but the relationship between alcohol consumption and T2DM is not fully explained. Furthermore, the mechanisms involved in the augmentation of insulin sensitivity by modest alcohol consumption are not clearly understood.

2.2.4 Obesity and Fat Distribution

Being overweight (body mass index (BMI) ≥ 25 kg/m^2 or obese (BMI ≥ 30 kg/m^2) is a well-established risk factor for insulin resistance and diabetes.[21, 116, 117] Obesity confers a 20-50 fold increased risk for developing T2DM.[21, 118, 119] In the US, only about a third of adults are considered to be of "normal" weight,[120] and similar trends are being observed worldwide.[121] The prevalence of obesity is increasing and, in the US, varies by race/ethnicity.[122] Data from NHANES found that 49.5% of Blacks, 39.1% of Hispanics, and 34.3% of Whites are obese.[123] African-Americans and Hispanics are more likely to be obese at the time of T2DM diagnosis than their White counterparts.[124, 125]

The relationship between race and diabetes risk may be modified by body mass index (BMI). Black and White Americans with higher BMIs appear to have a similar risk for diabetes, whereas Blacks with lower BMIs have a higher risk of diabetes (OR of 1.87 and 1.76 for men and women, respectively) than their White counterparts.[41] This data comes from the NHANES, Epidemiologic

Follow-up Study (1971-1992) which included over 1,000 incident cases of diabetes during 20 years of follow-up.

In contrast cross-sectional data from NHANES indicate that Hispanic men and women appear to have greater risk for diabetes than White adults across the BMI spectrum.[125, 126] Black and Hispanic adults appear to have higher insulin resistance than White adults even after adjustment for BMI.[116, 127, 128] Trends in the prevalence of diabetes by race/ethnicity over time demonstrate that ethnic disparities are worsening among normal and overweight groups but not among the obese.[129]

One hypothesized reason for these differential effects may be differences in fat distribution, particularly central adiposity. Central adiposity is highly correlated with increased insulin resistance which in turn increases risk for T2DM.[130, 131] Waist circumference appears to be a stronger predictor of T2DM risk than BMI with the relationship between waist circumference and T2DM risk being found even among people within the "normal range" of BMI (BMI < 25 kg/m^2).[132] The ARIC study found that central adiposity accounted for nearly 50% of the excess risk of T2DM in Black women vs. White women. However, the results in men were not consistent.[22] The anthropometric indices of waist circumference (WC) and waist-to-height ratio (WHR) are associated with insulin resistance.[23-25] Results from a cross-national study using NHANES data from England and the US demonstrated ethnic differences in the prevalence of diabetes, even among those characterized as normal weight and suggested that differences in WC or WHR may account for some of these differences.[133]

2.2.4.1 Mechanisms

Most obese individuals, even those who are insulin resistant, do not develop hyperglycaemia. Among most individuals, the pancreatic islet beta cells (the cells that store and release insulin) increase insulin release to compensate for the reduced efficiency of insulin action, thereby maintaining normal glucose tolerance.[134] For obesity and insulin resistance to be associated with

T2DM, beta cells must be unable to offset decreased insulin sensitivity.[135, 136] Adipose tissue also affects metabolism by releasing non-esterified fatty acids (NEFAs) and glycerol, hormones (including leptin and adiponectin), and pro-inflammatory cytokines.[137-139] It has been suggested that the release of NEFAs "may be the single most critical factor in modulating insulin sensitivity."[140] Increased NEFA levels are observed in obesity and T2DM, and are associated with the insulin resistance observed in both.[140] Insulin resistance develops within hours of an acute increase in plasma NEFA levels.[141]

The distribution of body fat is also a significant determinant of insulin sensitivity. Most obese individuals are insulin resistant. However, among lean individuals with different body fat distributions, insulin sensitivity can vary markedly. Lean individuals with more peripheral fat are more insulin sensitive than lean individuals with more centrally distributed fat (i.e. the abdominal and chest areas).[135, 142] There are differences in the characteristics of peripheral and central adipose tissue that may explain, in part, why the metabolic effects differ. For example, intra-abdominal fat expresses more secretory protein encoding genes and proteins responsible for energy production.[143]

Recent decades have seen major advances in our understanding of the mechanisms underlying obesity, insulin resistance and T2DM. However, despite these advances in understanding there is still much to be explored regarding racial/ethnic disparities in these conditions and the mechanisms underlying these disparities.

2.3 Psychosocial

Psychosocial factors may also play an important role in the development of T2DM. Specifically, increases in the prevalence of short sleep duration and depressive symptoms have been implicated as risk factors for T2DM.[144, 145] Studies have also demonstrated the association of various psychosocial stressors with diabetes, including adverse life events[28] and a low sense of coherence.[29]

2.3.1 Sleep

Scientists are now beginning to recognize the downstream health consequences of sleep-related problems, including increased risk for obesity[146, 147] which in turn increases risk for T2DM.[148-151] Data from NHANES indicate that sleeping fewer than five hours a night more than doubles the risk of pre-diabetes.[152] Recent research indicates that sleep restriction results in physiological changes that may have profound implications for T2DM related diseases.[153] There are several mechanisms by which sleep disturbances and/or deprivation may contribute to weight gain and incident obesity conferring increased T2DM risk. Short sleep increases cortisol and insulin secretion thereby promoting fat storage. Increases in ghrelin and reductions in leptin which stimulate appetite and inhibit satiety regulating signals to the brain, respectively, can lead to increased intake of high fat and high carbohydrate foods.[147] Sleep loss also leads to increased systemic inflammation as measured by CRP concentrations.[154] In addition, insufficient or inadequate sleep may lead to decreased energy expenditure, further increasing the risk for weight gain and incident obesity.[155, 156] Increased insulin production coupled with impaired glucose metabolism, greatly increase the risk for T2DM.[157] Short sleep increases blood pressure and sympathetic hyperactivity.[158] Sleep restriction and poor sleep quality are now being seen as major risk factors for obesity and obesity-related disease, right along with the two of the most commonly identified risk factors: lack of exercise and overeating.[147, 159]

Sleep problems appear to differentially affect racial/ethnic minorities,[160-162] with most studies documenting worse sleep among minority groups, including several smaller cross-sectional studies and the National Health Interview Survey (N=32,749 adults).[161-167] For example, Patel *et al*, found that African-Americans were 65% more likely than Whites to report poor sleep quality and Hispanics were 59% more likely.[168] Research suggests that the racial disparities in sleep are partially explained by (mediated by) SES and other related factors (e.g. occupation and financial strain).[162, 169-173] Low income, education, and overall SES were frequently associated with reduced opportunities to obtain sufficient sleep and with adverse environmental conditions that

compromise sleep quality.[170, 174] The BACH study examined the effect of self-reported short sleep duration and poor quality of sleep on racial/ethnic disparities in the development of obesity and T2DM.[175] However, we did not find that sleep quantity or quality mediated the effect of race/ethnicity on these conditions. While we utilized longitudinal data to examine the incidence of disease, our measures of sleep were subject to considerable measurement error. Nonetheless, research to date appears to suggest that sleep could play a role in racial/ethnic disparities in obesity and T2DM.[175]

2.3.2 Depressive Symptoms

Depressive symptoms can potentially contribute to lifestyle changes which may in turn confer T2DM risk. While it has been suggested that depression and T2DM may be associated in a bi-directional manner, a meta-analysis of nine longitudinal studies indicated that depression confers a 25% to 37% increased risk of developing T2DM.[145] These findings were consistent in sensitivity analyses attempting to control for undiagnosed diabetes at baseline. The pathophysiological mechanisms underlying this relationship are unclear. One potential mechanism is that depressive symptoms are associated with increased levels of pro-inflammatory markers and declining insulin sensitivity.[176, 177]

2.3.3 Chronic stress

Psychosocial stress, including adverse life events,[28] job strain,[178] low sense of coherence,[29] appears to be associated with T2DM. While one pooled analysis of over 100,000 participants indicated work-related stress was associated with an increased risk of T2DM[178] another meta-analysis of nine studies did not.[179] The biological pathways of the stress—diabetes association are not fully understood, however several theories have been proposed. For example, perceived psychological stress coupled with a reduced sense of control/increased helplessness leads to an activation of the hypothalamic-pituitary-adrenal (HPA) axis. This in turn results in abnormal endocrine function including increased cortisol and decreased sex steroid levels. This endocrine

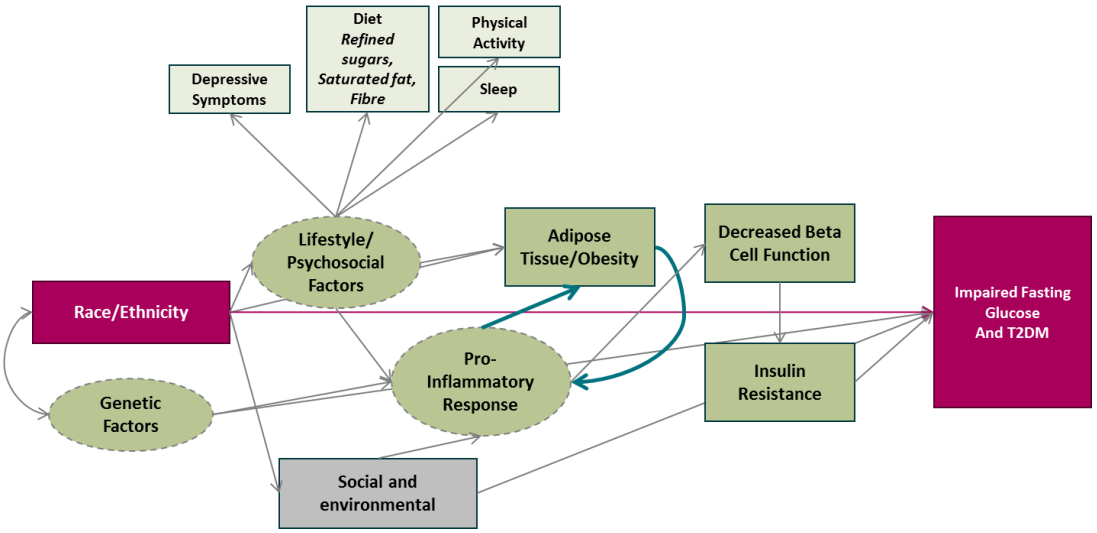
dysregulation antagonizes the effects of insulin.[180] These imbalances also can lead to obesity, particularly visceral adiposity, which plays an important role in insulin resistance and T2DM (see **Section 2.4.1**). Cross-sectional findings have found an association between stressful life events with visceral adiposity and T2DM.[28, 181] Internal versus external sense of control is also thought to be a key mediator between stressful events and health, as individuals with a low internal sense of control are less likely to deal successfully with stressors.[29, 182]

2.4 Biophysiologic

2.4.1 Low-grade inflammation

There is increasing clinical and observational evidence that low-grade inflammation may be an important pathway through which socioeconomic, lifestyle, and psychosocial factors influence T2DM risk (**Figure 2-1**). Low-grade chronic inflammation affects insulin signalling and increases beta-cell death.[26, 183, 184] Markers of inflammation, such as interleukin-6 and c-reactive protein are associated with insulin resistance and diabetes incidence.[185-187] As noted previously, certain dietary patterns (e.g. high in refined sugars, high in saturated fat) are associated with increased inflammatory responses.[105] Regular physical activity is associated with lower systemic inflammation.[101] The adipose tissue associated with obesity, a key risk factor for T2DM, may be a source of local inflammation and lead to the activation of immune cells.[188-190] Over-nutrition and obesity increase insulin requirements and impose stress on beta cells. It is noteworthy that patients with pre-diabetes and T2DM appear to demonstrate a greater inflammatory response to dietary glucose.[191] This suggests that early in the progression towards T2DM, the ability to contain inflammation induced by diet may be compromised.

Figure 2-1. Lifestyle and psychosocial factors cause decreased beta cell function, insulin resistance, and T2DM via low-grade inflammation



2.4.2 Glucose Metabolism and Insulin Resistance

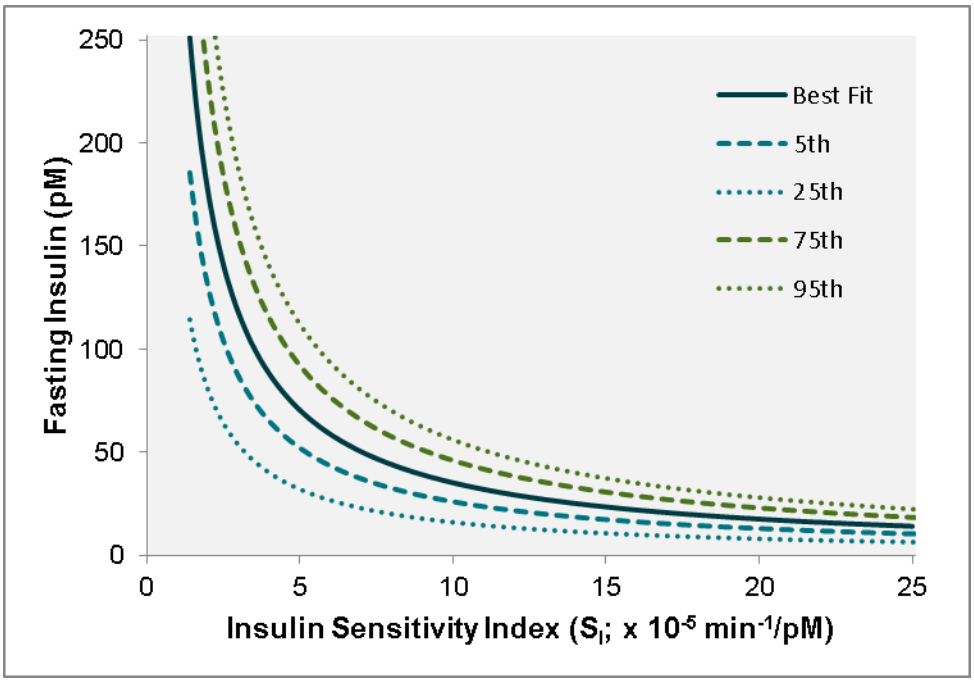
It has been suggested that the higher prevalence of T2DM in minority US populations is partially attributable to differences in glucose metabolism.[192] In several studies among non-diabetics, including longitudinal data from ARIC,[193] Blacks and Hispanics had higher fasting insulin and greater insulin resistance than Whites across various levels of BMI.[127, 193-196] An experiment conducted among Black and White Americans indicated that while glucose levels and C-peptide responses were identical in oral glucose tolerance testing, serum insulin levels (before and during) were greater (2-3 fold) among Blacks and hepatic insulin extraction was lower.[197] These results suggest that greater insulin resistance may be partially responsible for the higher prevalence of T2DM among Blacks and Hispanics. Several researchers have suggested that there is a biologic or genetic basis for these racial/ethnic differences in insulin resistance. However, more recent research with broader inclusion of ethnic groups and greater numbers of subjects found that Black, Asian, Caucasian and Hispanic Americans all became insulin resistant and had reduced beta cell function as glucose tolerance declined.[57] Although Black and Hispanic Americans had a greater degree of insulin resistance than Caucasians even after adjustment for BMI, the change in resistance observed in each group suggested that insulin resistance and

decreased beta cell function is a characteristic feature in the pathogenesis of T2DM in all racial/ethnic groups.[57]

2.4.3 Beta cell dysfunction

As mentioned in Section 2.2.4, for obesity and insulin resistance to be associated with T2DM, beta cells must be unable to offset decreased insulin sensitivity.[135, 136] In healthy individuals, there is a feedback loop between the insulin-sensitive tissues and the beta cells, with beta cells increasing insulin supply in response to demand from the liver, muscles and adipose tissue.[198] In order for glucose tolerance to remain unchanged, changes in insulin sensitivity must be matched by a proportionate yet opposite change in circulating insulin levels. For example, as **Figure 2-2** demonstrates, in individuals with marked insulin resistance, additional small changes in insulin sensitivity produce large changes in insulin levels, whereas in very insulin sensitive individuals, large changes in insulin sensitivity would be associated with small changes in insulin concentrations. Failure of this feedback loop results in a deviation from normal glucose tolerance and underlies the development of T2DM.

Figure 2-2. Relationship between insulin sensitivity and fasting insulin. Adapted from Kahn, 1993[198]



In T2DM, beta cell function is reduced, in that the cell fails to release insulin rapidly in response to glucose stimulation even though it clearly contains insulin.[198] In T2DM the numbers of beta cells are reduced by about 50%.[199-201] However, the degree of beta cell loss cannot fully account for the change in secretory response and function, because by the time the diagnostic level for diabetes occurs, beta cells are operating at 25% or less of its functional capacity.[202] There is a continual decline in beta cell function as T2DM progresses.[198] The extremely high blood glucose levels often observed in T2DM are a likely contributor to further disease progression through glucotoxic effects on the beta cell and harmful effects on insulin sensitivity.[203] In contrast, among healthy individuals exposure to high blood glucose levels has exactly the opposite effect; it improves insulin sensitivity and enhances beta cell function.[204] This suggests a pre-existing abnormality or risk, that is perhaps genetically determined, that is an important mechanism by which beta cell dysfunction occurs.[205]

Providing further evidence for the hypothesis of a pre-existing risk, groups of individuals at increased risk of T2DM exhibit beta cell dysfunction well before they would be considered to have reduced glucose tolerance.[57, 206-208] Longitudinal studies examining the progression from insulin resistance to T2DM with data collected from Whites, African Americans, Hispanics, and Pima Indians have found that those who did not progress to T2DM simply increased their insulin output as insulin sensitivity declines. However, among individuals who progressed to T2DM, the presence of a defect in insulin release was already present at baseline.[208, 209]

Racial/ethnic disparities in insulin resistance and beta cell function have been suggested in a number of studies,[127, 195-197, 210] whereas others have found no differences among racial/ethnic groups.[57] In a large cohort with adequate numbers of African American, Asian American, Caucasian, and Hispanic American participants, all were found to have similarly progressing insulin resistance and decreasing beta cell function as glucose tolerance declines.[57] The nature of the change in these two parameters was similar in all racial/ethnic groups studied.[57] These results suggest that the pathogenesis of insulin sensitivity and beta cell function are similar

among different racial/ethnic groups and therefore unlikely to explain disparities in risk between racial/ethnic groups.[57]

2.5 Contextual/Neighbourhood Influences

The literature discussed above focuses on the role of individual-level factors (genetic, lifestyle/behavioural, and biophysiologic). Epidemiologic literature, particularly in the US, tends to focus on these proximate risk factors for several reasons: (1) they are potentially controllable at the individual level and (2) they resonate with the value and belief systems of Western culture that emphasizes "personal responsibility"—the idea that individuals control their personal fate and responsible for their own actions.[15, 211, 212] While this research is important, interventions focusing on reducing diabetes risk factors at the individual-level (e.g. diet and exercise programmes, behaviour modification, medication, and surgical treatment) have met with limited success.[213-216] Individually-based determinants may fail to capture the entire causal pathway between race/ethnicity and T2DM. More recently, researchers have identified a number of environmental-level factors associated with obesity, diabetes, and other chronic diseases.[217] Neighbourhoods have emerged as a potential context in which disparities are fostered as they possess both physical and social attributes which can affect the health of individuals. The influence of neighbourhood context on health has been the focus of quite a body of research over the past decade, although most of the studies to date have focused on risk factors upstream to T2DM (i.e. dietary patterns,[218-220] physical activity,[219, 221] and body mass index/obesity[219, 220, 222]). However, studies linking neighbourhood characteristics directly with T2DM are limited.[31, 223-225]

Research has documented important differences in neighbourhood physical and social environments and health outcomes. However, the extent to which contextual factors contribute to disparities has remained elusive. This may be due, in part, to limitations inherent to neighbourhood and macro-environmental research. *Residential selection* refers to the fact that

individuals do not select residential environments at random and that race/ethnicity, culture, and familial influences all affect where individuals live.[226, 227] *Reverse causation* refers to the notion that lifestyles and behaviours may influence the choice of residential location, rather than the reverse. For example, individuals with better diets may seek out neighbourhoods with a healthier food environment.[228] These issues highlight the fundamental complexity in separating individual factors from contextual factors in research.

2.5.1 Built environment

Recently, the influence of built environment has received considerable attention, particularly in the US. The term 'built environment' typically refers to the man-made surroundings (e.g. density of fast food restaurants, distance to nearest park, and sidewalk completeness) that may or may not provide the setting for healthy behaviours, including healthy eating and physical activity. The domains and measures of the built environment used in scientific research vary considerably, in part, because of the large number of features that could potentially influence health behaviour.[229] Some aspects of the built environment, such as access to grocery stores, convenience stores, and restaurants, are highlighted as a target for research in large part because they are potentially modifiable features of neighbourhood environments.[230] Access to supermarkets and grocery stores were positively associated with healthy food behaviours and lower BMI in a number of studies including ARIC and the Women's Health Intiative,[33, 34, 231-234] while a high density of fast food restaurants has shown to have detrimental effects on BMI.[233-237] Differential rates of food store types by neighbourhood characteristics (i.e. neighbourhood deprivation, racial composition) may contribute to the differential prevalence of obesity, and subsequent T2DM, by race/ethnicity.[238, 239]

The nearby availability of parks and other "green spaces" (i.e. walking/biking trails) is increasingly viewed as a target for policymakers and urban planners for promoting healthier, more active lifestyles in disadvantaged communities. Proximity to parks has been linked to an increased frequency of, and the intensity of, physical activity,[240, 241] lower BMI,[242, 243]and lower

risk of T2DM in population-based studies and large cross-sectional investigations.[244] These health benefits are manifested even among people living in deprived neighbourhoods.[245] These findings indicate that increased access to parks and green space may potentially reduce obesity and T2DM disparities.

Walkability, a popular measure of a neighbourhood's conduciveness to walking for both transportation and recreation, has been associated with attaining the daily recommended physical activity[246, 247] and therefore, reduced rates of obesity.[248-250] In addition, some research suggests that neighbourhood walkability improves mental health[251, 252] which may also be a pathway by which neighbourhood determinants impact T2DM risk. Improved neighbourhood walkability may also increase social capital and collective efficacy.[253-255]

Research on the contextual environment presents many limitations. Many of the research studies cited above examine residential location (where an individual lives). However, other locations (i.e. work) may influence individual behaviour and therefore one's diabetes risk. Additionally, self-selection into neighbourhoods, also referred to as residential selection bias, can attenuate associations.[256]

These findings underscore the importance of several measures of built environment on healthy behaviours, body mass index/obesity, and subsequent diabetes risk. However, not all racial/ethnic and/or socioeconomic groups experience the same neighbourhood environments. Residential segregation often results in disparate neighbourhood environments, including the built physical environment.[257] Specifically, historical disinvestment in racially and/or socioeconomically segregated neighbourhoods may shape accessibility and the availability of neighbourhood services and amenities.[258] Therefore, the location of neighbourhood amenities (e.g. location of food stores, recreational areas) may contribute to socioeconomic and racial/ethnic disparities.[259]

2.5.2 Neighbourhood deprivation

It has previously been suggested that most of the racial/ethnic variation in T2DM is explained by social and economic factors at the neighbourhood-level.[260] Neighbourhood socioeconomic status (SES) appears to be a contributor to obesity,[234, 261, 262] cardiovascular disease risk factors ,[263-267] metabolic syndrome among women,[264] as well as T2DM prevalence[35] and incidence.[31, 223] The neighbourhood socioeconomic environment can influence the availability of grocery stores, recreational facilities, and educational resources which may influence diet, physical activity and subsequent T2DM. In addition, economically deprived neighbourhoods may increase exposure to chronic stress (i.e. noise, violence, and poverty) which is a potential risk factor for negative health outcomes including T2DM.[268, 269] These results suggest that neighbourhood-level SES may modify the relationship between individual-level SES and negative health outcomes. This underscores the potential importance of accounting for indicators of neighbourhood deprivation in studies examining health disparities. [270, 271]

A landmark experimental study, the Moving to Opportunity for Fair Housing Demonstration (MTO) study, offered housing vouchers to low-income families living in public housing projects in high-poverty neighbourhoods. The experimental group were offered the vouchers to move to low-poverty neighbourhoods. The MTO evaluated the impact of neighbourhood poverty and housing mobility on physical and mental health, economic self-sufficiency, criminal behaviour, and educational outcomes.[272] The significant finding was that the experimental group, who were offered the vouchers, had a reduced prevalence of obesity, morbid obesity, and diabetes (defined as an HbA1c ≥ 6.5). More than 90% of the households in the MTO experiment were headed by black or Hispanic women. This finding has powerful implications for the impact of neighbourhood mobility and neighbourhood poverty on racial/ethnic disparities in obesity and diabetes.[273]

2.5.3 Racial Segregation

Racial residential segregation, which refers to the physical separation of racial subgroups in space, is widespread in the Unites States and was previously supported by the federal government as well as economic and social institutions.[257] Although discrimination in housing and mortgage lending has been illegal for 50 years, explicit and implicit discrimination sustains high levels of segregation.[274] These continuing patterns of segregation have implications for the social, economic and health-related well-being of the segregated minority group[275-279] and are considered a fundamental cause of racial/ethnic health disparities.[280, 281] Segregation is hypothesized to influence health by perpetuating disparities in education and employment opportunities, clustering poverty spatially, shaping the social and physical neighbourhood context, and the availability of healthy resources.[277, 280] A few studies have examined the association between racial segregation and neighbourhood amenities. While some studies have indicated that high levels of residential segregation are associated with obesogenic characteristics (less access to healthy food options,[231, 282, 283] greater access to unhealthy food,[284] and less open spaces for recreational activities[285, 286]) other studies have found that spatial inequalities in racial/ethnic composition and socioeconomic disadvantage do not always result in disparate access to physical resources.[258, 287] Another potential mechanism by which segregation could impact health is stress. Stress related to disadvantage and discrimination can lead to coping behaviours such as increased sugar[288] and fat intake[289, 290] that may help reduce stress, but have adverse physical health effects.

Much of the current diabetes disparities literature fails to account for the fact that the US is largely segregated both racially and economically. The strong association of race with socioeconomic status both on the individual- and neighbourhood- level may lead to residual confounding in many studies.[291] One study, which examined an economically deprived but racially integrated neighbourhood in comparison to national data, suggested that when Blacks and Whites live under similar conditions, racial/ethnic disparities in many diseases, including

T2DM, disappear or are reduced.[270] Data from NHANES examined whether racial/ethnic segregation was associated with obesity and found that this association only held among women and was not mediated by neighbourhood socioeconomic factors.[292] However, data from national samples may be particularly susceptible to residual confounding due to overwhelming racial/ethnic stratification nationally.[270]

While neighbourhood disadvantage and segregation may be important mediators of racial/ethnic disparities in T2DM there are a number of limitations in measuring these constructs. Measurements of neighbourhood exposures rely heavily upon the definition of "neighbourhood" being used.[293] US Census tracts are one of the most frequently used measures of neighbourhood. While census tracts, when first delineated, were designed to be homogenous with respect to population characteristics, economic status, and living conditions,[294] they may not correlate with an individual's neighbourhood identification. New methods in neighbourhood research may alleviate some spatial misclassification. For example, the use of circulate or network buffers for an individual's residential address may be less prone to this bias.[293]

2.5.4 Crime, Safety and Perceived Neighbourhood Disorder

Racial/ethnic minorities, specifically African Americans and Hispanics, are more likely to live in neighbourhoods with higher levels of social, physical and economic disorder, which include crime, graffiti, lack of trust among neighbours, abandoned buildings, and concentrated poverty that contribute to social instability.[295, 296] Residents of neighbourhoods with high crime rates are less likely to walk and be physically active, particularly women and young children.[259, 297-299] This physical inactivity likely contributes to greater risk for obesity and T2DM. There is also evidence that residents' beliefs, or perceptions, about the safety of their neighbourhood may influence their behaviour thus influencing mediating the neighbourhood safety—T2DM risk association.[300] There are several studies that demonstrate evidence for this mediating effect. In two cross-sectional studies, perceived neighbourhood disorder potentially mediated the associations between neighbourhood disadvantage and self-rated health, physical function, adolescent

obesity and several chronic conditions.[301, 302] Reports of physical disorder (abandoned buildings, vacant lots, graffiti, etc.) have been shown to partly mediate the association between racial isolation and BMI, while incident crime was not associated with BMI.[303]

2.5.5 Summary

While there is a compelling body of research linking neighbourhood determinants to diet, physical activity, weight change, and obesity, the subsequent causal links towards T2DM risk have largely been assumed. Research detailing the complex pathways between specific aspects of neighbourhoods, obesity, and T2DM risk are needed.

Our research aims to address specific limitations in contextual research thus far. To date, most multilevel studies of neighbourhood effects on T2DM have been limited to aggregate census characteristics.[304] While census-derived measures, such as area poverty or racial segregation indices have shown important effects that persist despite adjustment for individual risk factors, they remain proxies for the actual physical and social characteristics of the actual neighbourhood. A further limitation to the use of these measures in the literature is that they are often used as a proxy for individual-level socioeconomic factors. Because of these limitations, there is still considerable debate regarding whether the associations between neighbourhood and T2DM reflect causal processes, and if they do, what specific aspects of neighbourhoods affect individual risk of T2DM.

2.6 Social and Economic Determinants

In this thesis, social determinants are defined as factors that involve a person's relationships to other people. These include social and economic structures of society (i.e. socioeconomic status) as well as social supports.

2.6.1 Socioeconomic Status

It is well established that health follows a social gradient—better health with increasing socioeconomic position.[305-308] In the past three decades the socioeconomic disparity in morbidity and mortality has grown.[309] Multiple inter-related pathways have been proposed to explain social inequalities in health, the most prominent mechanisms being health behaviours, psychosocial factors and access to material health promoting factors (i.e. healthy food, adequate health care).[306, 307, 310-312]

A social gradient in diabetes risk has been well documented in the US[313, 314] and in other developed nations.[35, 315-317] There are many pathways and mechanisms by which race/ethnicity and SES can combine to affect the development of diabetes.[318] *Early in life,* foetal exposures, such as poor maternal nutrition, may contribute to adult T2DM risk. Childhood socioeconomic circumstances may influence childhood nutrition, physical activity and illness (see **Section 2.6.2**). *Later in life, a*dult socioeconomic position may influence T2DM risk through a range of mechanisms including health behaviours (i.e. physical activity and diet) and psychosocial conditions (i.e. increased stress) (see **Section 2.6.3**). Differences in access to and use of health care services may further contribute to socioeconomic disparities in T2DM risk as opportunities for early prevention (i.e. behavioural risk factor modification) may be missed.

Studies of SES and diabetes have reported strong inverse associations between socioeconomic position and diabetes prevalence[319, 320] and incidence,[321, 322] and the US CDC has noted that these socioeconomic disparities in the incidence of diabetes appear to be worsening over time.[323] Several longitudinal studies have noted that socioeconomic disparities persist even after adjustment for lifestyle and behavioural covariates (unhealthy behaviours, obesity, and psychosocial factors).[322] Lower education and/or low income are also associated with several biomarkers of T2DM including higher levels of fasting insulin, fasting glucose, waist circumference and poorer glucose tolerance.[324]

Socioeconomic status (SES) is highly correlated with race in the US with African Americans and Hispanics tending to be poorer and less educated.[291, 325] Therefore, there is the potential for mediation by SES in research examining racial/ethnic disparities in diabetes. A few studies have postulated that SES explains racial/ethnic disparities in diabetes entirely.[13, 30, 32]

2.6.2 Childhood Socioeconomic Status

There is accumulating evidence that early-life socioeconomic circumstances have an effect on adult health outcomes. Observational studies and systematic reviews have demonstrated associations between childhood socioeconomic status and increased risk for obesity, coronary heart disease, stroke, all-cause-mortality, and T2DM.[326-333] Childhood socioeconomic status has also been linked to several T2DM precursors including the metabolic syndrome,[334, 335] insulin resistance,[336] and elevated blood glucose.[337]

2.6.2.1 Mechanisms

There are three major mechanisms by which childhood socioeconomic status can affect health status in adulthood. First, early-life circumstances may have a latent effect on adult health, independent of socioeconomic status later in life. Second, exposure to socioeconomic adversity may have a cumulative (or dose-response) effect through the life-course. Third, early-life socioeconomic status may affect adult socioeconomic status creating a pathway effect.

Maternal socioeconomic disadvantage is consistently associated with low birth weight, likely due to a clustering of risk factors including: access to prenatal care, malnutrition, smoking, alcohol consumption, drug use, and psychosocial stress.[338-345] Low birth weight is associated with adult T2DM in long-term longitudinal analyses even after considering ethnicity, childhood socioeconomic status, adult lifestyle factors[346] and adult BMI.[347] Low birth weight is associated with "catch-up" growth in early childhood which predisposes individuals to increased incidence of obesity.[348]

Childhood SES is also hypothesized to "program" a vulnerable phenotype with exaggerated inflammatory responses, thereby increasing the risk of developing T2DM as an adult.[349] Adverse socioeconomic circumstances have demonstrated an epigenetic effect on glucocorticoid signalling, which regulates the secretion of cortisol, and in turn exaggerates inflammatory responses.[350-352] Epigenetic changes refer to modification in the patterns of gene expression without changing the nucleotide sequence of its DNA.[353] Yet another pathway is through chronic psychosocial stress which is also related to alterations in inflammatory and immune activity.[354] SES differences in gene regulation of response to stress could be due to environmental and/or dietary influences over the life course or perhaps a direct consequence of early life developmental "programming."

The effect of lifetime socioeconomic circumstances on T2DM is partially mediated by traditional risk factors such as long-term obesity, physical activity, and diet.[332, 355, 356] Unhealthy behaviours, like lack of physical activity and poor dietary patterns tend to be more prevalent among adults with lower SES (see **Section 2.6.3**). Adult family members' health behaviours may be modelled as normative behaviours by children.[357] Early childhood is a critical period for the ability to self-regulate food consumption and in the development of food and flavour preferences.[358]

Parent socioeconomic circumstances may also affect both the health and education achievement of the child which has implications for adult socioeconomic status.[359] Childhood health also has implications for educational achievement and socioeconomic circumstances later in life.[360] Therefore adult SES may be an important explanatory mechanism for the association between childhood SES and adult T2DM. While many studies demonstrate that disparities by childhood socioeconomic status were independent of current socioeconomic status, lifestyle factors, and perceived stress, it is clear the effect of social adversity is not limited to early life experiences.

2.6.3 Adult Socioeconomic Indicators

2.6.3.1 Income, Education, and Occupation

As mentioned previously, there is a well-documented socioeconomic gradient in T2DM. Diabetes incidence data show a strong inverse relationship with income, education, and occupational status.[361]

Education is a major determinant of health and health inequalities. Education has traditionally been an important route out of poverty for disadvantaged groups. Education is also one of the most commonly used measures of SES, and a systematic review and meta-analysis indicated it was also the most consistently associated with T2DM.[362] Higher educational attainment is associated with a decreased risk of T2DM[363] and decreased T2DM attributed mortality.[308] There is some evidence that educational attainment may have a greater impact on diabetes risk among women than among men. Data from the NHANES I Epidemiologic Follow-up Study (1971-1992), demonstrated that women who had more than 16 years of education had a much lower risk for incident T2DM compared with women who had less than 9 years of education. Among men, these trends were evident, but not as strong.[361]

Evidence from high-income nations overwhelmingly indicates that lower education, occupation, and income are all associated with an increased risk of incident T2DM.[362] However, even though education generally leads to occupations that influence level of income, it has been argued that these measures of SES cannot be used interchangeably as they represent different causal processes and pathways.[364, 365]

2.6.3.2 Mechanisms

SES likely contributes to the development of T2DM through complex processes involving access to health-care services and information, availability of healthy foods and places to exercise, economic and occupational opportunities, as well as individual behaviours.[366]

Unhealthy behaviours including lack of physical activity and unhealthy dietary patterns tend to be higher in adults with lower SES.[367-372] The Whitehall II cohort demonstrated that modifiable risk factors such as health behaviours and obesity, could explain almost half of the social inequalities in T2DM.[373] The Australian Diabetes, Obesity and Lifestyle (AusDiab) study, found that behavioural risk factors attenuated the associations between socioeconomic measures and fasting glucose by 11-70% depending on gender and the specific socioeconomic measure of interest (education or income).[324] Unhealthy behaviours are often strongly social patterned. Material constraints, limited knowledge, and limited opportunities to act upon health promoting messages may act as barriers for lower SES populations to adopt healthier lifestyles.[374-376] However, in a meta-analysis of 21 studies on SES and T2DM, most of the included studies concluded that unhealthy behaviours could not fully explain the SES differences in T2DM.[362] Therefore, it is highly likely that other mechanisms are involved.

Education may capture the transition from childhood SES to adult SES. The skills and knowledge attained through education may shape T2DM risk through its influence on an individual's capacity to access and interpret health information including the importance of a healthy lifestyle.[324]

Adult socioeconomic status may also affect inflammation-related gene regulation. Several studies, including Whitehall II and NHANES, have demonstrated greater inflammation in people exposed to socioeconomic adversity.[377-379] Systemic inflammation is a potential mediator between socioeconomic status and T2DM. Biologically, inflammation affects insulin signalling and increases beta-cell death, and markers of chronic inflammation have been shown to be associated with T2DM prevalence and incidence (see **Section 2.4.1**). Linking together evidence that relates socioeconomic status to inflammation and inflammation to T2DM, research from the Whitehall II Cohort demonstrated that chronic inflammation explained a substantial portion of the association between socioeconomic status and T2DM.[349]

Psychosocial stress may also be a pathway by which SES impacts T2DM risk. Lower SES is related to higher stress levels[380] and psychosocial stress affects the adrenal system which in turn may lead to T2DM (see **Section 2.3.3**). Allostatic load is negatively associated with education and income independent of race, sex, and lifestyle/behavioural factors. This suggests yet another potential mechanism through which SES, and SES-related stress in particular, may increase T2DM risk.[381]

2.6.4 Health Literacy

Low health literacy, the inability to obtain, process, and understand health information needed to make appropriate health decisions, is a significant challenge worldwide. Most health-related reading materials are written at the high school level. Whereas most US adults comprehend at the 7th or 8th grade level.[382] The relationship between health literacy and diabetes outcomes has been studied in several cross-sectional studies[383,384] and a randomized intervention indicated that improving literacy could improve T2DM outcomes.[384, 385]

Limited health literacy differentially affects racial and ethnic minority groups with the proportion of adults with basic or below basic health literacy ranging from 28% of White adults to 65% of Hispanics adults.[386] Health literacy may play a role in the racial/ethnic disparities observed in health outcomes among patients already diagnosed with diabetes.[387-389] Disadvantaged populations are likely more vulnerable to the challenges posed by low health literacy given the inherent limitations posed by socioeconomic determinants and lower access to health care.

2.6.5 Access to health care/quality of care

Access to health care, as measured by health insurance status (insured versus uninsured) and visits to a healthcare provider in the past year, has been linked to a significantly higher odds (70%) of having undiagnosed diabetes.[390] While the number of undiagnosed cases was moderate (N=110), this data comes from a large, nationwide, health survey (NHANES). This evidence may, in part, explain why racial/ethnic minorities tend to have more advanced disease at the time of

diabetes diagnosis, which in turn leads to adverse outcomes.[391] Unequal access to health care, and poorer quality of care, are common explanations for racial/ethnic disparities in the complications of T2DM.[13] Racial/ethnic minorities are more likely to lack health insurance or have less comprehensive health insurance coverage.[13, 392-394] Minorities are disproportionately enrolled in health plans with poorer performance[395] and there is some evidence that they receive inferior medical care even when they have equivalent health care coverage.[395-398]

2.6.6 Acculturation

There are 40 million foreign-born residents in the U.S., accounting for 12.9% of the current U.S. population.[399] There has been significant research documenting differences in health status of immigrants versus native-born Americans in recent decades. Hispanics are the largest minority group in the US and experience a disproportionate burden of poverty and poor health outcomes including T2DM.[400]

Understanding risk factors and health outcomes among Hispanics can be challenging since health behaviours and therefore health outcomes vary as a function of acculturation.[401] Acculturation is a multidimensional process of the adoption of host country cultural norms, values and lifestyles and is shaped by the cumulative experience of the interaction of individuals with their environments across the life cycle.[402, 403]

Current research indicates that recent Hispanic immigrants tend to report healthier behaviours and better health than do native-born Americans, but this health advantage erodes over time.[404-407] Acculturation is associated with several negative health behaviours including: poorer nutrition, greater tobacco use, and substance abuse.[402, 408] Specifically, higher acculturation is associated with lower dietary quality in terms of higher total fat and saturated fat and lower consumption of fruit, vegetables, grains and legumes.[409, 410] This is despite the fact that acculturation among Hispanics is positively associated with higher socioeconomic status, greater access to health care, and some positive health behaviours (i.e. leisure-time physical activity).[408,

[409] Overall, the evidence suggests that acculturation may increase obesity[408, 411] disparities among Hispanics because it is consistently associated with less-healthy dietary patterns.

However, studies examining the association between acculturation and T2DM have shown mixed results,[408] and results from NHANES noted that the association appeared to be modified by country of origin.[412] The reason for this disconnect between acculturation and disparities in obesity versus T2DM is not known. However, several theories have been articulated. It is possible that higher health care access associated with acculturation among Hispanics facilitates access to preventive metabolic control screenings and improved prevention efforts.[400] Acculturated Hispanics also tend to have higher socioeconomic status and greater leisure-time physical activity, which may both in turn reduce exposure to chronic stress (**Section 2.3.3**) and therefore low-grade inflammation (**Section 2.4.1**), two important T2DM pathways.

2.6.7 Discrimination

Racism, the system of beliefs that members of specific racial/ethnic groups possess characteristics regarded as inferior or superior to another racial/ethnic group(s), is an added burden for Black and Hispanic Americans. Racism often leads toward the development of negative attitudes and beliefs towards racial groups (prejudice) and differential treatment of members of these groups by individuals and social institutions (discrimination).[413] Racism and discrimination can adversely affect health by restricting socioeconomic opportunities and social mobility.[318] Further, targets of discrimination often experience stress from overt discriminatory acts, micro-aggressions, as well as the perceptions of unfair treatment. Experiencing discrimination may promote distressing views of human nature, social relations, and result in a lower sense of control.[182]

In seeking to understand why racial/ethnic disparities in health are not entirely explained by socioeconomic factors, social epidemiologists have pursued three major lines of inquiry: (1) that the measures of SES are not equivalent across race,[291, 365] (2) that childhood SES and early life

psychosocial and economic adversity are not fully captured (**Section 2.6.2**), and (3) that racial discrimination can adversely affect health.[413, 414]

Chronic racial discrimination may be a factor in racial health disparities.[413] Racial discrimination may also exacerbate certain health conditions, in part, due to psychological stress.[415] **Section 2.3.3** discusses the links between psychosocial stress and diabetes and it follows that if racial discrimination is causally associated with psychosocial stress[416] then disparities in the experience of racial discrimination could amplify health disparities.

Evidence examining the effect of racial discrimination on diabetes prevalence or incidence is limited. However, discrimination has been linked to poorer health outcomes among diabetics, including higher HbA1c levels, greater physical burden, and poorer physical function.[417] Discrimination is also associated with greater nutritional risk among Black adults[418] which may lead to downstream health problems like diabetes.

2.7 Conclusion

There is an epidemic increase in obesity and diabetes in the US and around the world. While lifestyle and behavioural factors such as diet and exercise may play a large role in the creation/amplification of racial/ethnic disparities in T2DM, these explanations appear inadequate to explain these disparities. Racial/ethnic disparities in T2DM are a complex and widespread phenomenon that may be reinforced by genetics, lifestyles/behaviours, psychological factors, physiology, familial structure and history, as well as social, economic, and political factors. A greater understanding of the complexity of this causation may frame future research and subsequent interventions.

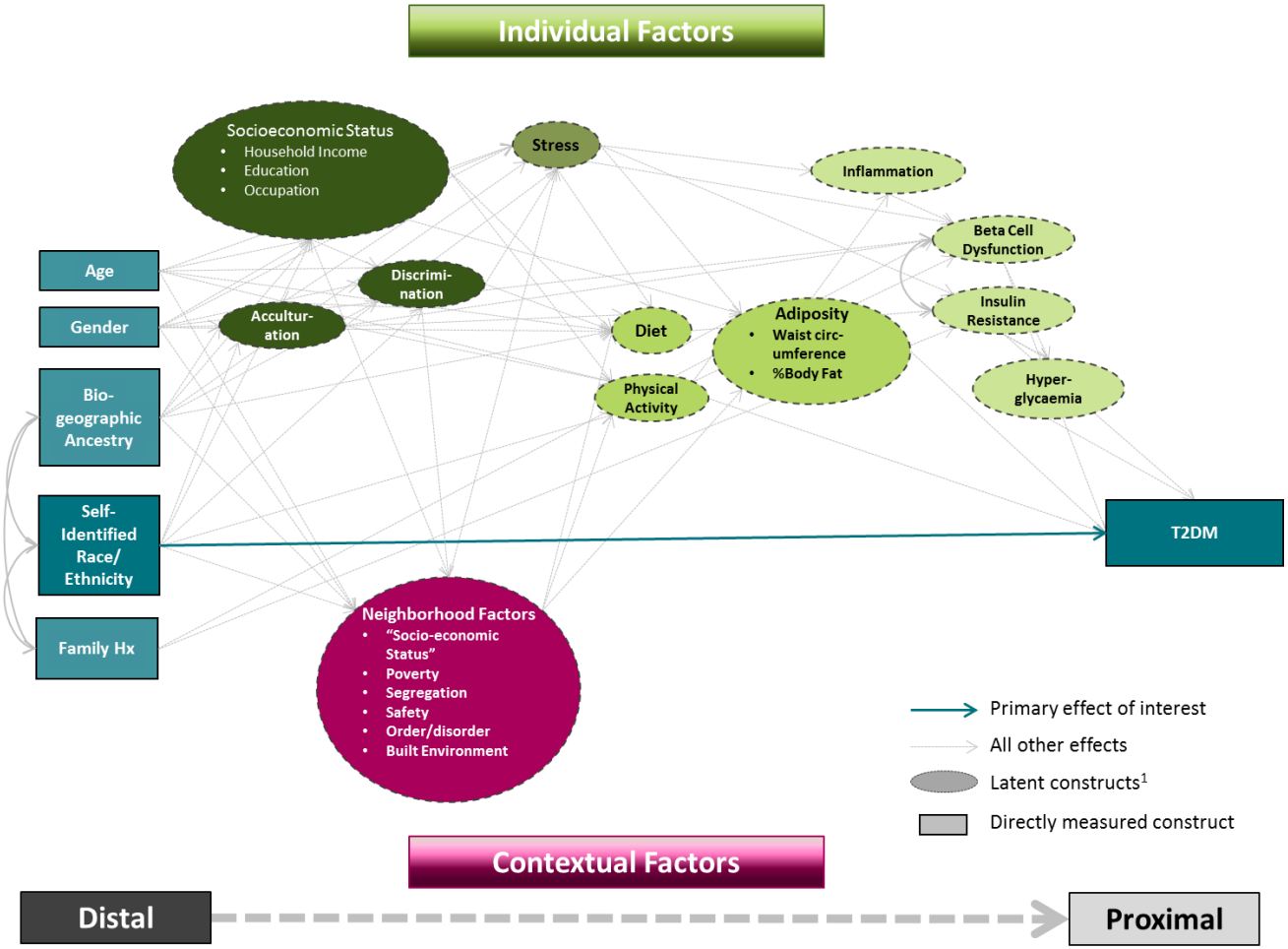
3 Methods

3.1 Conceptual Model

My conceptual framework, adapted from McKinlay and Marceau,[419] combines a population health framework with a causal modelling framework to elucidate the causes of racial/ethnic disparities in T2DM. This model (**Figure 3-1**) identifies distal, intermediate, and proximate factors that influence T2DM. Distal factors, which may be population-level determinants, include population-level and individual-level social conditions (i.e. socioeconomic factors, racial/ethnic discrimination). The intermediate determinants of T2DM include neighbourhood- or community-level physical and social environments. Proximate determinants of T2DM include biophysiological and genetic factors as well as individual health behaviours.

This conceptual model attempts to overcome two major constraints of modern epidemiologic research into T2DM disparities.[14] First, rather than focusing on proximate risk factors, it moves the focus upstream for a more comprehensive analysis of the causes of T2DM disparities within the population. In **Figure 3-1** distal factors are identified on the left-hand side, while more proximal factors are on identified on the right-hand side. Second, rather than focus exclusively on the individual as the site of etiologic action,[14] we focus individuals in the context of their neighbourhood and social environments. In **Figure 3-1** individual-level determinants are identified on the top-half of the figure, while neighbourhood-level determinants are identified on the lower-half of the figure. The conceptual framework can be represented as a Directed Acyclic Graph (DAG) which informs the development of multilevel structural equation models of contributors to racial/ethnic disparities in T2DM.[291]

Figure 3-1. Conceptual Model



3.2 The Boston Area Community Health (BACH) Survey

The Boston Area Community Health (BACH) Survey is an epidemiologic cohort study involving a community-based, stratified random sample of 5,502 Boston, Massachusetts, residents. The baseline BACH Survey (2002-2005) was designed to explore the mechanisms conferring increased health risks on minority populations. To this end, the cohort was designed to include adequate numbers of racially/ethnically diverse (Black, Hispanic, White) men and women across a broad age distribution (30-79). Follow-up surveys were conducted approximately 5 (BACH II, 2008) and 7 (BACH III, 2010) years later. The BACH Survey's measures were designed to cover seven broad categories: sociodemographics, health care access/utilization, lifestyles, psychosocial factors, health status, physical measures, and biochemical parameters. BACH III (2010-2012) was designed and conducted with the aim of quantifying the relative contributions of these influences to racial/ethnic disparities in prediabetes. To this end, the BACH III survey incorporated additional measures assessing type 2 diabetes and its precursors including insulin resistance, beta cell function, impaired fasting glucose, prediabetes, and metabolic syndrome. **Section 4** describes the BACH III survey design and collection in additional detail. Additional details regarding the specific measures used follow in **Section 3.3**.

3.3 Measures

3.3.1 Race/Ethnicity

As discussed in chapter 3, race and ethnicity are interrelated concepts that have a long history in the fields of human biology and public health.[420] Although the terms are often used interchangeably in the literature and there are no definitive definitions, race and ethnicity tend to have distinct meanings. Race is typically used to refer to groups that share biological similarities that are thought to be genetic in origin,[64] whereas ethnicity refers to shared cultural

similarities.[69] In many cases, race and ethnic groups may overlap considerably. Nonetheless, several researchers have argued that race and ethnicity are useful concepts when attempting to elucidate health disparities.[421, 422]

The racial/ethnic labels used in this research are 1) non-Hispanic Black, 2) Hispanic, and 3) non-Hispanic White. Race/ethnicity was self-reported by survey participants according to two separate survey questions: "Do you consider yourself to be Spanish, Hispanic, or Latino (Latina)?" and "What do you consider yourself to be? Select one or more of the following" with response categories of American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White or Caucasian, and Other (Specify). These questions are the standard ones used in the United States as recommended by the Office of Management and Budget.[423] "Non-Hispanic Black" (hereafter referred to as Black) is used to categorize people who self-identify as "Black or African-American" and identified as "not Hispanic or Latino." Hispanic is used to categorize people with Spanish or Latin American descent who identify as Hispanic irrespective of racial identification. White is used to categorize people who self-identify as "White or Caucasian" and identified as "not Hispanic or Latino."

Numerous authors have critiqued the reliance on race/ethnicity in the biomedical and epidemiologic literature as an etiologic quantity.[291, 422, 424] "Race" largely represents a complex mixture of behavioural, environmental, and social exposures. [69, 425] For example, Black Americans often are poorer, have less education, are more likely to live in disadvantaged communities, and have less access to health care.[69, 426] Because socioeconomic differences between racial groups are so ubiquitous, attempts to separate a "racial" effect often suffer from residual confounding.[291] This may make it difficult to validly estimate the relative contributions of the "genetic" versus "other" components of race.

The BACH study attempted to overcome these challenges in several ways. First, the stratified, two-stage cluster sampling design ensured that there were sufficient numbers of Black, Hispanic, and White participants in the study to permit examination of conditions across the population subgroups of interest. Further, the sampling design resulted in a study population of Black, Hispanic, and White participants with overlapping socioeconomic circumstances which allows for better control of confounding related to socioeconomic factors. Details on the distribution of socioeconomic factors by race/ethnicity are given in **Table 3-1**. Finally, we included several non-standard indicators of social and economic position including: neighbourhood socioeconomic indicators, language, country of birth, acculturation,[427] discrimination,[428] sense of control,[429] alienation,[430] and biogeographic ancestry.

Table 3-1. Socioeconomic Characteristics by Self-Reported Race/Ethnicity at BACH III

	Black N=1026	Hispanic N=1036	White N=1093	Total N=3155
Income				
<$20,000	413 (33.7%)	621 (43.4%)	304 (20.7%)	27.0%
$20,000 - $49,999	360 (35.3%)	307 (35.3%)	247 (18.5%)	25.1%
≥ $50,000	252 (31.0%	108 (21.3%)	542 (60.8%)	47.9%
Education				
Less than High School	160 (10.2%)	389 (28.0%)	69 (2.9%)	7.9%
High school or equivalent	378 (37.0%)	346 (36.2%)	225 (16.4%)	24.4%
Some college	28.7 (32.1%)	180 (18.8%)	204 (15.8%)	20.6%
College or advanced degree	201 (20.7%)	121 (17.1%)	595 (65.0%)	47.1%
Census Tract SES[431]				
Low	448 (43.3%)	373 (37.8%)	141 (7.1%)	21.6%
Middle	393 (45.5%)	415 (44.9%)	384 (44.7%)	45.0%
High	90 (11.2%)	150 (17.3%)	374 (48.3%)	33.5%

3.3.2 Type 2 Diabetes

3.3.2.1 Incident Type 2 Diabetes

Most diabetes surveillance data depends on self-report.[432] BACH I, II, and III used the same methods of self-report utilized by the CDC and NHANES.[432, 433] Specifically, participants were asked "Have you ever been told by a health care provider that you now have or previously had non-insulin dependent or adult-onset diabetes Type II?" A new report of a diagnosis of T2DM among those reportedly T2DM-free at baseline (BACH I) was considered to represent an incident case of T2DM.

3.3.2.2 Prevalent Type 2 Diabetes Including Undiagnosed T2DM

T2DM often develops in the absence of clinical symptoms.[21] Even in the presence of symptoms, many individuals often do not recognize them or seek care.[21] Further, because of the insidious nature of these symptoms, physicians often do not recognize, appropriately screen for, and diagnose T2DM.[434] Therefore, without routine screening many individuals with diabetes remain undiagnosed. It is estimated that 5% of the adult population of the US has undiagnosed diabetes accounting for 25-40% of all diabetes.[3]

Undiagnosed prevalence as a fraction of total diabetes prevalence differs by race/ethnicity and immigration status.[3] Therefore, in order to capture the true magnitude of racial/ethnic disparities in T2DM, I included likely cases of undiagnosed diabetes in the cross-sectional analyses of prevalent diabetes (BACH III).

Prevalent diabetes was defined as a self-report of T2DM (**Section 3.3.2.1**) or a fasting glucose (FG) > 125 mg/dL or an HbA1c ≥ 6.5%. FG was measured with a HemoCue 201 point-of-care analyser. HbA1c was measured by Quest Laboratories in Cambridge, MA. The cut-points for FG

and HbA1c were based on the guidelines promoted by American Diabetes Association (ADA) for T2DM diagnosis (**Table 3-2**).

Table 3-2. Criteria for Clinical Diagnosis of Prediabetes and Diabetes
Source: ADA Standards of Medical Care in Diabetes, 2012[21]

	HbA1c	Fasting Plasma Glucose	Oral Glucose Tolerance Test
Diabetes	≥ 6.5%	≥ 126 mg/dl	≥ 200 mg/dl
Pre-Diabetes	< 6.5% ≥ 5.7%	< 126 mg/dl ≥ 100 mg/dl	< 200 mg/dl ≥ 140 mg/dl
Normal	< 5.7%	< 100 mg/dl	< 140 mg/dl

3.3.3 Genetic Influences

3.3.3.1 Ancestry Informative Markers

We measured 63 Ancestry Informative Markers (AIMs), also known as single nucleotide polymorphism (SNPs), which are distributed across the human genome. AIMs are helpful in discriminating the genetic contributions of main parental ethnic groups. These AIMs were selected based on their ability to estimate percent African, Native American, and European ancestry in admixed populations similar to the profile of the BACH study (White, Black, Hispanic).[75, 435] Samples were genotyped at the Genetic Analysis Platform (GAP) at the Broad Institute (Cambridge, MA) using iPLEX (Sequenom) in three batches. HapMap samples (Utah residents with Northern and Western European ancestry (CEU) and Yoruba in Ibadan, Nigeria (YRI)) were included in each batch for quality control. All Hap Map samples had 100% HapMap concordance. The average call rate for all assays was 97.4%; 1.6% of samples failed quality control with call rates <90% and two SNPs failed with call rates <90%.

Ancestry proportions were estimated for individual participants using ADMIXTURE Software (version 1.12) under the assumption of three ancestral populations (K=3).[436] Representatives of two parental populations were included (West African (YRI) and European (CEU)) for quality control. Studies with a single known, admixed population may often weight towards a specific ancestry. However, for these purposes, ancestry proportions were estimated blinded to self-reported race/ethnicity. Since these SNPs were selected based on their ability to discriminate between African versus European ancestry or Native American versus European ancestry, each SNP was given an equal weight and was used to define, for each individual, the degree to which their whole genome is more West African, Native American, or European.

3.3.4 Mediating Influences

Details on the measurement of mediating factors are discussed in detail in **Section 6.2.3** (neighbourhood influences) and **Section 7.3.1** (all other influences).

3.4 Statistical Analyses

As described in **Section 4**, the BACH survey has a number of novel features that pose statistical challenges and opportunities. This section describes several methodological issues that are central to the statistical analyses of the BACH data included in the thesis papers.

3.4.1 Survey Weighting

As mentioned in **Section 4**, the BACH III survey is the second follow-up instalment to the BACH Survey. The BACH baseline survey was designed to ensure adequate representation of Black and Hispanic minority groups living in Boston. To this end, a 2-stage, stratified cluster sampling design was used to recruit approximately equal numbers of persons in 24 pre-specified design groups defined according to age group (30-39, 40- 49, 50- 59, 60- 79), race/ethnicity (Black, Hispanic, White), and gender (male, female).[437] Weighting of the BACH Survey data is therefore

required to "map" the sample back to the Boston population according to the 2000 US Census for BACH I or 2010 US Census for BACH II/III.[438]

The probability of selection at baseline was estimated as the product of three sampling fractions: (1) $f_{1h,}$ the probability of selecting the census block, (2) f_{2hi}, the probability of selecting a household within the selected block, and (3)f_{3h}, the probability of retaining the household under the design objective of filling 24 cells (race/ethnicity by gender by age decade) equally. The initial weights w_{hi} were computed as the inverse probabilities of selection.

$$w_{hi} = 1/(f_{1h} * f_{2hi} * f_{3h})$$

At baseline the "weighting class method"[439] was used to adjust for survey non-response. This method assigns survey respondents and non-respondents to classes (or cells). In the BACH Survey there were 24 design cells (**Table 3-3**).

Table 3-3. BACH study design (age, sex, and racial/ethnic composition of the BACH sample)

Demographic composition of the BACH I baseline survey (2002-2005)

	Age at baseline (years)					
	30-39	**40-49**	**50-59**	**60-69**	**70-79**	**Total**
Men	614	661	509	329	188	**2301**
Black	164	224	156	103	53	**700**
Hispanic	249	229	156	92	40	**766**
White	201	208	197	134	95	**835**
Women	793	835	776	517	280	**3201**
Black	259	284	249	179	96	**1067**
Hispanic	337	319	256	138	60	**1110**
White	197	232	271	200	124	**1024**
Total	**1407**	**1496**	**1285**	**846**	**468**	**5502**

A combined procedure was used to simultaneously adjust for design cell non-completion and post-stratification weighting with the target population defined as the Boston 2000 census population within each of the 24 cells. The final weights for use at T1 were defined as

$$W_{hi} = N_i x\ w_h/(\sum_{h=1,12} \sum w_{hi})$$

to correct the weights so that they sum up to the population N_i in each design cell while simultaneously adjusting for non-response.

Follow-up weights (BACH II and BACH III) were calculated using the propensity weighting class method.[438] A logistic regression model was fit using variables from BACH I and BACH II that informed follow-up non-response. The estimated response probabilities from these models were then categorized into deciles.[439] The non-response weighting adjustment was then computed as the inverse of the response rate in the decile. Post-stratification of the weights were calculated to reference the 2010 census.

The BACH Survey sampling weights are used explicitly in all statistical analyses unless otherwise specified. The sample weights, as well as the sampling stratum and primary sampling unit are specified. The sampling weights must be used to produce unbiased estimates of the Boston, Massachusetts population.

3.4.2 Multiple Imputation

Analyses of large scale cohort studies are often complicated by missing data. Data items can be missing due to subject refusal, subject inability or ineligibility, or due to data collection/entry errors. Missing data methods, such as complete-case analysis or available-case analysis are easy to implement and popular, but these methods may yield biased results[440] and can be inefficient when they reduce sample sizes.[441]

Generally, less than 1% of data are missing in BACH with the exception of income which was missing among 3% of Whites, 4% of Blacks, and 11% of Hispanics at baseline.[30] In addition, there is unit non-response in a number of components of the questionnaire. For example, the blood draw was refused by 11% of Whites, 21% of Blacks, and 22% of Hispanics. In addition, the self-

administered questionnaires in BACH I and II which contained a number of sensitive questions, like erectile dysfunction (14%), were more frequently missing.[442] Currently there is no consensus on the best approach to dealing with unit non-response. Either sub-sample reweighting or multiple imputation can be used.[438, 439] The research team decided to proceed with multiple imputation to deal with unit non-response.

The term 'multiple imputation' refers to the procedure of replacing each missing value by more than one imputed value creating multiple complete datasets.[443, 444] Multiple imputation is gaining credence and popularity in the fields of public health and epidemiology.[445-448]

There are three steps in multiple imputation: (1) choose and fit the imputation model, (2) fit the model of interest/analysis model to each imputed dataset, and (3) combine/pool the results from the multiple datasets.

The R (R Foundation for Statistical Computing, Vienna Austria) package "Multiple Imputation by Chained Equations" (MICE) was used to create 15 multiply imputed datasets. [449] The MICE program for multilevel imputation allows for partially observed responses at the individual-level but does not allow for missing data at the neighbourhood-level. Since all BACH participant addresses are geo-coded, there are no missing neighbourhood identifications or neighbourhood-level variables. Nonetheless, individual participant's neighbourhood of residence were included in the imputation model, as were the survey weights. The imputations were conducted separately for each racial/ethnic by gender strata to preserve interaction effects.

4 Cohort Profile: The Boston Area Community Health Survey

4.1 Introduction

The BACH Survey, a prospective, longitudinal, cohort study of community-dwelling participants from Boston, Massachusetts was used for all analyses included in this thesis. This profile of the BACH Survey has been published in the International Journal of Epidemiology and provides details on the motivation for the study, participant selection procedures, follow-up, included measures, and key findings.

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
www.lshtm.ac.uk

Registry
T: +44(0)20 7299 4646
F: +44(0)20 7299 4656
E: registry@lshtm.ac.uk

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SECTION A – Student Details

Student	Rebecca Piccolo
Principal Supervisor	Neil Pearce
Thesis Title	Racial and Ethnic Disparities in Type-2 Diabetes: A Multilevel Perspective

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	International Journal of Epidemiology		
When was the work published?	2014 Feb; 43 (1): 42-51		
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Have you retained the copyright for the work?*	Yes	Was the work subject to academic peer review?	Yes

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4.2 Article Submitted

4.2.1 Abstract

The Boston Area Community Health (BACH) Survey is a community-based, random sample, epidemiologic cohort of N=5,502 Boston, Massachusetts, residents. The baseline BACH Survey (2002-2005) was designed to explore the mechanisms conferring increased health risks on minority populations with a particular focus on urologic signs/symptoms and type 2 diabetes. To this end, the cohort was designed to include adequate numbers of U.S. racial/ethnic minorities (Black, Hispanic, White), both men and women, across a broad age distribution. Follow-up surveys were conducted approximately 5 (BACH II, 2008) and 7 (BACH III, 2010) years later which allows for both within- and between-person comparisons over time. The BACH Survey's measures were designed to cover seven broad categories: sociodemographics, health care access/utilization, lifestyles, psychosocial factors, health status, physical measures, and biochemical parameters. The breadth of measures has allowed BACH researchers to identify disparities and quantify contributions to social disparities in a number of health conditions including: urologic conditions (e.g. nocturia, lower urinary tract symptoms, and prostatitis), type 2 diabetes, obesity, bone mineral content and density, and physical function. BACH I data are available through The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Central Repositories (www.niddkrepository.org). Further inquiries can be made through the New England Research Institutes, Inc., website (www.neriscience.com/epidemiology).

4.2.2 Why was the cohort set up?

Despite steady improvement in the overall longevity of the United States (U.S.) population,[450] racial and ethnic minorities, with few exceptions, experience higher rates of morbidity and mortality than non-minorities.[13, 451] The reasons for these health disparities are multifactorial and poorly understood, but are hypothesized to reflect differences in socioeconomic status, lifestyle and behavioural risk factors, environmental effects, genetic influences, and access to healthcare. Given these competing and interrelated potential explanations for health disparities, there was a compelling need for research that simultaneously examined and measured these multiple potential explanations using a multidisciplinary approach.

The Boston Area Community Health (BACH) Survey was designed to explore these relative contributions conferring increased health risks on minority populations.[452] In addition to the primary research interests on the effects of age, sex, and race/ethnicity the BACH Survey was also concerned with lack of adequate health insurance, lack of access to adequate medical care, and how these problems influence patterns of disease. The baseline BACH Survey was initiated in 2002 in response to a National Institutes of Health (NIH) consensus panel recommendation that research on urologic and gynaecologic conditions in racial/ethnic minorities be prioritized.[453] At that time, epidemiologic studies in the field of urology were limited by three key factors which the BACH Survey designed to address: (1) lack of representation of racial/ethnic minorities; (2) cohorts of patients who access medical care and receive a diagnosis (i.e., non-population-based studies); (3) reliance on variably-defined and diagnosed medical conditions. Prior to the BACH Survey, very little was known about the basic descriptive epidemiology (i.e., prevalence, incidence) of urologic symptoms in the general population, or about how they vary by major social determinants such as race/ethnicity. The goal of the baseline BACH Survey (BACH I: 2002-2005) was to measure the prevalence of urologic symptoms/conditions by race/ethnicity, age, sex, and socioeconomic status. To this end, the BACH Survey used a random community-

based sample of racially/ethnically diverse men and women across a broad age range (30-79 years) from the Boston, Massachusetts population. From the outset, this initial survey was intended to provide the baseline data for a longitudinal study[437] and in 2008 enrolment began for the first follow-up survey (BACH II: 2008-2010). Enrolment in a third wave (BACH III: 2010-2012) has recently been completed. All three waves of the BACH Survey were funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

4.2.3 Who is in the cohort?

Table 4-1. BACH study design (age, sex, and racial/ethnic composition of the BACH sample)

Demographic composition of the BACH I baseline survey (2002-2005)

	Age at baseline (years)					
	30-39	**40-49**	**50-59**	**60-69**	**70-79**	**Total**
Men	614	661	509	329	188	**2301**
Black	164	224	156	103	53	**700**
Hispanic	249	229	156	92	40	**766**
White	201	208	197	134	95	**835**
Women	793	835	776	517	280	**3201**
Black	259	284	249	179	96	**1067**
Hispanic	337	319	256	138	60	**1110**
White	197	232	271	200	124	**1024**
Total	**1407**	**1496**	**1285**	**846**	**468**	**5502**

Composition of the BACH II survey (2008-2010)

	Age at baseline (years)					
	34-39	**40-49**	**50-59**	**60-69**	**70-79**	**Total**
Men	403	480	381	245	101	**1610**
Black	105	168	120	71	22	**486**
Hispanic	150	147	105	67	22	**491**

Table 4-1. BACH study design (age, sex, and racial/ethnic composition of the BACH sample)						
White	148	165	156	107	57	**633**
Women	610	660	643	434	188	**2535**
Black	196	229	207	143	66	**841**
Hispanic	249	240	212	112	37	**850**
White	165	191	224	179	85	**844**
Total	**1013**	**1140**	**1024**	**679**	**289**	**4145**

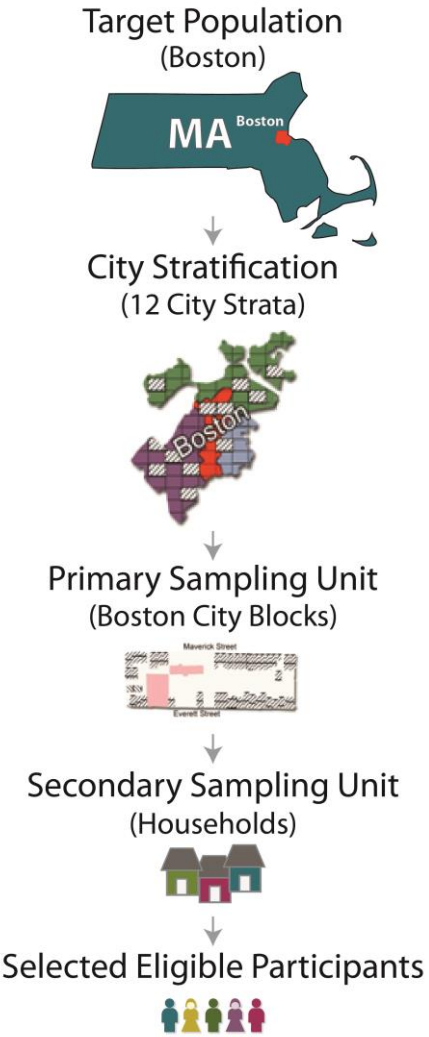
Demographic composition of the BACH III survey (2009-2012)						
	Age at baseline (years)					
	34-39	**40-49**	**50-59**	**60-69**	**70-79**	**Total**
Men	265	350	306	188	75	**1184**
Black	76	129	98	51	16	**370**
Hispanic	96	107	85	51	15	**354**
White	93	114	123	86	44	**460**
Women	460	529	514	332	132	**1967**
Black	156	187	163	108	43	**657**
Hispanic	192	193	180	85	29	**679**
White	112	149	171	139	60	**631**
Total	**724**	**879**	**820**	**520**	**207**	**3151**

The BACH Survey was designed to include adequate numbers of U.S. racial/ethnic minorities (Black, Hispanic, and White participants) and sufficient numbers of both men and women, and to balance across a broad age distribution (30-79 years, by 10-year age-groups). These requirements were intended to permit examination of rare conditions across major population subgroups of interest. The final baseline sample, by design cell, is provided in **Table 4-1**. A total of 5,502 participants were recruited with similar numbers across the three racial/ethnic groups considered (1,767 Black; 1,876 Hispanic; and 1,859 White).

4.2.4 How was this sample attained?

The sampling strategy for the BACH Survey has been published previously.[437] Briefly, to ensure a representative sample, a stratified, two-stage cluster sampling design was employed (**Figure 4-1**), with census blocks as the primary sampling units and households as the secondary sampling units. Census blocks were stratified by minority density and high minority strata were over sampled to attain a sample with roughly 1/3 Black, 1/3 Hispanic, and 1/3 White participants. The individual response rate, which was calculated as the number of participants interviewed divided by the number of participants for whom contact was attempted, was 57.3%.[437]

Figure 4-1. Stratified, two-stage cluster design employed in the BACH study



4.2.5 How often have they been followed-up?

Two follow-up surveys to BACH have been completed. BACH II was initiated in 2008 with n=4,145 participants participating. BACH III was initiated in 2010 with n=3,150 participants.

BACH II (2008-2010)

Approximately five years after the initial BACH Survey, a total of 4,145 participants completed the BACH II survey representing an 80.5% retention rate (**Table 4-2**). The average length of time between the baseline and follow-up interviews was 4.8 years. Attrition between BACH I and

BACH II was highest among racial/ethnic minorities and men. Retention rates for men were 77.3%, 68.1%, and 82.6% among Black, Hispanic, and White men, respectively. Retention rates for women were 84.1%, 79.1%, and 88.1% among Black, Hispanic, and White women, respectively. Retention rates were higher with increasing age, with the exception of the oldest age group (70-79 years at baseline). Lower retention rates were observed among lower SES participants.

Table 4-2. Retention and attrition of participants in the BACH Study cohorts

	BACH I	BACH II	BACH III
Respondents	5,502	4,145	3,151
Non-respondents			
Ineligible (deceased, too ill to participate, incarcerated, etc.)		348	324
Refusal		350	170
Unable to contact		657	535
Total eligible		5,152	3,856
Retention as % eligible		**80.5%**	**81.7%**

BACH III (2010-2012)

Participants were approached in 2010 to participate in BACH III (2010-2012) achieving an 81.4% retention rate (of those completing BACH II). Overall, 65.2% of eligible BACH I participants were retained through BACH III. Eleven participants participated in BACH III, but not BACH II.

The average length of time between BACH II and BACH III was 2.5 years. Retention rates were lowest among men from BACH II and BACH III. Retention rates (conditional on BACH II participation) were 81.0%, 77.8%, and 81.6% among Black, Hispanic, and White men, respectively; and 83.5%, 83.5%, and 82.4% among Black, Hispanic, and White women. Retention rates increased slightly with older age. Retention was not significantly related to SES.

4.2.6 Sub-studies

In addition to the three waves of the BACH Survey, a number of sub-studies have utilized the BACH cohort.

The **BACH/Bone Survey** is an observational research study of musculoskeletal health in 1,219 men recruited from the parent study, BACH.[454] The baseline examination occurred between 2002 and 2005. A follow-up survey (**BACH/Bone II**) is currently recruiting men from the original cohort to examine longitudinal changes in fall risk and bone density.

Endothelial Function and Erectile Dysfunction (ED/EnD) is an observational research study conducted among 400 men participating in the BACH/Bone Survey. This study investigates the association between endothelial function and erectile dysfunction (ED) and is designed to establish the role of endothelial dysfunction in the aetiology and natural history of ED. The study was initiated in January 2010.

Beneath the Urologic Iceberg is a qualitative study linked to the BACH Survey, consisting of focus groups and in-depth interviews. A primary objective was to explore factors underlying the care-seeking process for urinary symptoms.[455, 456] Participants were randomly sampled from each of the six subgroups of the BACH sample and included individuals who reported one or more lower urinary tract symptoms (LUTS) on the survey. Fifty-eight participants participated in a total of eight focus groups. In-depth interviews were conducted with 151 participants.

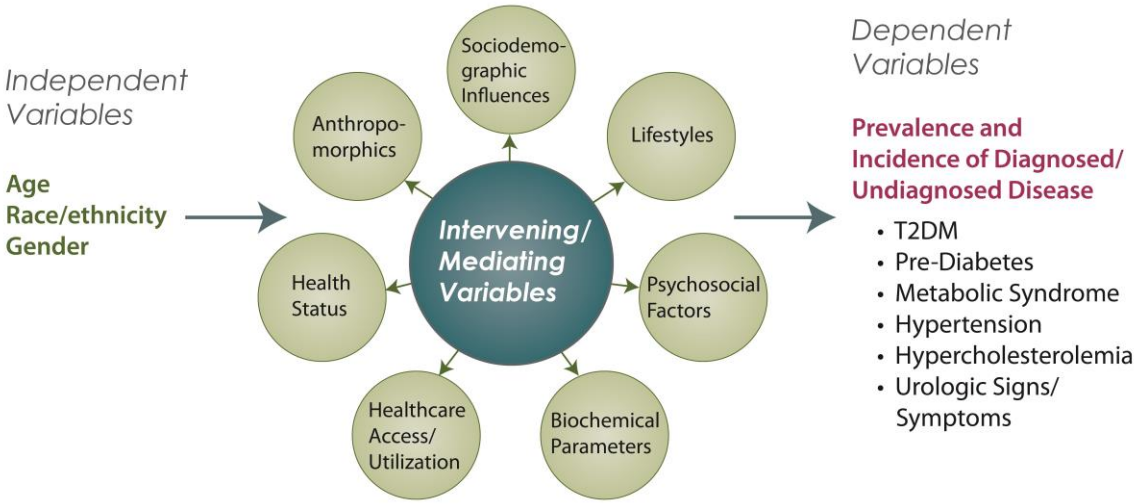
The Intra-Subject Hormone Variation Study was designed to measure intraindividual variation in hormones among men.[457] Male participants (n=134) were randomly selected from the BACH Survey's study strata. Two blood samples (drawn 20 minutes apart) were

obtained from two study visits (1-3 days apart) at study entry and again three and six months later.

4.2.7 What has been measured?

The main outcomes of interest in the first two waves were urologic symptoms and conditions. Extending beyond the initial outcomes of interest, the third wave of the BACH Survey focused on type 2 diabetes, pre-diabetes, and metabolic syndrome risk assessment. The characterization and explanation of social disparities (by age, racial/ethnicity, and sex) in the prevalence of disease has been the central focus of the BACH Survey through all three waves of the study. All three waves measured a number of other factors thought to contribute to the aetiology of disease or to mediate the relationship between social disparities (according to racial/ethnicity, SES, age, sex) and health outcomes (**Figure 4-2**). These variables can be categorized into seven groups: (1) sociodemographic characteristics, (2) health care access/utilization, (3) lifestyles, (4) psychosocial factors, (5) health status, (6) anthropomorphic measurements, and (7) biochemical parameters. **Table 4-3** gives details of the types of information collected in each wave of the BACH Survey.

Figure 4-2. Research model for the Boston Area Community Health study



When possible, previously validated questionnaires were utilized in the BACH Survey. Specifically, measures that were previously published in a peer-reviewed journal, had reported metric properties, were available in English and Spanish, and were already used in field epidemiology settings were preferred. A National Institutes of Health (NIH) scientific advisory committee offered recommendations on validated scales. The BACH questionnaires and project correspondence were translated into Spanish and then back-translated to ensure cross-cultural equivalence of meaning; 26% of the BACH interviews were conducted in Spanish (76% of interviews among Hispanics were conducted in Spanish). All protocols, questionnaires, and forms used in the BACH Survey were annually reviewed and approved by the New England Research Institutes' Institutional Review Board.

Table 4-3. Measures Available from the BACH Cohort study (2002-2012)			
Variable	BACH I (2002-05)	BACH II (2008-10)	BACH III (2010-12)
I. Sociodemographics			
Residential address (geo-coded), mobility	•	•	•
Income, education, work status, occupation, marital status	•	•	•
Sociological questionnaire including: acculturation, alienation, neighbourhood order/disorder, perceived discrimination, health literacy			•
II. Health Care Access/Utilization			
Health care access/utilization	•	•	•
Health insurance status/type	•	•	•
Quality of care, satisfaction with care			•
Inclination to seek care		•	•
III. Lifestyles			
Physical activity, diet	•	•	•
Abuse history	•	•	
Tobacco and alcohol use	•	•	•
Sleep	•	•	•
IV. Psychosocial Factors Depressive symptoms, interpersonal stress, major life events			
Depressive symptoms, interpersonal stress	•	•	
Major life events			•
V. Health Status			

Table 4-3. Measures Available from the BACH Cohort study (2002-2012)			
Variable	BACH I (2002-05)	BACH II (2008-10)	BACH III (2010-12)
Quality of Life (self-rated health, current and projected life satisfaction)	•	•	•
Chronic disease/events, family medical history, pain, fatigue, menopausal status	•	•	•
Inventoried Prescription/Non-prescription Medications and supplements	•	•	•
VI. Physical/Anthropomorphic Measures			
Height, weight, body fat percentage, hip/waist circumference, blood pressure, pulse	•	•	•
VII. Biochemical Parameters			
Total cholesterol, HDL, LDL, Triglycerides	•		•
Testosterone, estradiol, SHBG, FSH, LH (men only)	•		•
Cortisol, c-reactive protein	•		
Fasting blood glucose, HbA1c, insulin			•
Serum aliquots stored at -80F	•		•
Stored DNA, ancestry informative markers			•
HDL=High-density lipoprotein; LDL=Low-density lipoprotein; SHBG=Sex hormone-binding globulin; FSH =Follicle-stimulating hormone; LH=Luteinizing hormone			

An interviewer-administered questionnaire and anthropomorphic measures were included as a part of the BACH Survey at all three time points. For BACH I and BACH II, sensitive questions such as sexual functioning and abuse history were ascertained through a self-administered questionnaire. Blood samples were taken at the first and third study waves with serum aliquots stored at -80ºC for future use. DNA samples were isolated from the BACH III blood samples and

ancestry informative markers were collected. The ancestry informative markers are a panel of markers informative for geographic ancestry that can identify a participant's proportion of European, West African, or Native American ancestry.[75, 435] DNA samples are stored for future use.

4.2.8 What has it found? Key findings and publications

The BACH Survey's design and the breadth of measurements have allowed researchers to identify disparities and quantify contributions to social disparities in a number of health conditions; these have included racial/ethnic disparities in obesity,[458] exposure to prescription medications,[459] variation in markers of bone turnover[460] and bone mineral content and density,[461] higher rates of vitamin D deficiency,[462] and physical function.[463] The study has also explored potential explanations for these racial/ethnic disparities[464] with a particular focus on socioeconomic status. Recent publications from BACH demonstrate that socioeconomic status accounts for much of the racial/ethnic disparities seen in the rates of erectile dysfunction,[465] nocturia,[466] and diabetes.[30, 434] These findings are of critical importance for informing prevention and treatment strategies.

BACH has also contributed to the literature on gender disparities. BACH findings have suggested sex-specific effects in several health conditions,[467] explored previously un-researched areas of women's sexual health,[468-470] and has contributed significantly to the literature on the effects of abuse.[470-472]

The BACH Survey's novel "upstream" focus has led to new estimates on the magnitude of unmet need for drug treatment of urological symptoms[473] and has identified populations with unmet health insurance needs by studying both the uninsured and the underinsured.[474]

Basic epidemiologic data on health disparities (e.g. racial/ethnic specific prevalence and incidence) had not previously been estimated for many urologic conditions, and disparities in these conditions were poorly understood. The BACH Survey provided prevalence rates by racial/ethnicity for urine leakage,[475] LUTS,[476] painful bladder syndrome (PBS),[465] nocturia,[466] and prostatitis.[472] The BACH Survey contributed prevalence estimates and identified risk factors for female sexual dysfunction,[469, 470] erectile dysfunction,[442, 477, 478] and symptomatic androgen deficiency.[479]

Prior to the BACH Survey, urologic symptoms were not considered important clinical or public health problems. The BACH Survey helped identify an epidemic of urologic conditions and estimated that 52 million adults in the U.S. will have symptoms of LUTS, urine leakage, painful bladder syndrome, or prostatitis in 2025.[480] The BACH Survey demonstrated that urologic symptoms were significantly associated with other major medical conditions (type 2 diabetes, cardiac disease, hypertension, and depression) and a dose-response relationship between the severity and duration of urologic symptoms and chronic illnesses was identified.[481-484] Urologic symptoms were also shown to have a negative impact on quality of life[476, 477, 485-488] with an effect on quality of life similar to that of having diabetes, high blood pressure or cancer.[485]

Given the newfound importance of urologic symptoms and conditions, the BACH Survey's estimates on the risk factors for these conditions,[465, 478, 480, 481, 483, 489-491] the overlap between these conditions, [492-497] and the unmet medical care needs[498, 499] for these conditions are important contributions to the field of urology.

4.2.9 What are the main strengths and weaknesses?

Strengths

The strengths of the BACH Survey stem from its community-based random sample design. The study, by design, includes both sexes, a wide age range (30–79 years) and includes a large number of minority participants, representative of Black and Hispanic populations. Key strengths of the BACH Survey include: (1) the wide range of measurements covering six theoretical domains (Figure 2), that (2) allow for both individual-level and neighbourhood-level (multi-level) analyses, (3) its longitudinal design which allows for within- and between- person comparisons over a ten year period, (4) its focus on pre-diagnostic disparities (e.g. urologic symptoms, pre-diabetes) rather than disparities based on variably diagnosed conditions, and (5) the multi-disciplinary approach measures the prevalence of disease through both self-report and physiologic (objective) confirmation. In summary, the BACH participants are well-phenotyped in a number of key areas (variety of measures, over time, un-diagnosed and diagnosed conditions) that could lead to productive collaborations in many areas where data pooling is needed.

Representativeness and generalizability

While geographically limited to the city of Boston, Massachusetts, the BACH Survey sample has been compared to other large regional (Behavioral Risk Factor Surveillance System, Centers for Disease Control and Prevention) and national (the National Health and Nutrition Examination Survey, the National Health Interview Survey) on a number of different sociodemographic and health-related variables. The results suggest that the BACH Survey is highly representative of the city of Boston and that BACH Survey estimates of key health conditions are comparable with national trends. One key difference is that the BACH Survey does not include a number of other minority groups (e.g., Asian Americans).

Weaknesses

First, several key variables in the BACH Survey (e.g. history of certain medical conditions) rely on self-report data. Relying on self-report data is common among observational studies and research has shown that self-report of major medical conditions are well correlated with medical record review.[500-503] In addition, every attempt was made to directly measure key variables (e.g. height, weight, blood pressure, cholesterol, fasting glucose).

A second limitation of the BACH Survey was the exclusion of Asians from the study. While a sizeable minority population in the United States, Asians comprised only 7.5% of the Boston, Massachusetts population in 2000.[504] The feasibility of recruiting and interviewing Asians for inclusion in the BACH Survey (e.g. interviewer language requirements) was weighed against the potential public health impact.

Finally, the initial survey response rate was 57.3%. This response rate, while low, is comparable with response rates among other random sample cohort studies and was not entirely unexpected given the lengthy in-home interview (2 hours), the blood draw, and the sensitive nature of many of the questions. Nonetheless, the study has maintained high retention rates, thus presumably mitigating concerns regarding internal validity. The BACH Survey staff have fostered a close relationship with the study participants and with the inner-city Boston community. This close contact and continued communication through newsletter, holiday cards, and birthday cards helps to ensure a trust between the study participants and the study research team and staff that leads to high retention rates and good response rates to sensitive questions.

4.2.10 Can I get hold of the data? Where can I find out more?

BACH I data are available through The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Central Repositories (www.niddkrepository.org). Further inquiries can be made through the New England Research Institutes, Inc., website (www.neriscience.com/epidemiology).

5 The Contribution of Biogeographic Ancestry and Socioeconomic Status to Racial/Ethnic Disparities in Type 2 Diabetes: Results from the Boston Area Community Health (BACH) Survey

5.1 Introduction

This paper examines the contribution of biogeographic ancestry to racial/ethnic disparities in T2DM. Biogeographic ancestry is one example of a genetic influence thought to contribute to disparities. Previous research has shown that careful control of socioeconomic factors is necessary when examining biogeographic ancestry. Keeping this in mind, I used several different statistical techniques to separate genetic ancestral influences from socioeconomic influences.

This paper was accepted for publication to the Annals of Epidemiology and was published online in July 2014 and in print in September 2014.

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
www.lshtm.ac.uk

Registry
T: +44(0)20 7299 4646
F: +44(0)20 7299 4656
E: registry@lshtm.ac.uk

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SECTION A – Student Details

Student	Rebecca Piccolo
Principal Supervisor	Neil Pearce
Thesis Title	Racial and Ethnic Disparities in Type-2 Diabetes: A Multilevel Perspective

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conducted all analyses, designed all tables and figures included in this paper and wrote the first draft of the article. Andre Araujo, John McKinlay, and Neil Pearce all provided comments on the draft article, many of which I incorporated during revisions to the article.

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5.2 Article Submitted

5.2.1 Abstract

Purpose: Racial/ethnic disparities in the incidence of type 2 diabetes (T2DM) are well documented and many researchers have proposed that biogeographical ancestry (BGA) may play a role in these disparities. However, studies examining the role of BGA on T2DM have produced mixed results to date. Therefore, the objective of this research is to quantify the contribution of BGA to racial/ethnic disparities in T2DM incidence controlling for the mediating influences of socioeconomic factors.

Methods: We analyzed data from the Boston Area Community Health (BACH) Survey, a prospective cohort with approximately equal numbers of Black, Hispanic, and White participants. We used Ancestry Informative Markers to calculate the percentages of West African and Native American ancestry of participants. We used logistic regression with g-computation to analyze the contribution of BGA and socioeconomic factors to racial/ethnic disparities in T2DM incidence.

Results: We found that socioeconomic factors accounted for 44.7% of the excess risk of T2DM among Blacks and 54.9% among Hispanics. We found that BGA had almost no direct association with T2DM and was almost entirely mediated by self-identified race/ethnicity and socioeconomic factors.

Conclusions: It is likely that non-genetic factors, specifically socioeconomic factors, account for much of the reported racial/ethnic disparities in T2DM incidence.

5.2.2 Background

Disparities in type 2 diabetes (T2DM) by race/ethnicity are a pervasive public health problem in the United States and worldwide. Recent estimates from the US Centers for Disease Control

report that, compared to White adults, the prevalence of diabetes is 77% higher among Black and 66% higher among Hispanic adults in the US.[2] Racial/ethnic disparities have been shown to be associated with poorer diabetes control,[6] elevated rates of diabetes-related complications,[8] higher rates of hospitalization,[505] and greater health care costs.[494] It has been proposed in several studies that genetics, specifically, biogeographic ancestry (BGA), may explain a substantial proportion of these disparities.[80]

The concepts of genetics, race, and ethnicity are often confused.[61-63] The term 'race' is commonly defined in terms of biological differences between groups assumed to have different biogeographical ancestries. [64]Analysis of variance of genetic variation has indicated that approximately 75% of genetic variance is found 'within' racial/ethnic groups, while 10% of the variance is found 'between' races.[64] Furthermore, the US Census categorizations (White, Black, Asian, etc.) are largely artificial constructs, as is the concept of biological race itself.[63, 68]In contrast, ethnicity is a complex multidimensional construct that reflects biological factors, geographical origins, historical influences, as well as social, cultural, economic factors.[69]

A genetic basis for racial/ethnic differences in diabetes risk, the 'thrifty gene' hypothesis, was first proposed over 40 years ago [70]. The hypothesis has been heavily criticized from several different perspectives,[61] but has nevertheless been revived in recent years as the rapid evolution of science and technologies have facilitated an expansion in genetic research. Genetic studies have established approximately 70 loci that are associated with small increases in T2DM risk.[84-86, 506, 507] While early studies focused primarily on people of European descent, recent studies extended this research to Black and Hispanic populations.[88-90] These studies indicate substantial overlap in the susceptibility loci across racial/ethnic groups signifying that common genetic variants contribute similarly to diabetes risk across races/ethnicities[80, 85, 90, 91] and are therefore unlikely to explain racial/ethnic differences in diabetes risk.

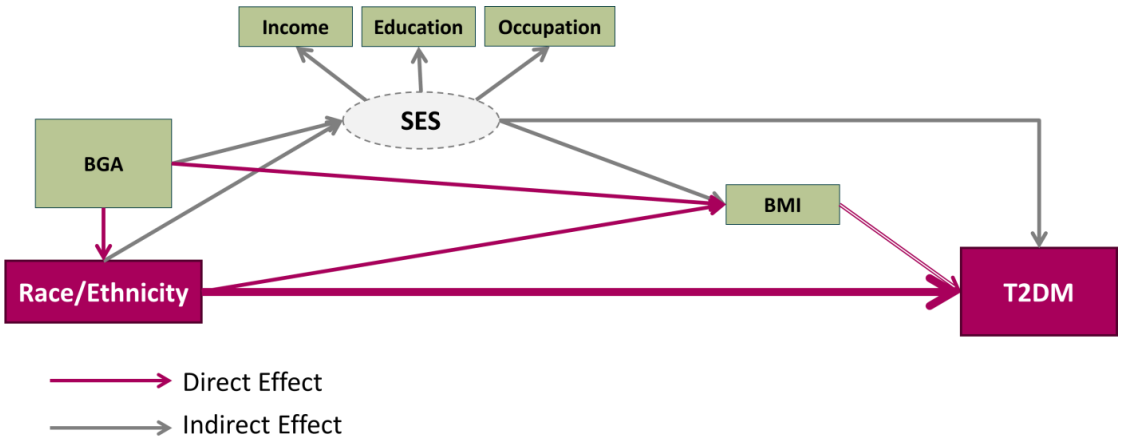
Since T2DM has a complex genetic etiology, it may be important to account for the substantial heterogeneity in genetic heritage that exists in admixed populations.[73-76] Individual proportions of European, African, and Native American ancestry can vary substantially among the commonly-used categories of Black,[73] Hispanic,[75] and White.[77] Several studies have suggested that the biologic mechanisms leading to increased T2DM risk in Black and Hispanic Americans may be related to genes associated with BGA.[58, 64, 80] However, studies examining this hypothesis by measuring Ancestry Informative Markers (AIMs), a method of estimating an individual's genetic marker-based race/ethnicity have produced mixed results. The Atherosclerosis Risk in Communities (ARIC) Study found that BGA was not associated with HbA1c among African Americans and found that the contributions of demographic and metabolic factors outweighed the contributions of BGA.[79] However, an analysis of ARIC/Jackson Heart data, found that BGA was associated with T2DM among African Americans, a finding that was robust to adjustment for lifestyle and socioeconomic factors.[80] Studies among Hispanic populations have similarly produced mixed results. In a study of Columbian and Mexican participants, the association between ancestry and T2DM was attenuated, if not eliminated, when adjusting for socioeconomic factors.[36] In contrast, a study of Puerto Rican participants living in the continental US showed a negative association between African ancestry and prevalent T2DM.[81] In one of the few studies to examine the associations between ancestry and diabetes risk among African and Hispanic Americans, the Women's Health Initiative (WHI) found that ancestry was significantly associated with diabetes risk, but that socioeconomic factors attenuated the effects among Hispanic but not African American women.[37]

In light of these conflicting findings, further research is needed in order to validly estimate the contributions of BGA and other factors to T2DM disparities. Therefore the objectives are two-fold: 1) to quantify the contribution of African and Native American ancestry to racial/ethnic disparities in T2DM incidence, and 2) to measure the contribution of socioeconomic status to

racial/ethnic and BGA disparities in T2DM incidence (**Figure 5-1**). The Boston Area Community Health (BACH) Survey [508] is uniquely positioned to address these research objectives given the racial/ethnic diversity of the cohort and its prospective cohort design.

1. What is the contribution of BGA to racial/ethnic disparities in T2DM? (pink arrows)
2. What is the indirect effect (mediation) of SES on racial/ethnic and ancestral disparities on T2DM?

Figure 5-1. Research Model



5.2.3 Materials and Methods

The Boston Area Community Health (BACH) Survey

The Boston Area Community Health (BACH) Survey is a prospective cohort study of men and women from Boston, Massachusetts. The BACH Survey used a random stratified cluster sample design to recruit 5,502 residents (2,301 men, 3,201 women) aged 30-79 years from three racial/ethnic groups (1767 Black, 1876 Hispanic, 1859 White). Participants completed an in-person interview at baseline (2002-2005) and were contacted approximately five (BACH II: 2006-2010) and seven (BACH III: 2010-2012) years later for follow-up assessments. BACH III interviews were conducted among 3,155 (BACH III) individuals (an 81.4% conditional retention rate).

At all three time points, a home visit was conducted that included anthropometric measurements and an in-person interview, conducted in English or Spanish, to obtain information about diabetes status, comorbidities, sociodemographics, and lifestyle. AIMs were collected at BACH III only. The detailed methods have been described elsewhere [508]. All participants provided written informed consent and the study was approved by New England Research Institutes' Institutional Review Board.

Measures

Biogeographical ancestry (BGA)

A panel of 63 uncorrelated single nucleotide polymorphism (SNPs) were genotyped. These AIMs were selected based on their ability to estimate percent African, Native American, and European ancestry in admixed populations [75, 435]. Samples were genotyped at the Genetic Analysis Platform (GAP) at the Broad Institute (Cambridge, MA) using iPLEX (Sequenom) in three batches. HapMap samples (Utah residents with Northern and Western European ancestry (CEU) and Yoruba in Ibadan, Nigeria (YRI)) were included in each batch for quality control. All Hap Map samples had 100% HapMap concordance. The average call rate for all assays was 97.4%; 1.6% of samples failed quality control with call rates <90% and two SNPs failed with call rates <90%. Ancestry proportions were estimated for individual participants using ADMIXTURE Software (version 1.12 http://www.genetics.ucla.edu/software/admixture/) using a *k* (the number of ancestral populations) of 3.

Race/ethnicity

Self-identified race/ethnicity was recorded using two separate survey questions as recommended by the Office of Management and Budget. The racial/ethnic categories used in

this research are 1) non-Hispanic Black (Black), 2) Hispanic of any race (Hispanic), and 3) non-Hispanic White (White).

Socioeconomic status (SES)

The individual SES indicators considered were: household income, educational attainment and occupation, measured at baseline. **Household income**, originally grouped into 12 ordinal categories, was collapsed into the following three categories of US dollars: <20,000, 20-49,999, and ≥50,000. These categories were specified *a priori* based on literature review. However, other parameterizations were considered to ensure adequate control of confounding. **Educational attainment** was categorized as: 1) less than high school; 2) high school graduate or equivalent; 3) some college; and 4) college or advanced degree. **Current or former occupation** was categorized as follows: 1) management, professional, sales and office occupations; 2) service occupations; 3) manual labor; and 4) never worked. We use the broader term 'SES' when referring to these three distinct socioeconomic factors in the aggregate, all of which are strongly related to overall health.

Type 2 diabetes

Participants were asked at baseline (BACH I) and follow-up (BACH II and III) whether a doctor or health care professional had ever told them that they have diabetes. Individuals diagnosed with diabetes at baseline were excluded from these analyses (n=432). Incident cases of T2DM were defined as new diagnoses of T2DM at BACH II or BACH III (n=260, 6.4%). The use of insulin or oral medications for diabetes was collected by medication inventory at all three time-points and sensitivity analyses were conducted to assess the potential for self-report bias. We also conducted confirmatory cross-sectional analyses using BACH III data. At BACH III prevalent diabetes cases were defined as fasting plasma glucose ≥ 126 mg/dL, HbA1c ≥ 6.5% or self-report of a diabetes diagnosis confirmed by medication inventory (**Section 5.4**).

Statistical methods

In order to reduce the potential for bias due to missing data and to minimize reductions in precision,[439, 509] multiple imputation was implemented for item non-response using Multivariate Imputation by Chained Equations (MICE) [510] in R (R Foundation for Statistical Computing, Vienna Austria). 822 participants (26%) were missing data on BGA (i.e. % West African, Native American, and European ancestry), 248 (8%) education, 184 (6%) household income, <1% occupation, and <1% BMI. Fifteen multiple imputation datasets were created for each racial/ethnic by gender combination. Analyses were replicated on the complete data and the results were essentially the same as those obtained from the multiple imputation. In this paper, we therefore present results from the multiple imputation models because the precision of the estimates is improved by the increased sample size, and the full data set is less likely to be subject to bias.[446, 511]

Statistical analyses were performed using SUDAAN 11 (Research Triangle Park, North Carolina), Stata/SE Version 12 (StataCorp, College Station, Texas), and Mplus Version 7 (Muthen and Muthen, Los Angeles, CA). To account for the BACH survey design (a stratified, two-staged cluster sample including oversampling of Black and Hispanic participants),[437, 508] data observations were weighted inversely to their probability of selection at baseline to produce unbiased estimates of the Boston population. Survey weights were adjusted for non-response bias at follow-up using the propensity cell adjustment approach,[438] and post-stratified to the Boston census population in 2010.

Logistic regression models were used to estimate risk ratios (RRs) and 95% confidence intervals (CIs) based on the predicted marginal risk in SUDAAN. All p-values are two-sided. BMI and other relevant lifestyle/behavioral mediators were considered including physical activity, dietary patterns, alcohol consumption, high blood pressure and high cholesterol. BGA was modeled as the proportion of West African (ranging from 0 to 1) and Native American ancestry (also ranging

from 0 to 1). The RRs for 100% West African and 100% Native American ancestry versus 100% European ancestry are reported for ease of interpretation.

We performed mediation analysis to assess what degree of the racial/ethnic (or ancestry) effect is explained by socioeconomic status (the mediating influence). The excess relative risk (ERR) was calculated to quantify the risk attributable to a given exposure (i.e. Black race or Hispanic ethnicity). The unadjusted ERR is one method to estimate the "total effect" of race/ethnicity. The "indirect effect" or "mediated effect" due to SES was estimated using the SES-adjusted ERR. An estimate of the percent of the total effect that is mediated by SES was calculated as: (unadjusted ERR - adjusted ERR)/unadjusted ERR. Since BMI is likely influenced by SES (**Figure 5-1**), BMI was introduced only in the SES-adjusted models and is not included in the calculation of mediation effects.

There are limitations to using standard regression techniques to estimate mediation[512] and under some circumstances, these techniques may fail to produce valid estimates. For example, traditional regression techniques may not adequately control for confounding between the mediator and the outcome[513]. Therefore, we also used g-computation[514] to supplement the traditional regression techniques. The g-computation procedure estimates the total causal effects as well as natural direct and indirect effects[513, 514]. Since the g-computation procedure in Stata (gformula) has only been developed on an additive (risk difference) scale and does not currently support survey sample weights, we conducted an unweighted analysis with three estimates: 1) excess relative risk estimates using unweighted data (for comparison to the weighted estimates), 2) risk differences estimates from traditional regression techniques, and 3) risk differences obtained from g-computation. All models were age and gender adjusted. We included BMI in the g-computation estimate as an exposure dependent confounder of the mediator outcome association.

5.2.4 Results

The demographic characteristics of the 2,723 men and women in the analytic sample are presented in **Table 5-1.** The mean and standard error (SE) time between the baseline (BACH I) and follow-up (BACH III) assessments was 7.2 (0.3) years. Over 25% of the sample had a household income < $25,000, over one-third had a high school education or less, and over two-thirds were overweight or obese.

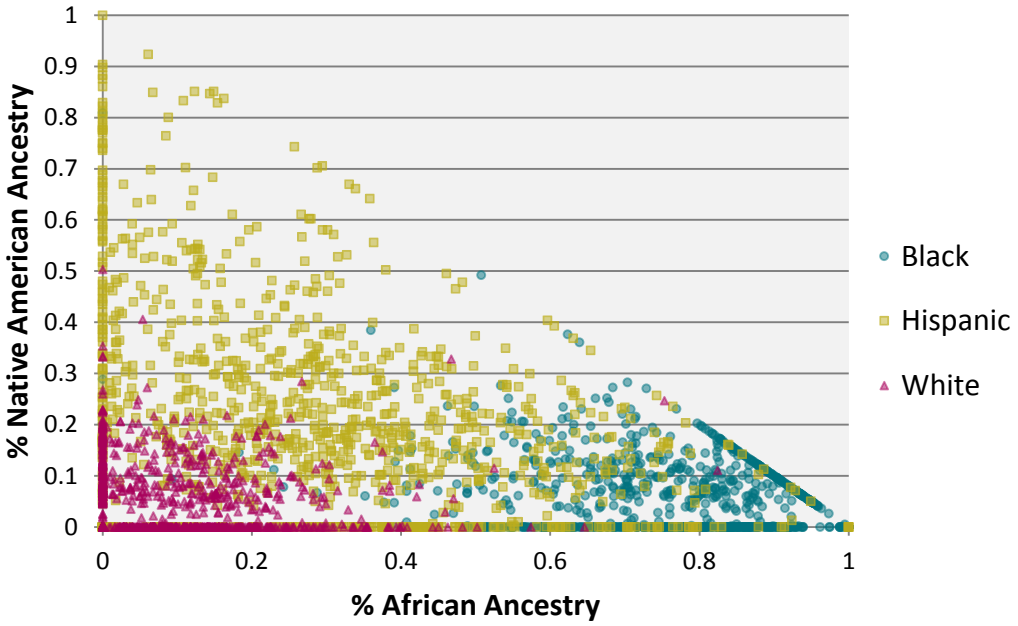
We estimated individual ancestry with respect to three ancestral populations: West African, Native American, and European (**Figure** 5-2). For Black participants, the ancestral composition is on average 78% West African (95% CI: 75-80%), 5% Native American (4-6%), and 17% European (15-20%). Hispanic participants were on average 29% West African (26-33%), 22.4% Native American (19-26%), and 48% European (45-52%) and had the greatest degree of variability around these measures due to the high degree of admixture. White participants were on average 9% West African (8-9%), 5% Native American (4-6%), and 87% European (86-88%).

Figure 5-2 demonstrates that while BGA (represented as % Native American and % African ancestry) was highly correlated with self-identified race/ethnicity, there was substantial variability in the individual proportions, particularly among Blacks and admixed Hispanics. For example, among self-identified Black participants, the minimum percentage of West African ancestry was 0.001% and the maximum was 99.99% (not imputed). Similarly wide ranges were seen for Native American ancestry (min: 0.001%, max: 80.9%) among Black participants; for African (min: 0.001%, max: 99.99%) and Native American (min: 0.001%, max: 99.99%) ancestry among Hispanic participants; and even African (min: 0.001%, max: 82.4%) and Native American (min: 0.001, max: 50.3%) ancestry among White participants (**Figure** 5-2). The overall cumulative incidence of T2DM over the follow-up period was 6%, with a cumulative incidence of 10% among Black, 6% among Hispanic, and 5% among White participants.

Table 5-1. Demographic Characteristics by Self-Reported Race/Ethnicity at Baseline

	Race/ethnicity Number (%)			
	Black N=863	**Hispanic N=870**	**White N=990**	**Total N=2723**
Age				
30-39	225 (50.38)	278 (63.72)	199 (39.11)	702 (45.10)
40-59	281 (23.27)	267 (21.34)	247 (24.34)	795 (23.69)
60-69	210 (14.56)	198 (8.62)	260 (14.41)	668 (13.74)
70-79	108 (7.75)	96 (4.49)	194 (13.09)	398 (10.62)
80+	39 (4.04)	31 (1.84)	90 (9.05)	160 (6.84)
Gender				
Male	312 (42.57)	292 (45.77)	420 (48.33)	1024 (46.49)
Female	551 (57.43)	578 (54.23)	570 (51.67)	1699 (53.51)
Biogeographical Ancestry (mean %, SE)				
African	77.72 (1.25)	29.24 (1.70)	8.52 (0.46)	29.41 (1.33)
Native American	5.01 (0.41)	22.35 (1.62)	4.93 (0.30)	7.08 (0.32)
European	17.27 (1.19)	48.41 (1.95)	86.55 (0.54)	63.51 (1.35)
Income				
<$20,000	372 (38.16)	552 (51.34)	237 (17.82)	1161 (27.31)
$20,000 - $49,999	322 (38.62)	252 (35.53)	281 (26.70)	855 (30.94)
≥ $50,000	169 (23.22)	66 (13.13)	472 (55.48)	707 (41.75)
Education				
Less than High School	137 (11.26)	367 (36.58)	74 (4.04)	578 (9.93)
High school or equivalent	375 (45.47)	293 (35.53)	235 (19.13)	903 (28.12)
Some college	181 (22.60)	109 (12.29)	131 (11.02)	422 (14.25)
College or advanced degree	170 (20.67)	101 (15.60)	550 (65.81)	821 (47.70)
Occupation				
Professional, Managerial, Sales, and Office	449 (58.55)	270 (37.72)	735 (80.03)	1454 (69.17)
Service	223 (21.10)	341 (36.81)	121 (8.17)	685 (15.09)
Manual labor	180 (19.52)	209 (20.74)	118 (9.42)	507 (13.48)
Never worked	11 (0.83)	50 (4.73)	16 (2.39)	77 (2.26)
Neighborhood SES				
Low	581 (66.24)	482 (51.00)	255 (18.24)	1318 (34.97)
Middle	143 (16.42)	192 (24.16)	372 (39.55)	707 (31.54)
High	138 (17.34)	196 (24.84)	363 (42.21)	697 (33.49)
BMI				
Normal (<25)	177 (21.48)	175 (28.01)	314 (34.39)	666 (30.18)
Overweight (25-30)	269 (29.33)	359 (38.69)	351 (39.53)	978 (36.72)
Obese (≥30)	417 (49.19)	336 (33.30)	325 (26.08)	1078 (33.10)

Figure 5-2. Biogeographical Ancestry by Self-Identified Race/Ethnicity



What is the contribution of African and Native American ancestry to racial/ethnic disparities in T2DM incidence?

In age and gender adjusted models, Black participants were 2.3 times as likely to report having developed diabetes (RR=2.3; 95% CI: 1.4-3.7) and Hispanics were 1.7 times as likely to report new diabetes (RR=1.7; 1.0-2.8) than White participants (Table 5-2). The excess relative risk (ERR) indicates that Black participants are 128% more likely, and Hispanic participants 67% more likely, to develop T2DM over the study period compared to White participants. Adjustment for BGA increased these estimates slightly and widened the confidence intervals (Black vs. White: RR=2.6; 0.9-7.2; Hispanic vs. White: RR=2.0; 1.1-3.8).

We examined the relationship between 1 unit increments of African and Native American ancestry on incident T2DM (Table 5-3). In age- and gender-adjusted models, the risk of developing T2DM was, on average, 1.6 times higher (RR= 2.6; 1.3-5.0) for an individual with

100% African ancestry versus an individual with 100% European ancestry. There was no relationship between Native American ancestry and developing T2DM (RR=1.0; 0.2-4.9).

What is the contribution of socioeconomic status to racial/ethnic and ancestral disparities in T2DM?

Adjusting for SES (income, occupation, and education) attenuated the racial/ethnic disparities (Black vs. White: RR=1.7; 0.6-5.1; Hispanic vs. White: RR=1.1; 0.6-2.2, Table 5-2). The traditional mediation analyses indicated that SES accounted for 64% of the total effect attributed to Black race and 100% of the total effect attributed Hispanic ethnicity. Further adjustment for BMI only changed the risk ratios slightly. Estimates adjusting for other lifestyle/behavioral factors are not reported since their effects were negligible (< 3%). Consistent with previous studies and with the results by self-report race/ethnicity, the effects of BGA were attenuated with adjustment for socioeconomic factors (African ancestry: RR=1.5; 0.8-3.0; Native American ancestry: RR=0.4; 0.1-2.3, Table 5-3). The mediation analyses indicated that SES accounted for 67% of the total effect attributed to West African ancestry. We tested for statistical interaction between ancestry and socioeconomic factors and found no statistically significant interactions.

Table 5-2. Risk Ratios for Diabetes Incidence by Self-Identified Race/Ethnicity (Longitudinal)[1]

	Black vs. White			Hispanic vs. White			Adjusted for
	RR	CI	ERR	RR	CI	ERR	
Base model	2.28	1.40-3.71	1.28	1.67	1.00-2.80	0.67	*Gender and age*
Ancestry adjusted	2.57	0.92-7.19	1.57	2.02	1.07-3.80	1.02	*Gender, age, African, and Native American ancestry*
SES adjusted	1.46	0.88-2.44	0.46	0.84	0.47-1.51	-0.16	*Gender, age, income, education, and occupation*
Ancestry and SES adjusted	1.71	0.58-5.07	0.71	1.02	0.50-2.09	0.02	*Gender, age, African, and Native American ancestry, income, education, and occupation*
Ancestry, SES, and BMI adjusted	1.55	0.52-4.61	0.55	1.11	0.55-2.21	0.11	*Gender, age, African, and Native American ancestry, income, education, occupation, and BMI*

% mediated by SES[2]	64%	100%	*Indirect effect through SES/Total effect of race/ethnicity * 100*

[1] Corresponds to the Black arrows in Figure 1
[2] % mediated (indirect effect over the total effect) is calculated as:
$((ERR_{Base\ model}) - (ERR_{SES\ adjusted\ model})) / (ERR_{Base\ model})$
RR=Relative Risk
ERR=Excess Relative Risk (RR-1)

Table 5-3. Risk Ratios for Diabetes Incidence by Biogeographical Ancestry (Longitudinal)[1]

	100% West African vs. 100% European			100% Native American vs. 100% European			Adjusted for
	RR	CI	ERR	RR	CI	ERR	
Base model	2.56	1.33-4.95	1.56	1.01	0.21-4.90	0.01	*Gender and age*
Race/ethnicity adjusted	0.86	0.19-3.94	-0.14	0.42	0.07-2.66	-0.58	*Gender, age, and self-identified race/ethnicity*
SES adjusted	1.52	0.77-3.01	0.52	0.43	0.08-2.31	-0.57	*Gender, age, income, education, and occupation*
Race/ethnicity and SES adjusted	0.82	0.18-3.76	-0.18	0.46	0.07-2.96	-0.54	*Gender, age, self-identified race/ethnicity, income, education, and occupation*
Race/ethnicity, SES, and BMI adjusted	0.83	0.18-3.90	-0.17	0.40	0.06-2.59	-0.60	*Gender, age, self-identified race/ethnicity, income, education, occupation, and BMI*
% mediated by SES[2]	67%			N/A[4]			*Indirect effect through SES/Total effect of race/ethnicity * 100*
% mediated by Race/ethnicity and SES[3]	100%			N/A[4]			*Indirect effect through Race/ethnicity and SES/Total effect of race/ethnicity * 100*

[1] Corresponds to the Black arrows in Figure 1
[2] % mediated (indirect effect over the total effect) is calculated as:
$((ERR_{Base\ model}) - (ERR_{Race/ethnicity\ and\ SES\ adjusted\ model})) / (ERR_{Base\ model})$
[4] The base model indicated no total effect, % mediated was not calculated
RR=Relative Risk
ERR=Excess Relative Risk (RR-1)

The findings from the G-computation (**Table 5-4,** unweighted data) largely agree with the findings from the standard regression techniques. The g-computation estimated the proportion mediated by SES to be lower, indicating that 45% of the Black vs. White effect, and 55% of the Hispanic vs. White effect was mediated by SES. Both the traditional regression techniques and the g-computation indicated that African ancestry was 82% mediated by race/ethnicity and SES and that there was no direct effect of Native American Ancestry on T2DM.

Table 5-4. The Total, Direct, and Indirect Effects of Race/Ethnicity and Biogeographical Ancestry on T2DM, Estimated Using Standard Regression Models and G-computation Using Unweighted Data

	Excess Relative Risk Method[1]				Risk difference Method[1]				G-computation[1,2]			
	Black		Hispanic		Black		Hispanic		Black		Hispanic	
		CI		CI		CI		CI		CI		CI
Total effect	0.90	0.39, 1.59	1.19	0.61, 1.98	0.05	0.03, 0.07	0.07	0.05, 0.09	0.01	-0.002, 0.03	0.03	0.01, 0.04
Direct effect	0.42	0.01, 1.00	0.40	-0.02, 1.01	0.03	-0.009, 0.07	0.03	-0.009, 0.07	0.008	-0.008, 0.02	0.01	-0.005, 0.03
Indirect/ Total effect[3]	**53.3%**		**66.4%**		**60.0%**		**42.9%**		**44.7%**		**54.9%**	
	African Ancestry		**Native American Ancestry**		**African Ancestry**		**Native American Ancestry**		**African Ancestry**		**Native American Ancestry**	
		CI		CI		CI		CI		CI		CI
Total effect	0.84	0.29, 1.64	1.12	0.04-3.32	0.06	0.02, 0.10	0.10	-0.02, 0.22	0.05	0.02, 0.07	0.008	-0.01,0.03
Direct effect	0.15	-0.49, 1.60	-0.28	-0.75, 1.09	0.01	-0.07, 0.09	-0.03	-0.11, 0.05	0.009	-0.02, 0.04	-0.0006	-0.02, 0.02
Indirect/ Total effect[4]	**82.1%**		**100.0%**		**83.3%**		**100.0%**		**82.1%**		**100.0%**	

[1] All estimates are adjusted for age and gender

[2] BMI is allowed to be an intermediate confounder in the mediator – outcome relationship

[3] The indirect/total effect is the % that of the racial/ethnic effect on T2DM that is mediated by SES

[4] The indirect/total effect is the % that of the BGA effect on T2DM that is mediated by race/ethnicity and/or SES

5.2.5 Discussion

In this population-based study, we report on two key findings. First, we found that racial/ethnic disparities in T2DM were potentially mediated by SES, whereas BGA had no effect on this relationship. Second, we found that while African ancestry is significantly associated with T2DM incidence, a large proportion of this association was mediated by self-identified race/ethnicity and socioeconomic factors. These findings were consistent with the results from g-computation, which indicated that SES accounted for approximately half of the racial/ethnic disparities in T2DM incidence and nearly all of the BGA differences.

Our estimates of the magnitude of racial/ethnic disparities in T2DM risk are in line with national trends [2]. In the BACH sample, the approximate 7-year incidence of T2DM was twice as high among Black versus White participants, and 60% higher among Hispanic versus White participants. In our unadjusted estimates of the effect of BGA we found that having 100% African ancestry versus 100% European ancestry conferred a 1.5 fold risk of T2DM. Due to the conflicting findings regarding BGA to date, the finding that socioeconomic status explains a large proportion of this association agrees with some studies[36, 37, 79] but is in contrast with others.[37, 80, 81]

Race/ethnicity is a complex multidimensional construct reflecting biological factors, geographical origins, as well as social, cultural, and economic factors.[69] These analyses indicate that while genetic factors, including bio-geographic ancestry, may play a role in T2DM, it is likely that the social, cultural, and economic facets of race/ethnicity better explain T2DM disparities in the US. Specifically, the lower average SES of Blacks and Hispanics in the US, compared with that of Whites, provides a plausible explanation for a large proportion of the excess risk of T2DM.

Strengths and limitations

A potential limitation of this study is the reliance on self-report for incident diabetes outcomes. However, our sensitivity analyses (available as an Appendix), which use objective measures of diabetes status, largely agree with the data presented here. In addition, research has shown that self-report of major medical conditions correlate well with medical record review [501] and over 80% of self-report incident cases were confirmed by medication inventory. Another limitation to this analysis is the lack of detailed information on changes in risk factors over time. While BGA and race/ethnicity are constant, the effects of socioeconomic and lifestyle/behavioral factors may be fine-tuned in a proportional hazards regression model. However, our study does provide evidence for a temporal effect between SES and diabetes incidence whereas many studies of BGA have been limited to cross-sectional [36, 80, 81] or limited measures of SES [36, 37, 81]. Finally, although the sample is geographically limited to Boston, Massachusetts, the BACH Survey sample has been compared to other large regional (Behavioral Risk Factor Surveillance System) and national (the National Health and Nutrition Examination Survey) on a number of socio-demographic and health-related variables.[437] The results suggest that the BACH Survey estimates of key health conditions are comparable with national trends.

The key strengths of this study stem from the community-based random sample design of the BACH Survey. To our knowledge, this is the first study to report the effects of BGA in a large cohort of Black, Hispanic, and White men and women. Most of the literature on the effects of BGA on T2DM have been restricted to one racial or ethnic group, such as African Americans [80] or Hispanics [36, 81] with the exception of the WHI.[37] Limiting the sample to one racial/ethnic group may restrict on the cultural, social, and economic factors that most directly appear to influence T2DM.

Another key strength of this study is the analytic strategy which was grounded in a causal modeling framework. The sensitivity analyses using the G-computation formula allow us to

estimate the total causal effect as well as natural direct/indirect effects and allowed flexibility to the modeling assumptions [513].

Conclusions

Racial/ethnic disparities in T2DM are well documented. However, it is likely that a proportion of the excess risk in T2DM attributed to race/ethnicity is explained by differences in social and economic circumstances. These results have profound implications for informing appropriate prevention strategies. It is likely that non-genetic factors, namely socioeconomic factors, lead to the observed racial/ethnic disparities in T2DM incidence, and the continued focus on genetic causes of disparities in T2DM is likely misplaced. Appropriate prevention strategies need to address the root causes for these disparities, which appear to be largely socioeconomic in nature.

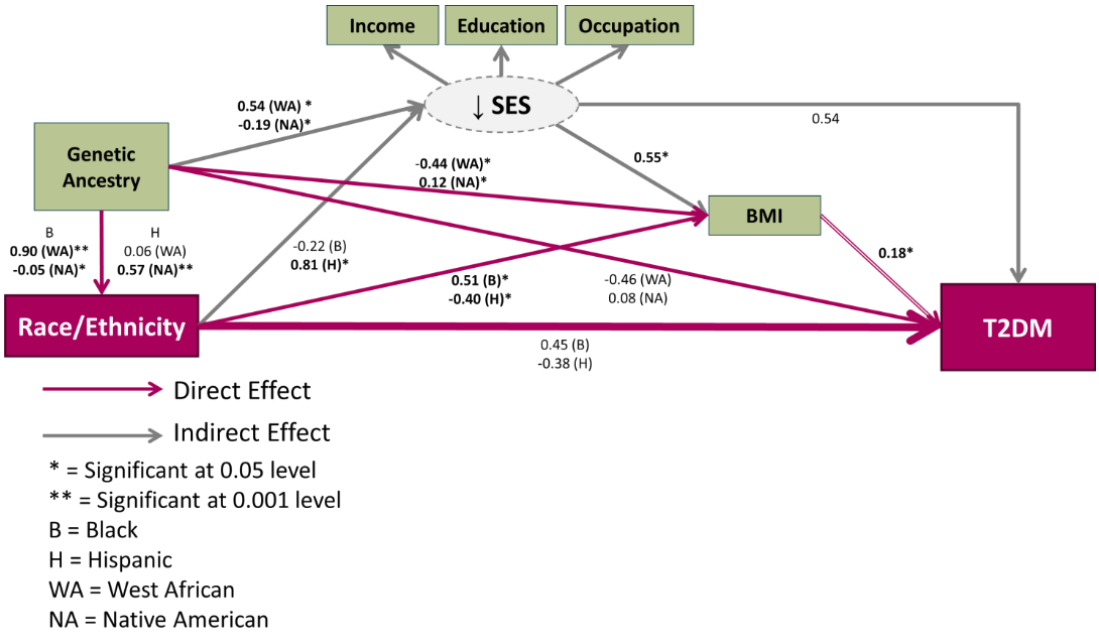
5.3 Supplementary Structural Equation Modelling

In order to estimate the full pictures of the relationships between BGA, race/ethnicity, SES, BMI, and T2DM as depicted in **Figure 5-1**, we used structural equation modelling (SEM). SEM (also referred to as path analysis) provides several distinct advantages over traditional regression techniques. First, BMI could be treated as a secondary mediator of interest and allowed to contribute to the direct or indirect paths. Second, SES is a complex construct that is imperfectly measured by income, education, and occupation. In the path analysis, SES can modelled as a latent (indirectly observed) variable. SEMs were estimated using Mplus, which fits path and latent variable models using linear and logistic regression to complex survey data using maximum likelihood. Overall model fit was assessed using the root mean square error of approximation (RMSEA), which is based on comparisons between observed correlations to those implied by the model. By convention, models are said to fit the data well if the RMSEA is 0.08 or less.[515] Standardized coefficients are reported (β) and are interpreted as a 1 standard deviation

difference in the predictor is associated with a "β" standard deviation difference in the outcome. Due to space limitations the following analyses were not included in the submitted paper.

The full structural model for BGA, race/ethnicity, SES, BMI and T2DM is presented in **Figure 5-3**.

Figure 5-3. Results from the supplementary structural equation modelling



The data fitted the *a priori* model well (RMSEA = 0.072). As expected, there were strong, highly significant relationships between BGA and an individual's self-reported race/ethnicity (β=0.90, $P < 0.001$ for African ancestry predicting Black race and β=0.57, $P < 0.001$ for Native American ancestry predicting Hispanic race). When BGA was accounted for, Black race was not associated with low SES (β=-0.22, *P*=0.18) while Hispanic ethnicity was (β=0.81, P=0.009). Low SES (β=0.55, *P*=0.02), Native American ancestry (β=0.12, *P*=0.05) and Black race (β=0.51, *P*=0.001) were all associated with increased BMI and BMI had the only positive, significant association with incident T2DM (β=0.18, *P*=0.02). Although low SES did not have a significant direct effect on T2DM (β=0.54, *P*=0.08), it had a larger effect on BMI (β=0.55) and on T2DM (β=0.54), than any other measured construct.

The SEM reinforces our findings from the submitted paper. Both the traditional regression techniques as well as the g-computation demonstrated that racial/ethnic disparities in T2DM were largely mediated through SES, whereas BGA had little effect on this relationship. However, the SEM clarifies this relationship by demonstrating that SES appears to influence T2DM largely through BMI. This finding demonstrates the complexity of the relationships between genetic, socioeconomic, and lifestyle/behavioural characteristics and T2DM. **Chapter 7** further examines these complex relationships.

5.4 Supplementary Cross-Sectional Analysis Examining the Contribution of Biogeographic Ancestry and Socioeconomic Status to Racial/Ethnic Disparities in Type 2 Diabetes

Peer reviewers of this paper noted that the analyses did not utilize additional data collected at BACH III, including fasting glucose measures which can be used to capture likely undiagnosed diabetes. Undiagnosed diabetes prevalence differs by race/ethnicity[3] meaning that analyses of diagnosed illness *only* may underestimate the true inequality in T2DM by race/ethnicity. To address these concerns, I also conducted confirmatory cross-sectional analyses of prevalent T2DM including undiagnosed T2DM and included them in a supplement which is in the online version of the published paper (http://dx.doi.org/10.1016/j.annepidem.2014.06.098) as well as below.

The prevalence of diabetes was 21.8% (980 prevalent cases). In age and gender adjusted models, Black participants were 2.1 times as likely to have diagnosed or undiagnosed diabetes (RR=2.1; 95% CI: 1.6-2.6) and Hispanics were 1.6 times as likely to have T2DM (RR=1.6; 1.2-2.1) than White participants (**Table 5-5**). Similar to the longitudinal findings, we found that income, education, and occupation accounted for much of the racial/ethnic disparity in prevalent T2DM. After adjustment for these socioeconomic factors the risk ratio for Black versus White participants was reduced to 1.6, but still remained statistically significant (95% CI: 1.2-2.0). The risk ratio for Hispanic versus White participants was reduced to non-statistical significance (95% CI: 0.7-1.3, **Table 5-5**).

However, in contrast to the longitudinal findings, we found some indication that biogeographic ancestry contributed to the Black/White disparities in T2DM prevalence. When BGA was added to the age, gender, and SES adjusted models, there was a further reduction in the risk ratio for Black vs. White participants (RR=1.5, 95% CI: 0.9-2.5) and the effect estimate was no longer

significant. This could be attributed to the high degree of correlation between biogeographic ancestry and self-identified race/ethnicity. However, results from the SEM suggest that this finding is not a statistical artefact.

Table 5-5. Risk Ratios for Diabetes Prevalence[1] by Self-Identified Race/Ethnicity (BACH III Confirmatory Cross-Sectional Analysis)[2]

	Black vs. White		Hispanic vs. White		Adjusted for
	RR	CI	RR	CI	
Base model	2.05	1.59-2.63	1.57	1.18-2.11	*Gender and age*
Ancestry adjusted	1.91	1.18-3.09	1.60	1.09-2.36	*Gender, age, African, and Native American ancestry*
SES adjusted	1.57	1.22-2.02	0.98	0.72-1.34	*Gender, age, income, education, and occupation*
Ancestry and SES adjusted	1.49	0.89-2.50	1.02	0.67-1.56	*Gender, age, African, and Native American ancestry, income, education, and occupation*
Ancestry, SES, and BMI adjusted	1.43	0.85-2.38	1.02	0.67-1.54	*Gender, age, African, and Native American ancestry, income, education, occupation, and BMI*
% Mediated by SES[3]	45.7%		100%		*Indirect effect/Total effect*

[1] Diabetes prevalence defined as fasting plasma glucose ≥ 126 mg/dL, HbA1c ≥ 6.5% or self-report of a diabetes diagnosis

[2] Corresponds to the Black arrows in Figure 1

[3] The excess relative risk which is the indirect effect over the total effect is calculated as: 100 * ((Base model -1) – (SES adjusted model - 1)) / (Base model - 1)

Table 5-6. Risk Ratios for Diabetes Prevalence[1] by Biogeographical Ancestry (BACH III Confirmatory Cross-Sectional Analysis)[2]

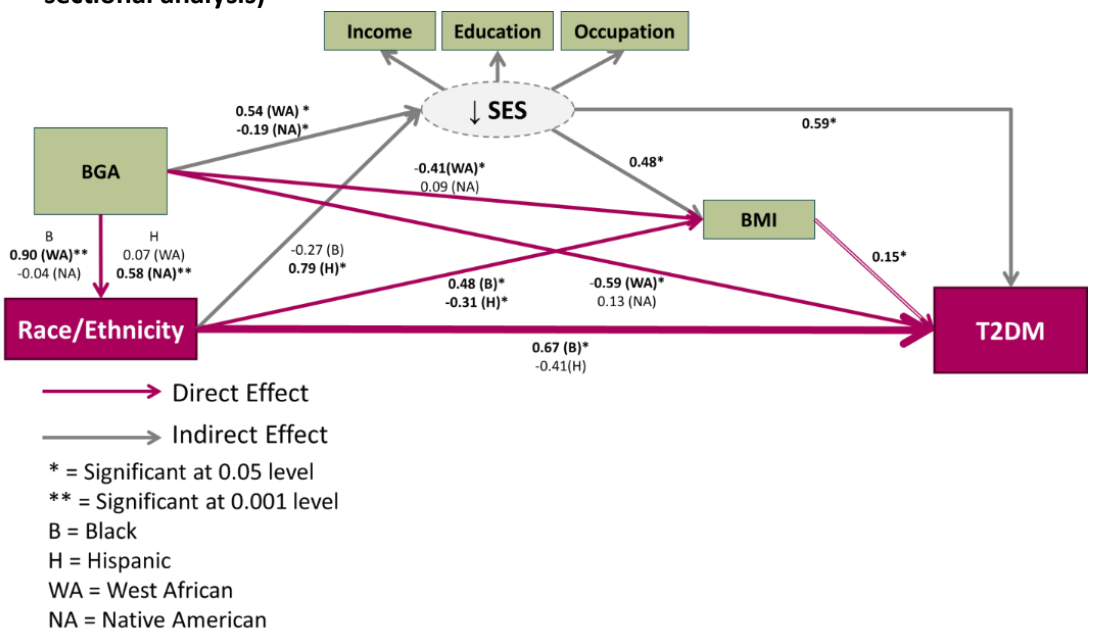
	West African		Native American		Adjusted for
	RR	CI	RR	CI	
Base model	2.35	1.72-3.21	1.41	0.65-3.05	*Gender and age*
Race/ethnicity adjusted	1.13	0.58-2.21	0.80	0.27-2.36	*Gender, age, and self-identified race/ethnicity*
SES adjusted	1.74	1.26-2.39	0.73	0.29-1.85	*Gender, age, income, education, and occupation*
Race/ethnicity and SES adjusted	1.10	0.55-2.20	0.76	0.26-2.24	*Gender, age, self-identified race/ethnicity, income, education, and occupation*
Race/ethnicity, SES, and BMI adjusted	1.11	0.56-2.21	0.79	0.28-2.22	*Gender, age, self-identified race/ethnicity, income, education, occupation, and BMI*
% Mediated by Self-Identified Race/ethnicity and SES[3]	92.5%		100%		*Indirect effect/Total effect*

[1] Diabetes prevalence defined as fasting plasma glucose ≥ 126 mg/dL, HbA1c ≥ 6.5% or self-report of a diabetes diagnosis

[2] Corresponds to the gray arrows in Figure 1

[3] The excess relative risk which is the indirect effect over the total effect is calculated as: 100 * ((Base model -1) – (Race/ethnicity and SES adjusted model - 1)) / (Base model - 1)

Figure 5-4. Results from the Structural Equation Modelling (BACH III confirmatory cross-sectional analysis)



The SEM for the cross-sectional analyses of BGA, race/ethnicity, SES, and BMI on T2DM is presented in **Figure 5-4**. Similar to the longitudinal analyses, when BGA was accounted for, Black race was not associated with low SES (β=-0.27) while Hispanic ethnicity was (β=0.79). Low SES (β=0.59), West African ancestry (β=-0.41) and Black race (β=0.48) were all associated with increased BMI. However, an important difference between the longitudinal results and the cross-sectional results is that lower SES (β=0.59), higher BMI (β=0.15), lower West African ancestry (β=-0.59), and self-identified Black race (β=0.67) were all associated a higher prevalence of T2DM.

These findings could be due to an increase in statistical power due to the greater number of events when examining prevalent versus incident cases. Future studies should consider examining incident T2DM in a larger population and over a longer period of time to fully explore these findings.

It is important to note that research from the BACH III Survey also demonstrated that West African ancestry is associated with higher fasting glucose and HbA1c among non-diabetic individuals.[82] These results did not change with adjustment for socioeconomic indicators (the same socioeconomic indicators captured here). These results indicate that West African ancestry may play a role in a biophysiologic pathway toward T2DM. These implications will be examined in further detail in **Chapter 7.**

6 The role of Neighborhood Characteristics in Racial/Ethnic Disparities in Type 2 Diabetes: Results from the Boston Area Community Health (BACH) Survey

6.1 Introduction

This paper examines the contribution of neighbourhood factors to racial/ethnic disparities in T2DM. The residential addresses of BACH III participants were geocoded and merged with contextual information gathered from InfoUSA (geocoded addresses of supermarkets, grocery stores, fast food outlets, and convenience stores), the Boston Police Department (X and Y coordinates of violent and property crime), and the US Census Bureau (e.g. poverty, racial composition measured at the census tract level). The goal was to not only quantify the contribution of neighbourhood factors to racial/ethnic disparities in T2DM, but to also identify *which* factors contributed the most. Geospatial analyses as well as multilevel modelling techniques were used to address these objectives.

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London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
www.lshtm.ac.uk

Registry
T: +44(0)20 7299 4646
F: +44(0)20 7299 4656
E: registry@lshtm.ac.uk

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Student	Rebecca Piccolo
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6.2 Article Submitted

6.2.1 Abstract

Racial/ethnic disparities in the prevalence of type 2 diabetes mellitus (T2DM) are well documented and until recently, research focused almost exclusively on individual-based determinants as potential contributors to these disparities (health behaviours, biological/genetic factors, and individual-level socio-demographics). Research on the role of neighbourhood characteristics in relation to racial/ethnic disparities in T2DM is very limited. Therefore, the aim of this research is to identify and estimate the contribution of specific aspects of neighbourhoods that may be associated with racial/ethnic disparities in T2DM.

Data from the Boston Area Community Health III Survey (N=2,764) was used in this study, which is a community-based random-sample survey of adults in Boston, Massachusetts from three racial/ethnic groups (Black, Hispanic, and White). We applied two-level random intercepts logistic regression to assess the associations between race/ethnicity, neighbourhood characteristics (census tract socioeconomic status, racial composition, property and violent crime, open space, geographic proximity to grocery stores, convenience stores, and fast food, and neighbourhood disorder) and prevalent T2DM (fasting glucose > 125 mg/dL, HbA1c ≥ 6.5%, or self-report of a T2DM diagnosis).

Black and Hispanic participants had 2.89 times and 1.48 times the odds of T2DM as White participants, respectively. Multilevel models indicated a significant between-neighbourhood variance estimate of 0.943, providing evidence of neighbourhood variation. Individual demographics (race/ethnicity, age and gender) explained 22.3% of the neighbourhood variability in T2DM. The addition of neighbourhood-level variables to the model had very little effect on the magnitude of the racial/ethnic disparities and on the between-neighbourhood variability.

For example, census tract poverty explained less than 1% and 6% of the excess odds of T2DM among Blacks and Hispanics and only 1.8% of the neighbourhood variance in T2DM.

While the findings of this study overall suggest that neighbourhood factors are not a major contributor to racial/ethnic disparities in T2DM, further research is needed including data from other geographic locations.

6.2.2 Background

Racial/ethnic disparities in the prevalence and incidence of type 2 diabetes mellitus (T2DM) are an important public health problem in the United States (US) and worldwide. Disparities are defined here as differences in the incidence, prevalence, mortality, and burden of diseases and other adverse health conditions that exist among specific population groups such as racial/ethnic minorities. To illustrate, compared to White adults, the prevalence of diabetes is 77% higher among Black and 66% higher among Hispanic adults in the US.[2, 433] Racial/ethnic disparities in diabetes are associated with poorer diabetes control,[6, 7] greater diabetes-related complications,[8, 9, 16] higher rates of hospitalization,[505] and increased health care costs.[494] Extensive research has been conducted on individual-level explanations for these disparities including: variations in lifestyles and behaviours, biological and genetic factors, family history and individual-level socio-demographic characteristics. However, this prevailing paradigm, which puts emphasis on the individual, fails to consider contextual factors (such as residential neighbourhoods) which may in part explain existing disparities in T2DM.

The notion that where we live can influence our health is not new. The influence of neighbourhood context on health has been the focus of an extensive body of research over the past decade. The worldwide increase in T2DM is largely attributed to increases in obesity (BMI ≥ 30 kg/m^2), poor diet, and physical inactivity.[21, 118, 119] There is an abundance of research linking neighbourhood resources and precursors to/risk factors for T2DM (i.e. dietary patterns,[218-220]

physical activity,[219, 221] and body mass index/obesity[219, 220, 222, 516-518]). However, to our knowledge, studies linking neighbourhood characteristics directly with T2DM are limited.[31, 223-225] Furthermore, few studies focused on the local contextual environment as a fundamental contributor to racial/ethnic disparities in health—including T2DM. The emerging socio-ecological framework attempts to identify both individual and contextual characteristics that may amplify, or moderate, racial/ethnic disparities in health. Neighbourhoods are a context in which disparities may be fostered as they possess both social and physical attributes which can affect the health of individuals.

Neighbourhood Deprivation and Socioeconomic Status

It has previously been suggested that most of the racial/ethnic variation in T2DM is explained by social and economic factors at the neighbourhood-level.[260] Neighbourhood socioeconomic status (SES) appears to be an important contributor to obesity,[234, 261, 262] cardiovascular disease risk factors ,[263-267] metabolic syndrome among women,[264] as well as T2DM prevalence[35] and incidence.[31, 223] The neighbourhood socioeconomic environment can influence the availability of grocery stores, recreational facilities, and educational resources which may influence diet, physical activity and subsequent T2DM. In addition, economically deprived neighbourhoods may increase exposure to chronic stress (i.e. noise, violence, and poverty) which is a known risk factor for negative health outcomes including T2DM.[268, 269] These results suggest that neighbourhood-level SES may modify the relationship between individual-level SES and negative health outcomes. This underscores the potential importance of accounting for indicators of neighbourhood deprivation in studies examining health disparities. [270, 271]

Racial Composition

Contextual research on the local environment often fails to account for the fact that the US is largely racially segregated. Racial segregation, which refers to the physical separation of racial subgroups in space, is a by-product of institutional discrimination and often affects the social,

economic and health-related well-being of the segregated minority group.[275, 276] Racial and socioeconomic segregation are also considered to be a fundamental cause of racial/ethnic disparities in health outcomes.[257, 280] Racial segregation often perpetuates disparities in educational and employment opportunities, results in concentrated poverty, and shapes the social and physical contextual environment.[280] These patterns of segregation are posited to influence obesity[519] and T2DM by shaping disparities in neighbourhood environments. A few studies have examined the association between racial segregation and neighbourhood amenities. While some studies have indicated that high levels of residential segregation are associated with obesogenic characteristics (less access to healthy food options,[231, 282, 283] greater access to unhealthy food,[284] and less open spaces for recreational activities[285, 286]) other studies have found that spatial inequalities in racial/ethnic composition and socioeconomic disadvantage do not always result in disparate access to physical resources.[258, 287]

Built Environment

The term 'built environment' refers to the man-made surroundings of a neighbourhood (e.g. density of fast food restaurants, distance to nearest park, and sidewalk completeness) that may or may not provide the setting for healthy behaviours, including healthy eating and physical activity. The domains and measures of the built environment used in scientific research vary considerably, in part, because of the large number of features that could potentially influence health behaviour.[229] Some aspects of the built environment, such as access to grocery stores, convenience stores, and restaurants, are the focus of research because they are potentially modifiable.[230] Access to supermarkets and grocery stores are positively associated with healthy food behaviours such as increased fruit and vegetable intake, more healthful diets, and lower BMI in a number of studies.[33, 34, 231-234] On the other hand, a high density of fast food restaurants has been associated with detrimental effects on BMI.[233-237] Differential rates of local area food store type availability by neighbourhood characteristics (i.e. neighbourhood deprivation, racial

composition) may contribute to the differential prevalence of obesity, and subsequent T2DM, by race/ethnicity.[238, 239]

The distribution of parks and other "green spaces" e (i.e. walking/biking trails) are increasingly viewed as a target for policymakers and urban planners for promoting healthier, more active lifestyles in disadvantaged communities Proximity to parks has been linked to and increased frequency of and the intensity of physical activity,[240, 241] lower BMI,[242, 243] and lower risk of T2DM[244]. These health benefits are manifested even among people living in deprived neighbourhoods.[245] These findings indicate that increased access to parks and green space may potentially reduce obesity and T2DM disparities.

Crime/Safety and Neighbourhood Disorder

Racial/ethnic minorities, specifically African Americans and Hispanics, are more likely to live in neighbourhoods with higher levels of social, physical and economic disorder, which include features such as crime, graffiti, lack of trust among neighbours, abandoned buildings, and concentrated poverty that contribute to social instability.[295, 296] Residents of neighbourhoods with high crime rates are less likely to walk and be physically active, particularly women and young children.[259, 297-299] This physical inactivity likely contributes to greater risk for obesity and T2DM. There is also evidence that residents' beliefs, or perceptions, about the safety of their neighbourhood may influence their behaviour thus influencing (or mediating) BMI and T2DM risk.[300] There are several studies that demonstrate evidence for this mediating effect. In two studies, perceived neighbourhood disorder mediated the associations between neighbourhood disadvantage and self-rated health, physical function, adolescent obesity and several chronic conditions.[301, 302] Reports of physical disorder (abandoned buildings, vacant lots, graffiti, etc.) have been shown to partly mediate the association between racial isolation and BMI, while incident crime was not associated with BMI.[303]

In summary, the influence of neighbourhood context on diet, physical activity and obesity has been the subject of considerable research over the past decade. However, few studies have examined the role of neighbourhood characteristics as a fundamental contributor to racial/ethnic disparities in T2DM. Further, very little research has examined which specific aspects of neighbourhoods influence these facets of health, including T2DM.

Research Objective

Our research aims to fill two key gaps in the literature. **First,** we aim to quantify the contribution of neighbourhood versus individual factors to racial/ethnic disparities in T2DM. In particular, we aim to assess whether neighbourhood characteristics will explain a substantive proportion of the disparities in T2DM beyond the contribution of individual-level factors/mediators (i.e. individual-level socioeconomic status, diet, exercise, BMI). **Second,** we aim to identify specific aspects of neighbourhoods that are associated with disparities in T2DM and measure their relative contributions to disparities. Specifically, we propose to examine the roles of five important contextual factors as potential mediators of racial/ethnic disparities: (1) neighbourhood socioeconomic status, (2) racial composition, (3) built environment, (4) safety, and (5) neighbourhood disorder.

6.2.3 Methods

The Boston Community Health (BACH) Survey

The Boston Area Community Health Survey (BACH) is a longitudinal, community-based random sample survey of 5,502 residents (2,301 men, 3,201 women) aged 30-79 years from three racial/ethnic groups (Black, Hispanic, and White) in Boston, MA.[508] BACH was initiated in 2002 and was conducted in participants' homes approximately every 5 years, with a total of three surveys to date. The current analysis uses cross-sectional data from the third round conducted between 2010 and 2012. A total of 3,155 men and women participated in BACH III. Only participants who had a geocodable address (99.9%) and who resided in Boston proper at the

third round were included in the analysis, leaving 2,764 subjects. Participants who moved out of Boston proper were more likely to be White (vs. Black), younger (< 45), and of higher income (≥ $50,000 vs. < $20,000). In all surveys, data were collected during a two-hour interview in English or Spanish, after written informed consent. The study was approved by New England Research Institutes' Institutional Review Board.

Address geocoding

BACH III participants provided their house number, street name and nearest cross-street in addition to other geographic information (e.g. zip code). All addresses were pre-processed before geocoding to improve their quality. For example, addresses were cross-checked against previous reported addresses for misspelled street names. The ArcGIS 10.1 (ESRI, Redlands, CA) North America Geocode Service (ArcGIS Online) address locator was used to geocode participants' addresses to the building level. Positional error for ArcGIS in comparison to aerial photography is on average 40 meters[520] and addresses with a match rate ≥80 have been found to be positionally accurate in a previous study.[521] All failures (match rate <80) were cross-checked with Google Maps to assist in remedying incorrect addresses. Geocoded residences were then used to link participants with 2010 US census tract-level data. BACH III participants were located within 155 of the 179 census tracts within Boston. We used census tracts as the primary measure of the contextual unit following conventions established in previous studies of neighbourhoods and health,[522] including in Boston.[258, 285] Census tracts generally contain 2500-8000 people and when first delineated, were designed to be homogeneous with respect to population characteristics, economic status, and living conditions.[294] Neighbourhood socioeconomic status, neighbourhood racial composition, neighbourhood recreational open space and neighbourhood crime were measured at the census tract level.

Neighbourhood measures

Neighbourhood Socioeconomic Status (SES). Neighbourhood SES was based on methods used by Diez-Roux.[431] A composite index Z-score was created for census tract based on six measures including: log median household income; log median value of owner occupied housing; percent of households receiving interest, dividend or net rental income; percent of adults 25 and over with a high school degree; percent of adults 25 and over with a college degree; and percent of individuals ages 16 and over in management and professional occupations. An increasing score signifies increasing neighbourhood socioeconomic advantage. Census tracts were designated as low, middle, or high SES according to the tertiles of the Z-score.[263] Census tract poverty was categorized using standard categories: less than 5% poverty, 5-9.9% poverty, 10-19.9% poverty, and 20% or greater poverty.[523]

Neighbourhood racial composition. The percentages of non-Hispanic Black, non-Hispanic White, and Hispanic residents in a census tract were used to measure racial composition (surrogates for residential segregation) and have been used in previous research.[285, 295]

Recreational open space. The percentage of recreational open space per census tract was estimated from shapefiles obtained from the Massachusetts Office of Geographic Information (MassGIS).[524] This data layer of outdoor recreational facilities includes parks, playing fields, school fields, and playgrounds, whether privately or publicly owned.

Crime. Crime incident reports provided by the Boston Police Department were downloaded from the City of Boston website at https://data.cityofboston.gov/. Data were coded using conventions described by others.[525] The property crime rates in 2010-2011 were calculated as the number of offenses of burglary, larceny, and motor vehicle theft per 1,000 population. Violent crime was calculated as murder, robbery, and assault (including sexual assault) per 1,000 population.

Food environment. Data on food establishments located in the Boston metro area were purchased from InfoUSA Inc., a proprietary information service. Food environment was

operationalized as the distance to the closest grocery store, convenience store, and fast food restaurant from each participant's residence.[526, 527]

Neighbourhood disorder. Social and physical neighbourhood order and disorder were measured using the "Perceived Neighbourhood Disorder" scale developed by Ross and Mirowsky.[528] Social disorder refers to people hanging around on the streets, drug and alcohol use, trouble with neighbours, and a general perception of lack of safety. Physical disorder refers to graffiti, vandalism, abandoned buildings, cleanliness, and maintenance of homes and apartments. The physical and social disorder indices were created by reverse coding "order" items and summing the six items in each subscale with higher scores indicating greater perceived disorder.[182, 430]

Individual Factors

Race/ethnicity. Race/ethnicity was self-reported by survey participants according to two separate survey questions: "Do you consider yourself to be Spanish, Hispanic, or Latino (Latina)?" and "What do you consider yourself to be? Select one or more of the following" with response categories of American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White or Caucasian, and Other (Specify). These questions are the standard used in the US as recommended by the Office of Management and Budget.[423] Consistent with our previous work,[437] the racial/ethnic categories used in this research are 1) non-Hispanic Black (Black), 2) Hispanic of any race (Hispanic), and 3) non-Hispanic White (White).

Socioeconomic Status (SES). The individual SES indicators considered were: self-reported household income, educational attainment and occupation. Household income was collapsed into three categories of US dollars: <20,000, 20-49,999, and ≥50,000. Education was categorized as less than high school, high school graduate or equivalent, some college, and college or advanced degree were combined due to smaller numbers. Current or former occupation was

categorized into four groups: (1) management, professional, sales and office occupations; (2) service occupations; (3) manual labour which includes construction, maintenance, farming, production, and transportation occupations; and (4) never worked. We use the broader term 'SES' when referring to these three distinct socioeconomic factors in the aggregate, all of which have strongly been related to overall health.[529]

Lifestyle/Behavioural Factors. BMI was measured by trained field interviewers during an in-home visit. Physical activity was categorized as low, moderate, or high using the Physical Activity Scale for the Elderly (PASE).[530-532] Participants completed the Block 2005 food frequency questionnaire to assess dietary patterns.[533, 534] Diet was operationalized as indicator variables representing intake of vegetables, fruit, meat and grain servings per the USDA MyPyramid.[535]

Type 2 Diabetes (T2DM)

Trained field interviewers (phlebotomists) collected fasting blood samples in BACH III using a HemoCue 201 point-of-care analyser. Self-reported diabetes status was identified by affirmative answers to the question, "Have you ever been told by a health care provider that you now have or previously had non-insulin dependent or adult-onset diabetes Type II?" The primary outcome for this study was operationalized as fasting glucose > 125 mg/dL, HbA1c ≥ 6.5% or self-report of a diabetes diagnosis.[21]

Statistical Methods

Descriptive statistics of the study population were calculated in SUDAAN 11 (Research Triangle Park, North Carolina). ArcGIS 10.1 (ESRI, Redlands, CA) was used to geocode participants' addresses, measure distances, link individual to contextual data, and visually inspect the data for potential spatial patterns. We assessed the presence of overall spatial dependence in diabetes

with the Global Moran's *I* statistic, a common test statistic for spatial autocorrelation, using the k nearest neighbour (KNN) method.

We applied two-level random intercepts logistic regression to assess the associations between individual-level race/ethnicity, neighbourhood characteristics and T2DM. Multilevel regression methods accommodate clustering of participant observations within their census tract of residence. Multilevel models were constructed in steps of increasing complexity. First, an intercept-only model was constructed to quantify the between neighbourhood variance (σ^2_B) of the outcome and to test for significant variation in T2DM by neighbourhood. A pseudo intra-class correlation coefficient (ICC) was computed using the latent variable approach to approximate the ICC for a binary outcome, where the within-neighbourhood variance for a standard logistic regression is $\pi^2/3$. The ICC roughly quantifies the amount of variability in T2DM attributable to the neighbourhood level relative to the sum of within ($\sigma^2_W = \pi^2/3$) and between neighbourhood variances (σ^2_{BW}) (i.e. total variability) (ICC = $[\sigma^2_B/(\pi^2/3 + \sigma^2_B)]$)[536].

Next, multilevel random intercepts models were constructed, with individual-level predictors modelled as fixed effects, to examine the influence of neighbourhood characteristics on racial/ethnic disparities in T2DM. We first included exogenous demographic variables (race/ethnicity, gender, and age), and then individual-level socioeconomic factors, both are hypothesized to influence neighbourhood of residence and therefore neighbourhood exposures. Next, lifestyle factors, hypothesized to be influenced by neighbourhood exposures and to be potential mediators, were added to the model. Finally, individual- and neighbourhood-level contextual factors were added to the demographic and socioeconomic adjusted random intercepts models. At each step two metrics were evaluated. First, the magnitude of the racial/ethnic disparities (ORs) were evaluated to determine the contribution of the individual- and neighbourhood- factors to racial/ethnic disparities in the prevalence of T2DM. Comparing these ORs allows us to evaluate whether individual- and/or neighbourhood- level factors

mediate or "explain" a proportion of the *racial/ethnic disparities* in T2DM.[537, 538] Second, the *proportion of neighbourhood variability* in T2DM that was explained by the model was calculated to determine whether neighbourhood variation persisted after accounting for these factors. Next, a parsimonious multilevel model was constructed by first including all variables marginally associated ($p < 0.20$) with T2DM in bivariate analyses. The model was then purposefully reduced to all individual- and neighbourhood-level factors either: 1) proving to have a confounding or mediating effect on the main determinant (race/ethnicity) outcome (T2DM) relationship (> 10%); or 2) were marginally significant in bivariates with the outcome (T2DM) ($p < 0.20$). All multilevel models were estimated using Mplus Version 7 (Muthen and Muthen, Los Angeles, CA). Residuals from the final regression model were tested using the Global Moran's *I* for evidence of spatial autocorrelation.

In order to minimize reductions in precision, multiple imputation was implemented using the Multivariate Imputation by Chained Equations (MICE)[510] algorithm in R.[539] Fifteen multiple imputation datasets were created. Imputations were conducted separately for each racial/ethnic by gender combination to preserve interaction effects, and the complex survey sample design was taken into account. 17% of participants were missing household income and 21% were missing dietary data. The proportion of missing data on other covariates was low with 9% having ambiguous diabetes status and less than 1% missing education, occupation, or weight. BACH's sampling design requires weighting observations inversely proportional to their probability of selection for results to be generalizable to the base population.[438, 540] Sampling weights were post-stratified in order to produce estimates representative of the Black, Hispanic, and White population of Boston, MA between the ages of 34 and 88 years (based on the 2010 US Census).

6.2.4 Results

The study population consisted of 2,764 BACH III participants (33.6% Black, 33.9% Hispanic, 32.5% White) living in 155 census tracts. The average age of participants was 55.9 years. Sample characteristics by race/ethnicity are shown in Table 6-1. Black and Hispanic participants tended to have lower incomes, less education, and live in neighbourhoods (census tracts) with lower SES and higher poverty. Black participants tended to live in high minority neighbourhoods; 54.9% lived in neighbourhoods where >75% of residents were non-White and 39.7% lived in neighbourhoods where 25-75% of residents were non-White (**Table 6-1** and **Figure 6-1**). Hispanic participants were more likely to live in mixed-race (25-75% non-White) neighbourhoods (57.2%) followed by high (>75% non-White) minority neighbourhoods (34.7%). White participants tended to live in mixed-race (25-75% non-White, 49.3%) or low minority (<25% non-White, 48.0%) neighbourhoods (p<0.001).

Table 6-1. Characteristics of the BACH III study population overall by diabetes status (N=2,764)

	Overall N=2764	Black N=929	Hispanic N=937	White N=898
Individual characteristics				
Age (continuous)[1]	55.89 (0.53)	53.99 (0.69)	50.58 (0.59)	57.80 (0.74)
Age (categorical)[2]				
34-44	406 (29.85)	138 (33.88)	171 (44.93)	97 (24.47)
45-54	741 (26.23)	286 (27.25)	262 (28.31)	193 (25.26)
55-64	813 (19.09)	261 (20.03)	281 (14.88)	271 (19.55)
65-74	536 (13.97)	165 (12.08)	161 (8.28)	210 (16.19)
75-88	272 (10.86)	81 (6.77)	63 (3.60)	128 (14.53)
Gender, % Male	1019 (44.57)	327 (40.96)	318 (45.39)	374 (46.19)
BMI (continuous)[2]	29.64 (0.23)	31.26 (0.41)	29.96 (0.31)	28.75 (0.29)
BMI (categorical)				
Normal	551 (24.33)	168 (18.76)	137 (16.99)	246 (28.75)
Overweight	934 (34.64)	295 (31.36)	338 (38.74)	301 (35.37)
Obese	1283 (41.03)	468 (49.88)	463 (44.26)	352 (35.88)
Diet				
3-4 Vegetable servings	277 (11.83)	114 (10.98)	46 (4.19)	116 (13.96)
2-3 Fruit servings	382 (17.90)	126 (12.67)	90 (12.76)	166 (21.66)
2-3 Meat servings	590 (22.41)	177 (20.59)	209 (22.87)	205 (23.22)
6-11 Grain servings	401 (18.15)	115 (12.61)	117 (16.80)	169 (21.22)

Table 6-1. Characteristics of the BACH III study population overall by diabetes status (N=2,764)

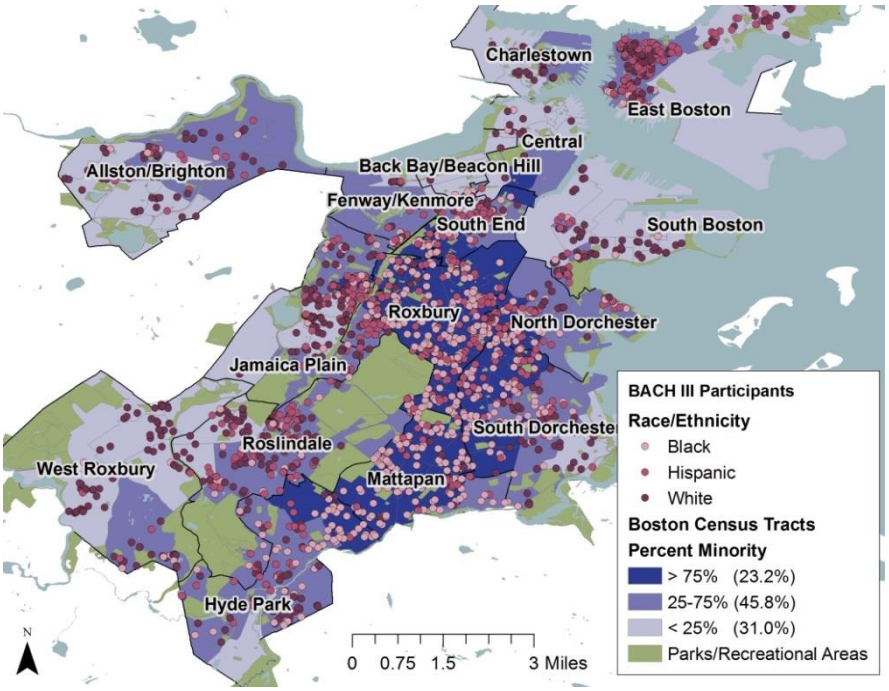
	Overall N=2764	Black N=929	Hispanic N=937	White N=898
Physical activity				
Low	1132 (34.67)	378 (33.63)	399 (33.03)	355 (35.56)
Medium	1288 (50.16)	417 (48.47)	432 (51.25)	439 (50.76)
High	348 (15.17)	136 (17.90)	107 (15.72)	105 (13.68)
Income				
<$20,000	1234 (30.50)	389 (36.26)	581 (47.34)	265 (23.86)
$20,000 - $49,999	801 (26.62)	321 (34.90)	271 (35.64)	209 (20.46)
≥ $50,000	733 (42.87)	221 (28.83)	87 (17.01)	425 (55.68)
Education				
Less than High School	560 (8.73)	146 (11.06)	363 (30.40)	51 (2.73)
High school or equivalent	867 (27.11)	348 (38.15)	318 (39.60)	201 (18.79)
Some college	579 (20.63)	258 (30.86)	151 (15.79)	170 (16.58)
College or advanced degree	762 (43.53)	179 (19.92)	106 (14.21)	477 (61.90)
Occupation				
Professional, Managerial, Sales, and Office	1328 (63.10)	473 (54.78)	227 (31.61)	628 (74.29)
Service	715 (18.85)	246 (24.46)	338 (31.95)	131 (13.12)
Manual labour	495 (13.92)	180 (17.48)	206 (21.85)	109 (10.36)
Never worked	229 (4.13)	32 (3.28)	166 (14.58)	31 (2.23)
Census Tract (CT) Characteristics				
Number of census tracts	155	111	115	126
CT SES				
Low	962 (21.57)	448 (43.31)	373 (37.83)	141 (7.05)
Middle	1192 (44.95)	393 (45.51)	415 (44.89)	384 (44.68)
High	614 (33.48)	90 (11.18)	150 (17.28)	374 (48.27)
CT Poverty				
< 5%	160 (9.57)	11 (0.79)	18 (1.61)	131 (15.76)
5-9.9%	280 (13.21)	37 (3.43)	81 (6.24)	162 (19.68)
10-19.9%	792 (35.55)	240 (31.36)	216 (28.02)	336 (39.34)
≥ 20%	1535 (41.66)	643 (64.42)	623 (64.13)	269 (25.22)
CT racial composition, continuous				
% Black	28.03 (1.14)	51.98 (1.89)	36.23 (2.04)	14.19 (0.98)
% Hispanic	16.62 (0.53)	19.71 (0.76)	25.89 (1.02)	13.38 (0.62)
% White	52.11 (1.30)	26.80 (1.69)	37.90 (1.89)	67.98 (1.36)
CT racial composition, categorical				
> 75% non-White	863 (20.75)	531 (54.93)	299 (34.72)	33 (2.70)
25-75% non-White	1439 (47.67)	357 (39.67)	564 (57.15)	518 (49.34)
< 25% non-White	462 (31.57)	41 (5.40)	74 (8.14)	347 (47.97)
Property crime per 1,000	6.35 (0.29)	7.22 (0.24)	7.44 (0.55)	5.67 (0.42)
Violent crime per 1,000	74.75 (3.18)	94.49 (3.31)	91.55 (5.90)	61.10 (4.46)

Table 6-1. Characteristics of the BACH III study population overall by diabetes status (N=2,764)

	Overall N=2764	Black N=929	Hispanic N=937	White N=898
Built environment Average distance to closest…, in miles				
Grocery Store	0.30 (0.01)	0.30 (0.01)	0.26 (0.01)	0.31 (0.02)
Convenience Store	0.23 (0.01)	0.23 (0.01)	0.20 (0.01)	0.24 (0.01)
Fast food	0.42 (0.02)	0.44 (0.01)	0.40 (0.02)	0.42 (0.02)
CT % open space, continuous	0.08 (0.01)	0.06 (0.01)	0.07 (0.01)	0.09 (0.01)
CT open space, categorical				
≤ 5%	1393 (47.95)	518 (58.36)	501 (55.80)	374 (41.73)
5.1-10%	686 (26.66)	198 (20.46)	229 (22.02)	259 (30.36)
10.1-20%	440 (16.07)	146 (14.45)	141 (15.28)	153 (16.96)
> 20%	245 (9.32)	67 (6.74)	66 (6.90)	112 (10.96)
Physical disorder	13.67 (0.14)	14.27 (0.22)	14.52 (0.24)	13.18 (0.20)
Social disorder	14.07 (0.16)	15.50 (0.26)	15.36 (0.29)	13.06 (0.21)

[1] Mean and standard error presented for continuous variables
[2] n and column percent presented for categorical variables
CT= census tract

Figure 6-1. Boston Area Community Health (BACH) III Survey participants by race/ethnicity by the racial composition of census tracts in Boston, MA



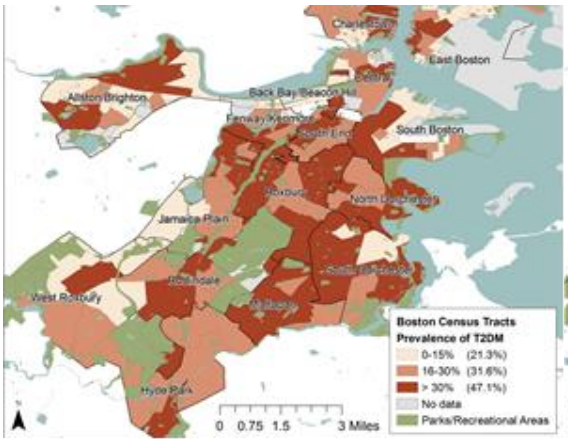
Overall, 892 (22.8%) of participants had diabetes (64.9% diagnosed, 35.1% undiagnosed). Black (33.3%) and Hispanic (23.5%) participants were more likely to have diabetes than White participants (18.0%, p<0.001).The prevalence of diabetes was higher among individuals with lower income (p<0.001), less education (p<0.001), and with non-professional occupations (p<0.001, bivariate results not shown). Diabetes was more prevalent among individuals living in low (34.1%) or middle (40.7%) SES neighbourhoods (p=0.002), high poverty neighbourhoods (48.0% among participants living in neighbourhoods with ≥20% of residents living in poverty, p=0.02), and greater minority populations (p=0.003). Participants with diabetes were more likely to perceive their neighbourhood as socially disordered (i.e. people hanging around on the streets, drug and alcohol use, trouble with neighbours, and a perception of lack of safety, p=0.003).

There appeared to be a spatial pattern in the distribution of T2DM (**Figure 6-2, map a**). This was confirmed statistically via the Global Moran's *I* statistic (*I*=0.09, p=0.03). **Figure 6-2, maps b-d** demonstrate the patterning of SES, poverty and % White in Boston measured at the census tract level. The Global Moran's *I* statistic evaluating spatial autocorrelation in the ordinary multilevel model of census tract-level poverty on T2DM, however, indicated no significant positive autocorrelation (*I*=0.003, p=0.77). Therefore analyses proceeded using ordinary multilevel models as opposed to spatial autoregressive models. Multilevel models indicated a significant between-neighbourhood variance estimate of $\sigma^2_B = 0.943$, providing evidence of geographic variation in T2DM (**Table 6-2**). The ICC indicated that 22.3% of the total variability in T2DM is due to variation between neighbourhoods, while the remainder of the variation in T2DM is due to variation within neighbourhoods (i.e. individual variation). With the addition of individual-level demographic variables (Model 1: race/ethnicity—our primary determinant of interest--age, and gender) to the

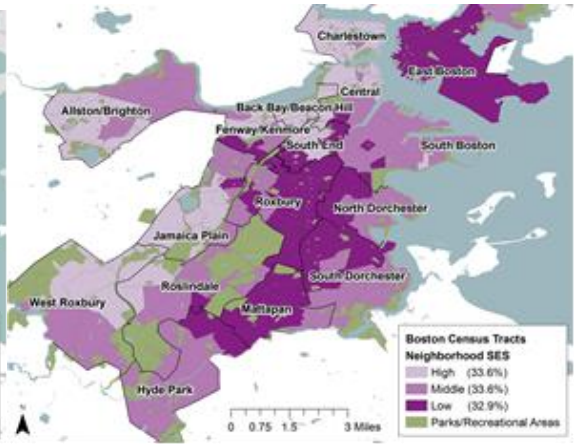
model, between-neighbourhood variance (σ^2_B) persisted but was reduced by 22.3% [(0.943-0.733)/0.943 x 100%]. In other words, the composition of the neighbourhood (i.e. clustering of demographic characteristics by neighbourhood) explained 22.3% of the neighbourhood variability in T2DM. Racial/ethnic disparities in T2DM were large, with Black participants having 2.89 times the odds of having T2DM as White participants (95% CI: 1.20-3.97) and Hispanic participants having 1.48 times the odds (95% CI: 1.91-3.51). With the addition of individual-level socioeconomic factors (Model 2), neighbourhood variation in T2DM was further reduced so that nearly 31.9% of the between-neighbourhood variability was explained by these factors. The excess odds of diabetes among Black participants was reduced by 34.4%, and the excess odds among Hispanic participants by 69.8%, with the introduction of individual socioeconomic factors ($OR_{Black\ vs.\ White}$=2.24, 95% CI: 1.61-3.13; $OR_{Hispanic\ vs.\ White}$=1.48, 95% CI: 1.03-2.12). Further inclusion of all individual lifestyle factors marginally associated with T2DM (physical activity, grains servings, and BMI) had little impact on between-neighbourhood variability in T2DM or the magnitude of the racial/ethnic disparities (**Table 6-2**, Models 3 and 4). The addition of neighbourhood-level variables to the model had very little effect on the magnitude of the racial/ethnic disparities and on the between-neighbourhood variability (Models 5-10). For example, the addition of census tract poverty (Model 5) explained less than 1% of the excess odds of T2DM among Blacks and 6% of the excess odds among Hispanics and explained only 1.8% of the neighbourhood variance in T2DM.

Figure 6-2. The Distribution of T2DM, Socioeconomic Status, Poverty, and Minority Status in Boston, Massachusetts

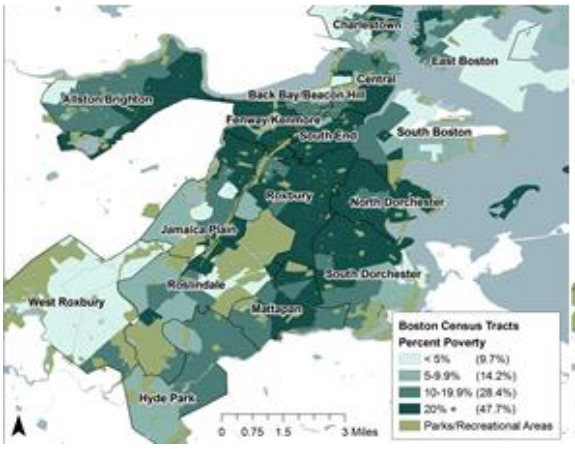
a. The distribution of T2DM prevalence in Boston, MA as measured by the BACH Survey



b. The distribution of socioeconomic status by census tracts in Boston, MA



c. The distribution of poverty by census tracts in Boston, MA



d. The racial composition of census tracts in Boston, MA

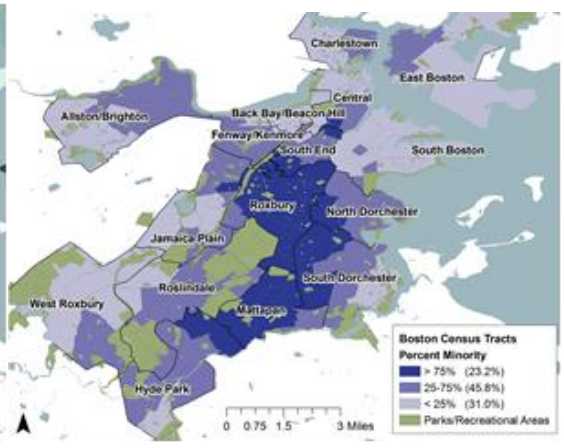


Table 6-2. Within and between neighbourhood variance estimates from null and adjusted multilevel models of diabetes from the Boston Area Community Health Survey

	OR (95% CI) Black vs. White	OR (95% CI) Hispanic vs. White	$\sigma^2_{between}$	% of neigh-bourhood variance explained	ICC[1]
Null Model (intercept only)			**0.943**	--	0.223
Random Intercept Models (Individual-level variables only)					
Model 1: Race/ethnicity, Age, Gender	2.89 (1.20-3.97)	2.59 (1.91-3.51)	0.733	22.3	0.182
Model 2: Model 1 + Socioeconomic factors	2.24 (1.61-3.13)	1.48 (1.03-2.12)	0.642	31.9	0.163
Model 3: Model 2 + BMI	2.33 (1.66-3.29)	1.74 (1.20-2.52)	0.652	30.9	0.165
Model 4: Model 3 + Grains, physical activity	2.30 (1.63-3.24)	1.57 (1.08-2.28)	0.650	31.1	0.165
Random Intercept Models (Contextual variables)					
Model 5: Model 2 + CT Poverty	2.23 (1.57-3.16)	1.45 (1.00-2.10)	0.625	33.7	0.160
Model 6: Model 2 + % Black	2.31 (1.58-3.39)	1.50 (1.04-2.16)	0.641	32.0	0.163
Model 7: Model 2 + Violent and Property Crime	2.22 (1.58-3.12)	1.47 (1.02-2.11)	0.642	31.9	0.163
Model 8: Model 2 + Built Environment (Distances)	2.26 (1.62-3.16)	1.47 (1.02-2.10)	0.628	33.4	0.160
Model 9: Model 2 + Open Space	2.24 (1.61-3.13)	1.48 (1.03-2.12)	0.639	32.2	0.163
Model 10: Model 2 + Disorder (Physical and Social)	2.23 (1.60-3.12)	1.47 (1.02-2.11)	0.642	31.9	0.163

[1] latent variable approach to approximate ICC for a binary outcome, where the within variance for a standard logistic regression is $\pi^2/3$.

Table 6-3 shows the most parsimonious model for racial/ethnic disparities in T2DM and includes all variables with either an influence on the magnitude of the racial/ethnic disparities or that were independently associated with T2DM. In this model, the between-neighbourhood variability (σ^2_B) was reduced to 0.614. While this still involved a significant between-neighbourhood variance (p=0.002), the compositional (race/ethnicity, gender, age, income, education, physical activity, and

BMI) and contextual (proximity to grocery stores, and census tract poverty) variables included in this model explained 34.9% of the between-neighbourhood variance in T2DM [(0.943- 0.614)/0.943 x 100%]. Only two contextual factors had marginally significant (p<0.20) associations with prevalent T2DM: (1) the distance to the nearest grocery store for each participant and (2) census tract poverty. Participants living one mile further from a grocery store had approximately half the odds of having T2DM though this result was not statistically significant (OR=0.53; 95% CI: 0.25-1.15). Participants living in lower poverty census tracts (< 5%, 10-20%) had lower odds of T2DM but again this finding was not statistically significant ($OR_{10\text{-}19.9\% \text{ vs. } \geq 20\%}$=0.79; 95% CI: 0.59-1.06).

Table 6-3. Full multilevel model, $\sigma^2_{between}$=0.614 (p=0.002)		
	Full Model	
	OR	**95% CI**
Demographics		
Race		
Black vs. White	**2.34**	**1.64-3.34**
Hispanic vs. White	**1.54**	**1.07-2.21**
Male vs. female	**1.68**	**1.31-2.15**
Age	**1.04**	**1.03-1.05**
SES		
Income		
<$20,000 vs. ≥ $50,000	**1.77**	**1.21-2.58**
$20,000-$49,999 vs. ≥ $50,000	1.18	0.81-1.72
Education		
Less than High School vs. college or advanced degree	**2.09**	**1.37-3.19**
High school or equivalent vs. college or advanced degree	1.4	0.96-2.04
Some college vs. college or advanced degree	1.21	0.82-1.78
Lifestyle		
Physical Activity		
Low vs. Medium or High	**1.37**	**1.06-1.78**
BMI		

Table 6-3. Full multilevel model, $\sigma^2_{between}$=0.614 (p=0.002)	Full Model	
	OR	**95% CI**
Overweight vs. Normal	**1.81**	**1.24-2.63**
Obese vs. Normal	**4.18**	**2.89-6.04**
Contextual Factors		
Distance to nearest grocery store (miles)	0.53	0.25-1.15
CT Poverty		
< 5% vs. ≥ 20%	0.92	0.49-1.71
5-9.9% vs. ≥ 20%	1.32	0.88-1.96
10-19.9% vs. ≥ 20%	0.79	0.59-1.06

Bold = significant at the 0.05 level

6.2.5 Conclusions

Racial and ethnic disparities in T2DM remain a major public health problem. While many studies investigating the potential causes for these disparities have focused on variations in individual lifestyles and behaviours, genetics, and/or individual-level socio-demographic factors, we examined the added influence of neighbourhood-level factors. We found that there was a large variation in the prevalence of T2DM by neighbourhood that could not be explained by the composition of the neighbourhood (i.e. individual-level factors). We also sought to identify specific aspects of neighbourhoods that were associated with variability in T2DM by race/ethnicity. However, despite the comprehensive list of contextual variables amassed in this study (built environment, neighbourhood socioeconomics, racial composition, safety, and neighbourhood disorder) we were unable to identify contextual elements that could explain the racial/ethnic disparities in T2DM nor the neighbourhood variability present in this study. While bivariate associations indicated that neighbourhood socioeconomic factors (SES, poverty), racial composition, and social disorder were

associated with higher odds of T2DM, these factors explained neither the racial/ethnic differences, nor the between-neighbourhood variance, in T2DM in multilevel models.

Our finding that there was significant neighbourhood variability in T2DM is consistent with results reported by others.[244] However, the extent to which this variability is explained by the contextual factors under consideration varies with the outcome of interest, the specific contextual measures included, the population examined, and the analytic techniques used. All of the contextual factors included in this study have been found to be associated with precursors to T2DM (dietary patterns,[218-220] physical activity, [219, 221] or body mass index/obesity[219, 220, 222, 516-518]) in previous studies. However, T2DM is a more distal biological manifestation of residential conditions than behavioural and BMI outcomes. This indirect relationship may be one potential explanation for the null findings of this particular study. It is worth noting that several studies have successfully made the link between neighbourhood socioeconomic factors like unemployment[541], economic disadvantage[31, 542], and racial segregation[270, 271, 543] and T2DM. Astell-Burt found that individuals residing in neighbourhoods with greater green space had lower odds of having T2DM[244] and lower insulin resistance.[544] Therefore, the mixed results to date may largely result from the specific contextual factors measured and from the specific locales and populations examined.

There are several potential explanations for our negative findings with regards to contextual factors. First, despite our attempts to address a comprehensive list of neighbourhood factors, it is possible we may be missing a key contextual factor that would explain the large between neighbourhood variability in T2DM. For example, we did not include a direct measure of neighbourhood "walkability," but rather measured individuals' distances to specific features of their

neighbourhoods thought to influence conduciveness to walking and linked this data to individual physical activity. Comprehensive measures of neighbourhood walkability have been linked to physical activity and body mass index,[545, 546] and thus could be an area for future type 2 diabetes research. Second, we recognize that we examined only one neighbourhood context, neighbourhood of residence. People experience and interact with multiple neighbourhood environments each day, known as spatial polygamy, which can influence their health and health behaviour.[547] Most notably people's work environment may influence their dietary and physical activity behaviours,[548] thus influencing their risk of T2DM. Third, it is important to note that the contextual characteristics measured here are shaped by the macroeconomic forces of the larger community. The degree of economic or racial segregation of the larger community may contribute to scant variation at smaller units. Boston has previously ranked as one of the most residentially segregated metropolitan areas in the US. The racial segregation index of Boston is 67.7[549] (a score of 60 and above is considered to be a high degree of segregation). Despite Boston being a segregated city, we found variation in individual versus neighbourhood racial composition. Therefore, we believe it is reasonable to expect co-variation between neighbourhood racial composition in relation to T2DM. Previous studies conducted in Boston found similarly high levels of residential segregation[258] but not necessarily segregation in the built environment.[258]

The heterogeneous findings across the literature may be attributable to differences in the contextual measures examined and differences in the way constructs were evaluated (e.g. distance to versus density of), but it is also possible that the patterning of neighbourhood social and physical attributes may be locale-specific. For example, in a study that examined the density of supermarkets, retail areas, recreational facilities, and health opportunities across three US cities,

neighbourhood racial/ethnic composition was significantly associated with access to facilities in both New York, NY and Baltimore, MD, but not in Winston-Salem, NC.[550] The macro-economic influences of living in this urban, northeast environment may not be generalizable to other contexts or to the conditions in which racial/ethnic disparities in T2DM are fostered in the US at large. Nonetheless, the BACH cohort has been compared to other large regionally (Behavioral Risk Factor Surveillance System), and nationally (National Health and Nutrition Examination Survey) representative samples and has been shown to have a similar chronic disease profile to these survey populations with the exception of the exclusion of Asians (Asians comprise approximately 7.5% of the Boston, Massachusetts population).[437]

A notable limitation of this study is the cross-sectional nature of the analyses which prevent causal inferences and limit our ability to determine temporality. While US Census data were available for previous rounds of the BACH Survey, a unique strength of the BACH III Survey was the inclusion of contextual data from a variety of sources such as InfoUSA (food environment), the Boston Police Department (crime data), and participants' perceptions (physical and social disorder). Another advantage to using the BACH III data was that on-the-spot diabetes testing was conducted (this was not done in any other BACH study) allowing us to examine both diagnosed and undiagnosed diabetes which may more accurately depict the true nature of racial/ethnic disparities in T2DM. Finally, BACH III participants had lived at their current address, on average, for over 15 years (Mean=15.5, SE=0.5) and over 80% of participants lived in the same neighbourhood for all three rounds of the BACH Survey. These findings may mitigate concerns regarding the temporality between neighbourhood exposure and diabetes onset.

It may be argued our results are influenced by the analytic approach. Exploratory analyses using the residuals from the census tract poverty-T2DM regression indicated no spatial autocorrelation. Therefore, we did not employ spatial modelling techniques. In addition, the modelling strategy presented here allowed individual-level variables to enter the model first to test the contribution of compositional factors. However, we also built the models introducing neighbourhood-level contextual variables first and the results were the same. In addition, the modifiable areal unit problem (MAUP) is an issue. However, we note that the neighbourhood definitions used in the current study are common in the social epidemiology of neighbourhood literature.

Finally, residential selection bias is a well-known limitation of many investigations of neighbourhood effects.[551] Neighbourhood selection is the result of residential mobility choices made by individuals and households within a restricted set of choices that can produce residential segregation patterns. To reduce the potential for bias relating to residential selection, we adjusted for variables that may be associated with neighbourhood selection (e.g. individual income, education, and occupation). We recognize that this is a crude method to account for selection into neighborhoods,[552, 553] but unfortunately there was not a variable in our dataset for neighbourhood selection. Finally, it is important to note that results from this study might only be generalizable to adults in similar urban locations to Boston.

There are a number of strengths to this study and the analytic approaches used here. Features of BACH that make it uniquely suitable for this investigation include: large diverse random sample of community-dwelling men and women; the utilization of established survey instruments; the collection of fasting blood samples at BACH III allow us to examine both diagnosed and undiagnosed

T2DM; and collection of neighbourhood measures from a wide variety of sources including the US Census Bureau, InfoUSA, as well as the individual participants' perceptions of their neighbourhood.

We attempted to compile a list of compositional and contextual factors representative of both the physical (food store availability, green space) and social (socioeconomics, racial composition, safety) environments in which individuals live. While many studies of neighbourhood effects rely solely on objective assessments of neighbourhood, we included residents' subjective characterization of their neighbourhood using a psychometrically validated scale.[528] In addition, the racial/ethnic diversity of our sample allowed us to examine the impact of neighbourhood characteristics on disparities, an understudied potential impact of the contextual environment.

In conclusion, using data from the BACH Survey, we have identified large, significant, neighbourhood variability in the prevalence of T2DM. However, the many neighbourhood factors we were able to examine did not explain this neighbourhood variability, nor did they appear to play a role in the amplification or creation of racial/ethnic disparities in T2DM. While the findings of this study overall suggest that neighbourhood factors are not a major contributor to racial/ethnic disparities in T2DM, further research is needed including data from other geographic locations, including both urban and rural areas and areas with both high and low residential segregation.

7 The Relative Contributions of Socioeconomic, Local Environmental, Psychosocial, Lifestyle/Behavioural, Biophysiologic, and Ancestral Factors to Racial/Ethnic Disparities in Type 2 Diabetes

7.1 Introduction

While previous papers looked at specific factors in depth, this paper aims to tie together the conceptual model of racial/ethnic disparities in T2DM. This paper examines the relative contributions of socioeconomic, local environmental, psychosocial, lifestyle/behavioural, biophysiologic, and genetic ancestral factors to racial/ethnic disparities in T2DM. Given the complexity of racial/ethnic disparities in T2DM, the conceptual model was simplified for modelling purposes. Two-level structural equation modelling was used to examine direct and indirect effects whilst accommodating the clustering of participants within their census tract of residence.

This paper is currently under consideration for publication in the International Journal of Epidemiology.

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
www.lshtm.ac.uk

Registry
T: +44(0)20 7299 4646
F: +44(0)20 7299 4656
E: registry@lshtm.ac.uk

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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SECTION A – Student Details

Student	Rebecca Piccolo
Principal Supervisor	Neil Pearce
Thesis Title	Racial and Ethnic Disparities in Type-2 Diabetes: A Multilevel Perspective

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	Diabetes Care
Please list the paper's authors in the intended authorship order:	Piccolo RS, Subramanian SV, Pearce N, Florez J, McKinlay JB
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conducted all analyses, designed all tables and figures included in this paper and wrote the first draft of the article. S.V. Subramanian and Neil Pearce helped to devise the modelling strategy. S.V. Subramanian, Neil Pearce, Jose Florez, and John McKinlay all provided comments on the draft article, many of which I incorporated during revisions to the article.

Student Signature: _____ **Date:** 8/Oct/2015

Supervisor Signature: _____ **Date:** 8/Oct/2015

7.2 Article Submitted

7.2.1 Abstract

Background: Racial/ethnic minorities in the US have a higher prevalence of type 2 diabetes mellitus (T2DM). While many independent risk factors for T2DM have been identified, these determinants are often viewed in isolation without considering the joint contributions of competing risk factors. The objective of this study was to assess the relative contributions of six domains of influence to racial/ethnic disparities in T2DM.

Methods: Cross-sectional analyses were conducted using the Boston Area Community Health (BACH) III Survey (2010-12), the third wave of a random, population-based sample of men and women from three racial/ethnic groups (Black, Hispanic, White) living in Boston, Massachusetts (N=2,764). Prevalent diabetes was defined by self-report of T2DM, fasting glucose>125 mg/dL, or HbA1c≥6.5%. Structural equation models (SEM) were constructed to evaluate the direct effects of each conceptual domain of influence on T2DM prevalence as well as their indirect effect on the race/ethnicity – T2DM relationship. All direct and indirect pathways were included.

Findings: The final model indicated that 38.9% and 21.8% of total effect of Black race and Hispanic ethnicity, respectively, on T2DM prevalence was mediated by the socioeconomic, environmental, psychosocial, and lifestyle/behavioural risk scores. The largest mediating influence was the socioeconomic risk score, which explained 21.8% and 26.2% of the total effect of Black race and Hispanic ethnicity, respectively.

Interpretation: Our study found that socioeconomic factors had the greatest impact on explaining the excess prevalence of T2DM among racial/ethnic minorities.

7.2.2 Background

Disparities in type 2 diabetes mellitus (T2DM) by race/ethnicity are an important public health problem in the United States and worldwide. Compared to White adults, the prevalence of diabetes is 77% higher among Black and 66% higher among Hispanic adults in the US.[2] Racial/ethnic disparities in T2DM are associated with disparities in diabetes control,[6] elevated rates of diabetes-related complications, and greater health care costs.[554]

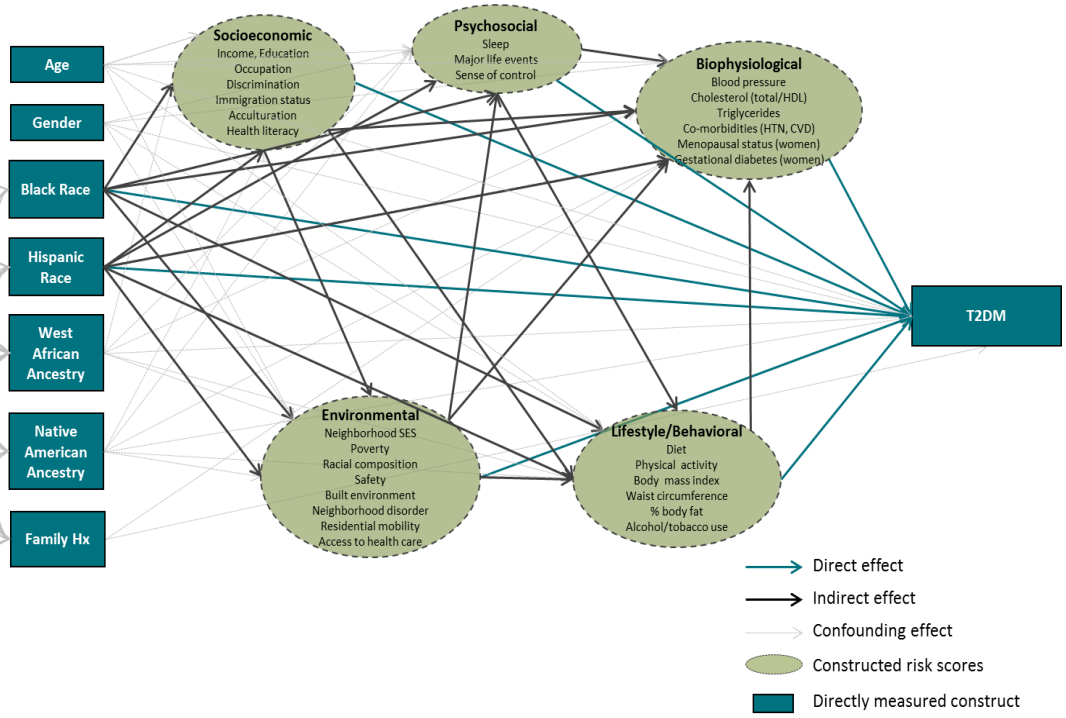
Many factors have been identified as contributing to these disparities,[555] including variations in lifestyles and behaviours, biophysiological, psychosocial, socio-demographic, and environmental factors, and biogeographic ancestry.[36, 37] However, research to date has largely focused on individual risk factors in isolation and the relative contribution of these influences have not been identified.[555]

Since racial/ethnic differences in T2DM appear to result from a broad range of influences, a more complete understanding requires a multilevel approach. A multilevel risk model, reflecting the many factors that contribute to T2DM risk, may advance understanding, and better inform the design of interventions to target the most relevant domains which disproportionately contribute to disparities.

The aim of this research is to develop and test a conceptual risk model that takes a multilevel approach to T2DM disparities (**Figure 7-1**). Statistical methods are available that allow us to test this conceptual model which includes both direct and indirect (mediating) effects. Our aim is to assess the relative contributions of six domains of influence to racial/ethnic disparities in T2DM: (1) socioeconomic, (2), local environmental, (3) psychosocial, (4) lifestyle/behavioural, (5) biophysiologic, and (6) biogeographic ancestry (BGA).

Figure 7-1. Conceptual Model of Potential Factors Influencing Racial/Ethnic Disparities in T2DM

Potential factors influencing racial/ethnic disparities in T2DM are grouped into five domains of influence: social structure, environmental, psychosocial, lifestyle/behavioural, Biophysiological. Race/ethnicity, age, gender, and genetic constructs are considered exogenous. Constructs operationalized in the BACH III Survey are listed in the ovals (conceptual domains).



7.2.3 Methods

Study Sample

The Boston Area Community Health (BACH) Survey is a longitudinal, random, population-based, cohort of 5,502 residents (2,301 men, 3,201 women) aged 30-79 from three racial/ethnic groups in Boston, MA. [437] BACH has conducted total of three surveys to date (BACH I: 2002-2006; BACH II: 2008-2010; BACH III: 2010-2012). The current analysis uses cross-sectional data from the third survey (BACH III, N=3,155). Analyses were restricted to 2,764 participants still residing in Boston,

Massachusetts at BACH III due to the availability of environmental parameters. Survey participants were interviewed in the morning after being instructed to fast overnight (≥ 8 hours) and after providing written informed consent. The interviews were conducted by trained, certified phlebotomists fluent in English and/or Spanish. The response rate, conditional on previous participation, was 81.4%.[508] The study was approved by the New England Research Institutes' Institutional Review Board.

Measures

The primary determinant of interest was self-identified race/ethnicity (non-Hispanic Black [Black], non-Hispanic White [White], and Hispanic). The primary outcome was prevalent T2DM. Fasting glucose (FG) was measured with a HemoCue 201 point-of-care analyzer. HbA1c was measured by Quest Laboratories in Cambridge, MA. Participants who (a) self-reported T2DM ("have you ever been told by a doctor or other health professional that you have type 2 diabetes?"), or (b) had FG > 125 mg/dL or HbA1c ≥ 6.5% were classified as having T2DM.[21] Medication inventory and age of diagnosis was used to further separate type 1 versus type 2 diabetes. Eight individuals younger than 35 years at diagnosis and on continuous insulin therapy were considered to have type 1 diabetes and were excluded. The medication inventory also confirmed over 80% of the self-reported cases of diabetes.

Our multilevel approach builds upon an earlier theoretical model[419] and includes six domains of influence (**Figure 1**) which are hypothesized to directly and/or indirectly, singly and in combination affect T2DM. The constructs measured within each domain are described in briefly below. Additional details on the measures can be found in **Section 7.3**.

Socio-economic influences considered included household income, educational attainment, occupation, perceptions of everyday discrimination,[556] immigration status, acculturation,[427] health literacy, type of health insurance, and number of visits to a health care provider in the past year. ArcGIS 10.1 (ESRI, Redlands, California) was used to geocode participants' residences and link participants with geographic features. ***Environmental influences*** considered included census-tract socioeconomic status,[431] percent poverty, percent non-Hispanic Black, percent non-Hispanic White, violent and property crime per 1,000 population, distance to the closest grocery store, convenience store, and fast food (miles), percentage of recreational open space, perceived social and physical disorder,[528] and number of years at current address. ***Spatial access to health care*** was assessed by distance to the closest community health centre, acute care hospital, or health care centre of either kind (miles). ***Psychosocial influences*** considered included hours of sleep each night, major life events,[557] and sense of personal control.[429] ***Lifestyle/behavioural*** factors assessed: dietary patterns (2005 Block food frequency questionnaire[558] assessed average daily intake of sodium, vegetables, fruits, meats/beans, grains, fibre, and saturated fat comprising a "healthy eating score" which was adjusted for total kilocalories), physical activity,[530] BMI, waist circumference, and body fat percentage were measured by trained field interviewers, and smoking history. ***Biophysiological influences*** considered included: blood pressure (average of three readings taken during the in-home visit), total cholesterol, HDL cholesterol, triglycerides (Quest laboratories, Cambridge, MA), reported high blood pressure or cardiovascular disease, and for women only menopausal status, and history of gestational diabetes.

To measure ***BGA***, we evaluated a panel of 63 ancestry informative markers, including 33 autosomal single nucleotide polymorphisms differentiating Native American versus European ancestry and 30

single nucleotide polymorphisms differentiating West African versus European ancestry. The 63 markers combined can provide an estimate of % West African, % Native American, and % European ancestry for each participant.[559, 560] Genotyping was conducted at the Broad Institute using the Sequenom iPLEX platform. ***Family history*** of diabetes was also considered as an independent risk factor for T2DM. Race/ethnicity, age, and gender, BGA, and family history of diabetes were considered exogenous factors.

Structural Equation Modelling

We applied two-level structural equation modelling (SEM) to assess the associations between race/ethnicity, confounding and mediating characteristics, and T2DM. Two-level SEM allows us to include both direct and indirect effects of each risk domain on T2DM as hypothesized in the conceptual model (**Figure 7-1**) while accommodating the clustering of participant observations (level 1) within their census tract of residence (level 2). Direct effects are depicted as arrows from independent to dependent variables. For example, socioeconomic risk may have a direct effect on T2DM (depicted in **Figure 7-1** by a single arrow from socioeconomic risk to T2DM, the final outcome variable). Indirect effects are depicted as a series of arrows operating through mediating construct(s). For example, socioeconomic risk may contribute to increased lifestyle/behavioural risk which in turn contributes to T2DM and serves as a mediating influence. We relied on published literature and inherent temporality to determine the direction of the effects. Correlations between the measurement errors of two variables are represented by bi-directional curves. Standardized coefficients (sβ)[561] and their *p*-values are reported. We performed mediation analysis to assess the percentage of the racial/ethnic effect explained by each the five mediating domains of influence.

The mediated, or indirect, effect is calculated as the product of the direct effects (sβ) among the independent, mediating, and any subsequent dependent variables.[562] The overall percent mediated was calculated as the indirect effect over the total effect. Descriptive statistics were estimated using SAS callable Sudaan Version 11 and SEMs were estimated using Mplus Version 7 (Muthen and Muthen, Los Angeles, CA).

Development of the Risk Scores

Data based on the five theoretical mediating domains of influence (socioeconomic, environmental, psychosocial, lifestyle/behavioural, and biophysiological) were used to create risk scores. Variables listed in **Figure 7-1** were reduced from those in the conceptual model using race/ethnicity-, age-, and gender-adjusted models (**Table 7-3**, **Section 7.3.2 Supplementary Analyses**). Variables that did not either (1) meet a minimal criterion for association with T2DM ($p < 0.10$) or (2) reduce the race/ethnic effect (OR) by 10% were not included in the domain risk score. For categorical variables, we created a weighted scoring system by rounding up all regression coefficients (ln(OR)) to the nearest integer, using methods similar to those utilized in Bang *et al*[563] which is the basis for the American Diabetes Association self-screening tool. For continuous variables, risk was based on clinically accepted "high risk" criteria (see **Table 7-1** for citations). If clinically accepted criteria were not available, tertiles were used. Following the construction of the final model all variables were added in the model singly to ensure their effects were adequately captured by the risk scores.

Table 7-1. Development of the "risk score"

Domain/Variable	High Risk (+1)	Very High Risk (+2)
Socioeconomic		
Income	$20,000 - $49,999	<$20,000
Education	High school or equivalent/Some college	Less than High School
Occupation	Manual labour/Never worked	
Born in the US	Yes	
Acculturation	High/Bicultural (≥2.5 for English domain)	
Health Literacy	Inadequate/Marginal	
Insurance Status	Public	
Visits to HCP in the past year	7+	
Neighbourhood		
CT Poverty	> 20%	
Psychosocial		
Sleep Duration	< 6 hours	> 9 hours
Major Life Events	> 1 MLE	
Sense of Control (tertiles)	< 1.0	< 0.43
Lifestyle/Behavioural		
Physical activity	Low	
Smoking history	Current	
BMI[563]	25-29	30-39 (> 40 adds 3 risk points)
Waist circumference[564]	≥ 102 cm (men) ≥ 88 cm (women)	
Body fat percentage (tertiles)	> 25% (men) > 35% (women)	> 33% (men) > 42% (women)
Biophysiological		
Blood pressure[564]	SBP ≥ 130 or DBP ≥ 85 or self-report of hypertension diagnosis	
Cholesterol (total)[565]	≥ 200 mg/dL	≥ 240 mg/dL
HDL Cholesterol[564]	< 40 mg/dL (men) < 50 mg/dL (women)	
Triglycerides[564]	≥ 150	
Cardiovascular disease		Yes
Menopausal status	Post	Surgical/Undetermined
Gestational diabetes		Yes

In order to minimize reductions in precision, multiple imputation was implemented using the Multivariate Imputation by Chained Equations (MICE)[510] algorithm in R (Vienna, Austria). Fifteen multiple imputation datasets were created. Imputations were conducted separately for each racial/ethnic by gender combination to preserve interaction effects, and the complex survey sample design was taken into account. DNA samples were obtained and isolated on 73.1% of participants, 24.4% of participants were missing household income, and 25.8% were missing dietary data. The proportions of missing data for other variables were 10%. BACH's sampling design requires weighting observations inversely proportional to their probability of selection for results to be generalizable to the base population.[540] Sampling weights were post-stratified in order to produce estimates representative of the Black, Hispanic, and White Boston, MA population.

7.2.4 Results

The prevalence of diabetes in the BACH III study was 23.4%. The demographic characteristics of the 2,476 participants the analytic sample are presented in **Table 7-2.** The sample was comprised of approximately 1/3 Black (29.0%), Hispanic (32.8%), and White (34.6%) participants and the average age of the participants was 54. Compared with non-diabetic participants, T2DM participants were older, had greater West African genetic ancestry, were of lower socioeconomic status, reported greater discrimination, lower health literacy, lived in lower SES/greater poverty census tracts and neighbourhoods with more minority residents, reported greater neighbourhood disorder, short (<6 hours) or long (>9 hours) sleep, reported a lower sense of control, less physical activity, greater BMI, waist circumference and body fat percentage, had higher blood pressure, total cholesterol, and triglycerides and lower HDL cholesterol.

Table 7-2. Characteristics of the BACH III study population overall by diabetes status (N=2,476)

	Overall N=2,764	Type 2 Diabetes N=892	No Type 2 Diabetes N=1872	*P*-value
Self-Identified Race/Ethnicity				
Black	929 (27.10%)	351 (39.51%)	578 (23.42%)	< 0.001
Hispanic	937 (12.20%)	340 (12.55%)	597 (12.09%)	
White	898 (60.71%)	201 (47.94%)	697 (64.48%)	
Age[1]				
34-44	405 (27.54%)	61 (14.68%)	344 (31.34%)	< 0.001
45-54	739 (26.97%)	177 (23.07%)	562 (28.13%)	
55-64	812 (19.99%)	300 (24.12%)	512 (18.77%)	
65-74	536 (13.76%)	236 (21.46%)	300 (11.49%)	
75-88	272 (11.74%)	119 (16.67%)	153 (10.28%)	
Gender, % Male	1018 (46.46%)	344 (52.00%)	674 (44.82%)	0.056
Genetic Influences				
% West African, Mean (SE)	29.84 (1.23)	39.02 (2.27)	27.12 (1.43)	< 0.001
% Native American, Mean (SE)	6.85 (0.29)	6.53 (0.56)	6.95 (0.36)	0.545
% European, Mean (SE)	63.31 (1.27)	54.45 (2.33)	65.93 (1.49)	< 0.001
Family History of Diabetes	1483 (46.52%)	602 (62.12%)	882 (41.91%)	< 0.001
Socio-economic Influences				
Income				
<$20,000	1234 (26.68%)	524 (44.69%)	710 (21.35%)	< 0.001
$20,000 - $49,999	798 (25.10%)	234 (25.63%)	564 (24.94%)	
≥ $50,000	732 (48.22%)	134 (29.67%)	598 (53.70%)	
Education				
Less than High School	560 (8.16%)	278 (16.21%)	282 (5.78%)	< 0.001
High school or equivalent	867 (24.44%)	298 (32.72%)	569 (21.99%)	
Some college	576 (21.17%)	176 (23.79%)	400 (20.39%)	
College or advanced degree	761 (46.23%)	140 (27.28%)	620 (51.84%)	
Occupation				
Professional, Managerial, Sales, and Office	1324 (65.27%)	345 (52.95%)	979 (68.92%)	< 0.001
Service	715 (17.52%)	224 (19.53%)	492 (16.92%)	
Manual labour	495 (13.67%)	209 (21.83%)	286 (11.25%)	
Never worked	229 (3.54%)	114 (5.70%)	115 (2.90%)	
Discrimination (0-45), Mean (SE)	9.34 (0.25)	10.31 (0.57)	9.05 (0.29)	0.057
Born in US	1645 (78.97%)	488 (77.50%)	1157 (79.41%)	0.490
Acculturation (English not First language)				
Low	669 (8.53%)	253 (10.54%)	416 (7.93%)	0.178
High/Bicultural	2095 (91.47%)	639 (89.46%)	1456 (92.07%)	

	Overall N=2,764	Type 2 Diabetes N=892	No Type 2 Diabetes N=1872	*P*-value
Health literacy				
Inadequate	708 (13.44%)	328 (24.12%)	380 (10.27%)	< 0.001
Marginal	298 (6.25%)	120 (10.28%)	178 (5.06%)	
Adequate	1759 (80.32%)	445 (65.60%)	1313 (84.67%)	
Environmental Influences				
CT SES				
Low	1269 (25.55%)	447 (34.07%)	822 (23.03%)	< 0.001
Middle	968 (39.87%)	315 (40.65%)	653 (39.64%)	
High	527 (34.58%)	130 (25.29%)	397 (37.33%)	
CT Poverty				
< 5%	159 (10.45%)	33 (6.84%)	126 (11.52%)	0.018
5-9.9%	280 (14.37%)	88 (12.22%)	192 (15.01%)	
10-19.9%	792 (35.78%)	210 (32.94%)	582 (36.62%)	
≥ 20%	1533 (39.40%)	561 (48.01%)	972 (36.86%)	
CT Racial Composition				
% Black, Mean (SE)	26.80 (1.07)	32.61 (1.86)	25.09 (1.18)	< 0.001
% Hispanic, Mean (SE)	16.62 (0.53)	18.25 (0.88)	16.14 (0.55)	0.017
% White, Mean (SE)	53.75 (1.25)	47.33 (2.06)	55.65 (1.38)	< 0.001
Property crime per 1,000, Mean (SE)	74.05 (3.58)	77.84 (4.28)	72.93 (3.84)	0.219
Violent crime per 1,000, Mean (SE)	6.35 (0.33)	6.51 (0.37)	6.30 (0.35)	0.505
Low Access to… (> 0.5 mi)				
Supermarkets	1316 (51.01%)	415 (49.53%)	901 (51.45%)	0.529
Grocery Stores	251 (11.58%)	69 (9.76%)	182 (12.12%)	0.370
Convenience Stores	164 (7.94%)	52 (8.40%)	112 (7.81%)	0.616
Fast Food	882 (33.66%)	269 (30.71%)	613 (34.53%)	0.578
CT % Open Space, Mean (SE)	0.08 (0.01)	0.07 (0.01)	0.08 (0.01)	0.105
Physical Disorder (6-30), Mean (SE)	13.55 (0.14)	13.82 (0.20)	13.48 (0.18)	0.191
Social Disorder (6-30), Mean (SE)	13.86 (0.16)	14.58 (0.26)	13.65 (0.18)	0.003
Years Lived at Current Address, Mean (SE)	15.51 (0.48)	17.17 (0.86)	15.02 (0.56)	0.031
Access to/Use of health care				
Distance to Community Health Centre (Miles), Mean (SE)	0.60 (0.03)	0.56 (0.04)	0.61 (0.03)	0.200
Distance to Acute Care Hospital (Miles), Mean (SE)	1.24 (0.04)	1.24 (0.06)	1.24 (0.05)	0.958

	Overall N=2,764	Type 2 Diabetes N=892	No Type 2 Diabetes N=1872	*P*-value
Distance to Any Health Care Centre (Miles) , Mean (SE)	0.53 (0.03)	0.49 (0.04)	0.54 (0.03)	0.326
Usual Source of Care	2714 (98.75%)	880 (98.48%)	1834 (98.82%)	0.651
Difficulty in Traveling to Health Care Provider				
Very difficult	54 (1.67%)	22 (1.96%)	32 (1.58%)	0.171
Somewhat difficult	199 (6.62%)	79 (9.26%)	120 (5.84%)	
Not too/Not at all Difficult	477 (17.19%)	181 (19.75%)	296 (16.43%)	
Not at all difficult	2034 (74.52%)	611 (69.02%)	1423 (76.15%)	
Insurance Status				
Private	1001 (51.41%)	218 (33.84%)	783 (56.61%)	< 0.001
Public	1671 (46.03%)	654 (64.14%)	1016 (40.67%)	
None	92 (2.56%)	20 (2.02%)	73 (2.72%)	
Visits to Health Care Provider in the past year				
0-1 times	395 (16.71%)	74 (9.49%)	321 (18.85%)	< 0.001
2-6 times	1459 (51.96%)	411 (49.12%)	1048 (52.81%)	
7+ times	910 (31.32%)	407 (41.39%)	503 (28.35%)	
Psychosocial				
Sleep Duration				
< 6 hours	622 (17.53%)	259 (27.98%)	363 (14.44%)	< 0.001
6-9 hours	2097 (81.28%)	617 (69.96%)	1480 (84.62%)	
> 9 hours	45 (1.19%)	17 (2.06%)	28 (0.93%)	
Major Life Events (0 to 10), Mean (SE)	0.60 (0.03)	0.68 (0.05)	0.57 (0.03)	0.080
Sense of Control (-16 to 16), Mean (SE)	0.72 (0.02)	0.61 (0.03)	0.76 (0.02)	< 0.001
Lifestyle/Behavioural Influences				
Dietary Influences				
< 1500 mg Sodium	615 (15.16%)	216 (18.03%)	399 (14.31%)	0.144
3-4 Servings of Vegetables	276 (12.47%)	83 (9.84%)	194 (13.25%)	0.239
2-3 Servings of Fruit	382 (18.09%)	114 (15.60%)	268 (18.83%)	0.299
2-3 Servings of Meat/Beans	588 (23.07%)	187 (19.96%)	401 (23.98%)	0.204
6-11 Servings of Grain	400 (18.99%)	111 (14.22%)	289 (20.39%)	0.051
25-30 g of Fibre	171 (7.17%)	51 (5.28%)	120 (7.73%)	0.172
< 14 g Saturated Fat	1040 (29.19%)	352 (31.29%)	688 (28.58%)	0.435
FFQ Score (0-7), Mean (SE)	1.24 (0.03)	1.14 (0.07)	1.27 (0.04)	0.092
Total Kcal, Mean (SE)	1745.4 (32.02)	1685.1 (79.47)	1763.2 (34.47)	0.370
Physical activity				

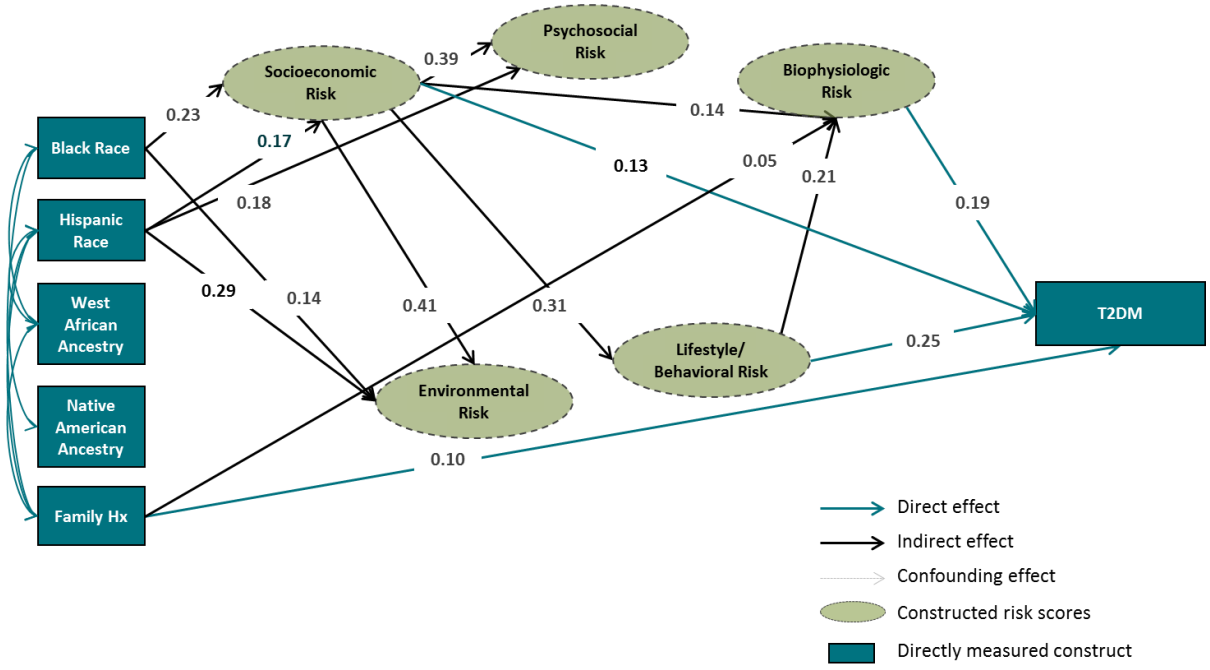
	Overall N=2,764	Type 2 Diabetes N=892	No Type 2 Diabetes N=1872	*P*-value
Low	1132 (33.21%)	480 (47.31%)	652 (29.03%)	< 0.001
Medium	1286 (50.51%)	337 (39.80%)	949 (53.68%)	
High	346 (16.28%)	76 (12.89%)	270 (17.29%)	
BMI, Mean (SE)	29.42 (0.22)	32.63 (0.42)	28.47 (0.22)	< 0.001
Waist Circumference (cm), Mean (SE)	97.05 (0.54)	106.58 (1.09)	94.23 (0.55)	< 0.001
Body Fat %, Mean (SE)	33.96 (0.32)	36.74 (0.57)	33.13 (0.37)	< 0.001
Smoking History				
Never	1220 (44.25%)	373 (37.55%)	847 (46.22%)	0.014
Former	1015 (38.80%)	346 (39.62%)	669 (38.56%)	
Current	529 (16.95%)	173 (22.83%)	356 (15.21%)	
Biophysiological Influences				
SBP, Mean (SE)	130.57 (0.61)	138.83 (1.32)	128.13 (0.66)	< 0.001
DBP, Mean (SE)	80.38 (0.37)	81.86 (0.79)	79.94 (0.43)	0.034
Total Cholesterol, Mean (SE)	187.03 (1.29)	176.10 (2.31)	190.26 (1.45)	< 0.001
HDL Cholesterol, Mean (SE)	54.89 (0.68)	50.39 (1.00)	56.22 (0.82)	< 0.001
Triglycerides, Mean (SE)	129.05 (3.88)	148.94 (5.87)	123.17 (4.67)	< 0.001
Hypertension	2110 (70.16%)	805 (89.44%)	1305 (64.46%)	< 0.001
Cardiovascular Disease	604 (16.09%)	315 (32.66%)	289 (11.19%)	< 0.001
Women Only				
Menopausal Status				
Pre/Peri- menopause	437 (36.63%)	67 (16.14%)	370 (41.90%)	< 0.001
Post-menopause	740 (36.79%)	241 (40.54%)	499 (35.83%)	
Undetermined/Other	569 (26.57%)	240 (43.33%)	329 (22.27%)	
Gestational Diabetes	125 (5.93%)	72 (17.07%)	54 (3.07%)	< 0.001

[1] n and column percent presented for categorical variables, *P*-value from a chi-squared test
[2] Mean and standard error presented for continuous variables, *P*-value from a t-test
CT= Census Tract

Using the results of the race/ethnic-, gender-, and age-adjusted models (**Table 7-3**), we identified 24 variables within the 5 mediating domains that were associated with T2DM prevalence and/or racial/ethnic disparities in T2DM (**Table 7-1**). This produced risk scores with the following ranges and means: socioeconomic (0-10, 4.3), environmental (0-1, 41.2%), psychosocial (0-5, 1.7), lifestyle/behavioural (0-8, 3.2), and biophysiological (0-11, 2.7).

The SEM specified in **Figure 7-1** fit the data well. Age and gender had direct effects on almost all factors with the exception of environmental risk. For simplicity, age and gender effects and non-significant pathways ($p \geq 0.05$) are not presented in **Figure 2** (full results are available in **eTable 2**). The lifestyle/behavioural domain was the largest direct predictor of T2DM status (sβ=0.25, $p<0.001$) followed by biophysiologic factors (0.19, $p<0.001$), socioeconomic factors (0.13, $p=0.003$), and family history of diabetes (0.10, $p=0.005$). There was a marginal direct effect of self-identified race/ethnicity on T2DM prevalence (Black, 0.18, $p=0.054$; Hispanic, 0.10, $p=0.069$). The standardized coefficients represented in **Figure 7-2** can be interpreted as a one standard deviation difference in the predictor (i.e. lifestyle/behavioural risk) is associated with a 0.25 standard deviation difference in the outcome (i.e. T2DM). Unstandardized coefficients are available online (Standardized coefficients (StdYX and StdY) are presented in the main body of the paper. However, unstandardized coefficients may be useful as well. All standardized and unstandardized coefficients are available in **Table 7-4,** below. The unstandardized coefficients may be interpreted in the typical manner: as a logistic regression coefficient for a binary outcome (environmental risk and T2DM) or as a linear regression coefficient for a continuous outcome (all other outcomes). For example, the unstandardized coefficients suggest that for every one unit increase in the lifestyle/behavioural risk score the odds of T2DM increase 35% (OR=1.35) and for every one unit increase in the biophysiological risk score the odds increase 29% (OR=1.29).

Figure 7-2. Final Structural Equation Model of Factors in the Pathway from Race/Ethnicity to T2DM



	Total Effect of Race/ Ethnicity	Direct Effect of Race/ Ethnicity	% Mediated by				
			Socio-economic Factors	Environ-mental Factors	Psycho-social Factors	Lifestyle/ Behavioural Factors	Bio-physiological Factors
Black	0.29	0.18	21.8%	1.3%	0.0%	11.21%	4.6%
Hispanic	0.18	0.10	26.2%	4.3%	5.0%	5.77%	4.6%

Self-identified Black race had a significant direct effect on socioeconomic risk (sβ=0.23, *p*=0.003) and environmental risk (0.14, *p*=0.001) only. There was no direct effect of self-identified Black race on psychosocial, lifestyle/behavioural, biophysiological risk, or T2DM. However, Black race has an indirect effect on these outcomes through socioeconomic factors. Socioeconomic risk is 43.3%

mediated by lifestyle/behavioural risk. The mediation analysis (**Figure 7-2**) indicate that 38.9% of total effect of Black race was mediated by the socioeconomic, environmental, psychosocial, lifestyle/behavioural risk scores with 21.8% of the total effect of Black race being explained by socioeconomic risk.

Self-identified Hispanic ethnicity had a significant direct effect on socioeconomic risk (0.17, $p<0.001$), environmental risk (0.29, $p<0.001$), and psychosocial risk (0.17, $p=0.04$). There was no significant direct effect of Hispanic ethnicity on lifestyle/behavioural risk, biophysiological risk, or T2DM. Mediation analyses indicate that 45.7% of total effect of Hispanic ethnicity was explained by the calculated risk scores. Again, the largest mediator, 26.2%, was the socioeconomic risk score.

Despite the considerable differences in BGA among type 2 diabetics versus non-diabetics in the bivariate results (**Table 7-2**), neither West African Ancestry (OR=1.02, $p=0.658$) nor Native American ancestry (OR=0.94, $p=0.428$*)* contributed to T2DM once self-identified race/ethnicity was included in the model (**Table 7-3**). The final SEM also indicated that there was no significant direct effect of West African (-0.003, $p=0.069$*)* or Native American ancestry (-0.016, $p=0.725$) on T2DM once self-identified race/ethnicity was accounted for.

7.2.5 Conclusions

To our knowledge, this study presents the first examination of a multilevel risk model aimed at explaining racial/ethnic disparities in T2DM. While many authors have proposed similar conceptual frameworks with the aim of understanding and eliminating health disparities,[419, 555, 566] to our knowledge the BACH study is the first survey to amass this data and test this model of health

disparities in T2DM in a community-based population with adequate numbers of Black, Hispanic, and White participants.

Under our conceptual framework, biophysiological and individual lifestyle/behavioural factors were considered more proximate to T2DM. The data supported this temporality as individual lifestyle/behavioural risk had the largest direct effect on T2DM and biophysiological risk the second largest direct effect. However, the mediation analyses indicate that only 5% and 11% of the total effect of Black race can be explained by excess biophysiological and lifestyle/behavioural risk, respectively. Among Hispanic participants, the % mediated was even lower. The mediation analyses indicate that the largest explainable proportion of the excess proportion of T2DM among Black and Hispanic participants is attributable to socioeconomic risk. The socioeconomic risk score developed, which is a composite of household income, education, occupation, immigration status, acculturation, health literacy, insurance status and utilization of health care explains 22% of the excess odds of T2DM among Black and 26% of the excess odds among Hispanic participants. The statistical analyses indicate that while much of the excess odds of T2DM among Blacks and Hispanics remains unexplained (61% and 54%, respectively), adverse socioeconomic conditions explains the largest explainable proportion of racial/ethnic disparities in T2DM.

Our data, supported by our previous findings,[567] suggest that the effects of BGA on T2DM are attenuated with further adjustment for self-identified race/ethnicity and nearly eliminated when socioeconomic and lifestyle/behavioural pathways are considered. This finding is supported by several studies.[36, 37, 79] However, other studies have found the effect of BGA on T2DM to be more robust to adjustment,[37, 80, 81] including research from the BACH study which demonstrate that the

effect of BGA on prediabetic illness may be robust to adjustment for social factors.[82] Race and ethnicity are complex multidimensional constructs reflecting biogeographic origin, biological factors, as well as social, cultural, and economic factors. [69] Our findings suggest that while BGA may be associated with T2DM, it is likely that the social, cultural, and economic facets of race/ethnicity may better explain T2DM disparities in the BACH study.

Family history of diabetes, which may have a genetic component, but may also be the result of similar socioeconomic, environmental, psychosocial, lifestyle, and biophysiological risk profiles between parent and offspring, had a modest direct effect of T2DM prevalence (0.10, p=0.005) and was highly associated with race/ethnicity.

While race/ethnicity had no direct effect on lifestyle/behavioural risk, it is important to note that socioeconomic risk, which was highly associated with race/ethnicity, did have a significant direct effect on lifestyle/behavioural risk. Overall, lifestyle/behavioural risk explained 43.3% of the socioeconomic effect on T2DM. Studies that aim to assess the role of lifestyle and behavioural factors on the socioeconomic gradient of health in T2DM have found similar results. For example, the Whitehall II cohort study found that lifestyle/behavioural factors accounted for 33-45% of the socioeconomic gradient in T2DM.[373]

Each domain of the conceptual model presented here suggests a particular structural intervention. Increased socioeconomic risk suggests policy interventions affecting social conditions; environmental risk--community intervention; psychosocial risk--primary prevention aimed at reducing psychological strain and increasing coping mechanisms; lifestyle/behavioural risk--primary prevention directed at increasing healthy behaviours and decreasing unhealthy behaviours; and

biophysiological risk--secondary prevention efforts aimed at stopping/slowing the progression of disease. The results of these analyses, as well as the results of several trials,[568] suggest that interventions targeting lifestyle/behavioural and biophysiologic risk may reduce T2DM risk overall. However, the results presented here demonstrate that interventions aimed at reducing disparities may need to target socioeconomic risk factors in order to lessen the racial/ethnic divide.

Strengths and limitations

A substantial limitation to this analysis is the cross-sectional design. One-time measurement of health behaviours may underestimate their contribution. Life-course and repeated measures designs have shown to increase the proportion of social inequalities that can be explained by potential modifiable risk factors.

Second, although the sample is geographically limited to Boston, Massachusetts, the BACH Survey sample has been compared to other large regional (Behavioral Risk Factor Surveillance System) and national (the National Health and Nutrition Examination Survey) on a number of socio-demographic and health-related variables. The results suggest that the BACH Survey estimates of key health conditions are comparable with national trends.[437]

Third, although we measured BGA markers, which are thought to estimate the genetic contribution to increased diabetes prevalence in certain populations, we do not have comprehensive markers of genetic risk. We therefore cannot make conclusions regarding genetic contributors to racial/ethnic disparities in T2DM.

The key strengths of this study stem from the community-based, stratified, random sample design of the BACH Survey which provided a large cohort of Black, Hispanic, and White men and women. Since this study was designed to test this specific conceptual model of disparities, validated scales with published metrics measuring the constructs of interest were used wherever available (**Section 7.3.1**). Finally, unlike many studies of T2DM, we did not rely solely on self-report for T2DM status. Participants were contacted in the morning in their home, giving a more accurate prevalence of T2DM.

Conclusions

Our study found that while lifestyle/behavioural and biophysiologic risk factors had the greatest direct effect on T2DM risk, socioeconomic factors had the greatest impact on explaining racial/ethnic disparities in T2DM.

7.3 Supplementary Materials

7.3.1 Measures

7.3.1.1 Race/ethnicity

Race/ethnicity was self-reported by survey participants according to two separate survey questions: "Do you consider yourself to be Spanish, Hispanic, or Latino (Latina)?" and "What do you consider yourself to be? Select one or more of the following" with response categories of American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White or Caucasian, and Other (Specify). These questions are the standard used in the United States as recommended by the Office of Management and Budget.[423] The racial/ethnic labels used in this research are 1) non-Hispanic Black (Black), 2) Hispanic of any race (Hispanic), and 3) non-Hispanic White (White).

7.3.1.2 Socio-economic Influences

As mentioned in **Section 2.6**, in this thesis social determinants are defined as factors that involve a person's relationships to other people. This includes social and economic structures of society (i.e. socioeconomic status) as well as acculturation, discrimination, health literacy, and access to health care. In the conceptual model of this thesis (**Figure 3-1**) acculturation and discrimination were separated from SES. Higher levels of acculturation have been associated with T2DM and it is hypothesized that higher SES may be a key mediator of this pathway. Poverty, low SES and lower social capitol may be causes for everyday discrimination in addition to, or independent of, race/ethnicity. In the development of the latent constructs (see **Section 7.3.2.3**), acculturation and

discrimination were captured as part of the socioeconomic domain although the exploratory factor analysis indicated they could considered as individual factors. Nonetheless, when the risk scores were developed, these constructs were captured within the socioeconomic risk score. Despite their temporality and complex interplay with SES, these factors are socio-economic constructs defined by relationships with other people and within one's culture.

Socioeconomic Status (SES)

The individual SES indicators considered were: household income, educational attainment and occupation. Household income, originally grouped into 12 ordinal categories, was collapsed into the following three categories of US dollars: <20,000, 20-49,999, and ≥50,000. Educational attainment was categorized as less than high school, high school graduate or equivalent, some college, and college or advanced degree were combined due to smaller numbers. Current or former occupation was categorized into four groups: (1) management, professional, sales and office occupations; (2) service occupations; (3) manual labour which includes construction, maintenance, farming, production, and transportation occupations; and (4) never worked. We use the broader term 'SES' when referring to these three distinct socioeconomic factors in the aggregate, all of which are strongly related to overall health.[529]

Discrimination

We measured perceptions of everyday discrimination using the Every Discrimination Scale (Short Version), a five item scale that attempts to measure chronic and/or routine experiences of unfair treatment without direct reference to the influence of race and a four item scale that measures the influence .[556] Metrics on this scale have been published previously.[556] The five items capture the

frequency of the following experiences in the day-to-day lives of the participants: being treated with less courtesy than others; less respect than others; receiving poorer service than others in restaurants or stores; people acting as if you are not smart; they are afraid of you; and being threatened or harassed. Scores for each item ranged from 0 to 5 with 0 indicating the event never occurred and 5 indicating an almost every day occurrence. Scores for the total scale ranged from 0 to 45, with a high score indicating greater perceived discrimination.

Acculturation

The Bidimensional Acculturation Scale (BAS) was used to assess the extent to which the individuals participate in the cultural domains of both their original culture and the culture of contact. The domains assessed are language use, language proficiency, and electronic media. The BAS has been tested in several Hispanic populations (Central and Mexican Americans populations) and correlates well with generational status, length of residence in the US, and ethnic self-identification.[427]

Health Literacy

To measure health literacy, we used the abbreviated form of the s-TOFHLA, Spanish or English version.[569] The abbreviated s-TOFHLA is a 36-item, timed reading comprehension test. Every fifth to seventh word in a reading passage is omitted, and 4 multiple-choice options are provided. The abbreviated s-TOFHLA contains two health care passages. The abbreviated s-TOFHLA is scored on a scale of 0 to 36. Using established convention, we categorized patients
as having inadequate health literacy if the s-TOFHLA score was 0 to 16, marginal health literacy if it was 17 to 22, and adequate health literacy if it was 23 to 36.

Access to Health Care

Type of health insurance (public or private), number of visits to a health care provider in the past year and spatial access to health care (assessed by distance to the closest community health centre, acute care hospital, or health care centre of either kind (miles)) were considered to be socioeconomic and environmental factors, respectively. While most would argue that number of visits to a health care provider in the past year would be influenced by the diagnosis of T2DM, rather than vice-versa, the case can be made that visits to a provider could influence the diagnosis of T2DM. Limited access to health care as measured by lack of insurance, visits to a health care provider in the past year, and routine patterns of health care utilization are associated with undiagnosed diabetes.[390] Diabetes may be identified anywhere along the spectrum from a "low-risk" individual who has a random glucose test, to a higher-risk individual who is tested due to suspicion of diabetes, to the symptomatic individual.[21] Essentially, the greater the visits to a health care provider, the greater the chance that a "missed patient" may be caught. Furthermore, data from a factorial experiment examining the effect of patient race/ethnicity on diabetes diagnosis demonstrated that even when presenting with the same signs and symptoms, a "missed diagnosis" of diabetes was patterned on race/ethnicity.[434]

7.3.1.3 Environmental Influences

Neighbourhood Socioeconomic Status (SES)

Census-tract (neighbourhood) SES was based on methods used by Diez-Roux. [431] A composite index Z-score was created for census tract based on six measures including: log median household income; log median value of owner occupied housing; percent of household receiving interest, dividend or

net rental income; percent of adults 25 and over with high school degree; percent of adults 25 and over with a college degree; and percent of individuals ages 16 and over in management and professional occupations. An increasing score signifies increasing neighbourhood socioeconomic advantage. Census tracts were designated as low, middle, or high SES according to the tertiles of the z-score.[263]

Safety

Crime incident reports provided by the Boston Police Department were downloaded from the City of Boston website at https://data.cityofboston.gov/. Data was coded using conventions described by others.[525] The property crime rates in 2010-2011 were calculated as the number of offenses of burglary, larceny, and motor vehicle theft per 1,000 population. Violent crime was calculated as murder, robbery, and assault (including sexual assault) per 1,000 population.

Built Environment

We used ArcGIS (Environmental Systems Research Institute, Redlands, CA) to draw circular buffers with 3 different radii (0.25mi, 0.5mi, and 1.0 miles) centred at each research participant's residence. A distance of 0.25 mi is approximately a 5 minute walk which has been estimated to be the average distance walked to a grocery store in large metropolitan cities with available public transit.[570] The food stores within each radius were categorized as supermarkets, grocery stores, fast food, and convenience stores. Information on food establishments located in the Boston metro area were purchased from InfoUSA Inc., a proprietary information service. Supermarkets and grocery stores were identified by a primary SIC code of 541105. Following precedents set by previous work,[526] supermarkets were differentiated from grocery stores on the basis of chain name recognition or annual payroll of greater than 50 employees. Convenience stores were identified as businesses with

a primary or secondary SIC code of 541102 or 541103. Following standards set by other researchers[527] fast food restaurants including restaurants, delicatessens, pizza shops and coffee shops (SIC codes: 581206,07,08,09,14,19,22,24,28) had to meet the following criteria: 1) be a franchised vendor, 2) ability to purchase food without wait staff, and 3) sale of both food and beverage. To ensure that our database was both comprehensive and appropriate for Boston, we gathered information on fast-food restaurants in the city from several other sources. In addition to the InfoUSA list, we also referred to a privately run Web site, Fast Food Source (http://www.fastfoodsource.com), to identify fast-food restaurants in Boston. We thus defined food environment exposures into three category measures defined as high access (<0.25 miles), medium (0.25-0.50 miles), and low access (>0.50 miles) to convenience stores, grocery stores, supermarkets, and fast food.

Neighbourhood disorder

Social and physical neighbourhood order and disorder were measured using the "Perceived Neighbourhood Disorder" scale developed by Ross and Mirowsky.[528] Social disorder refers to people hanging around on the streets, drug and alcohol use, trouble with neighbours, and a general perception of lack of safety. Physical disorder refers to graffiti, vandalism, abandoned buildings, cleanliness, and maintenance of homes and apartments. The physical and social disorder indices were created by reverse coding "order" items and summing the six items in each subscale with higher scores indicating higher perceived disorder.[182, 430] Number of years at current address was used to assess residential mobility and was considered as a potential mediator between neighbourhood determinants and downstream health effects.

Access to health care

The locations of community health centres and acute care hospitals were obtained from the Massachusetts Office of Geographic Information (MassGIS).[571] Distance to the closest community health centre, acute care hospital, and community health centre or hospital were calculated in miles. In addition, we assessed whether the participants had a usual source of care (Yes/No) and their perceived difficulty in getting to their primary care provider (Very/Somewhat/Not too/Not at all difficult).

7.3.1.4 Psychosocial Influences

Sleep

Hours of sleep each night was captured continuously and categorized as <6, 6-9, >9 hours over the referent period of the past month.

Sense of Control

The Mirowsky and Ross sense of control index[429] contains 8 items that assess internal sense of control over positive and negative outcomes (e.g. "I am responsible for my own successes" [positive] and "I am responsible for my failures" [negative]) as well as a sense of powerlessness over positive and negative outcomes (e.g. "the really good things that happen to me are mostly luck" [positive] and "most of my problems are due to bad breaks" [negative]). This 2x2 design eliminates defence and agreement bias from the measure. All items are coded -2 to 2 (external items are reverse coded). The sense of control score is calculated as the sum of the responses to the 8 items, and ranges from maximally denying (−16) to maximally claiming control (+16). Metrics for this scale on Black and White populations indicate high test-retest reliability and robust confirmatory factor analysis validation. [182, 572]

7.3.1.5 Lifestyle/behavioural influences

Dietary patterns

Participants completed the self-administered Block Food Frequency Questionnaire (FFQ) in English or Spanish. This FFQ has been validated to obtain data on usual dietary intake over the past year.[558] Based upon the USDA and AHA guidelines for healthy eating,[535] we calculated a healthy eating score composed of FFQ data on average daily intake of sodium, vegetables, fruits, meats/beans, grains, fibre and saturated fat. The healthy eating score was adjusted for total kilocalories.

7.3.2 Supplementary Analyses

7.3.2.1 Risk Score Creation

Table 7-3, below, presents the race/ethnicity-, age-, and gender-adjusted models. These results were used to create the weighted scoring system presented in the paper above. Variables that did not either (1) meet a minimal criterion for association with T2DM ($p < 0.10$) or (2) reduce the race/ethnic effect (OR) by 10% were not included in the domain risk score. For categorical variables, we created a weighted scoring system by rounding up all regression coefficients (ln(OR)) to the nearest integer. For continuous variables, risk was based on clinically accepted "high risk" criteria (see **Table 7-1** for citations). If clinically accepted criteria were not available, tertiles were used. Following the construction of the final model all variables were added in the model singly to ensure their effects were adequately captured by the risk scores.

Table 7-3. Results from logistic regression models (each potential variable added one at a time to race/ethnicity, age, and gender model)

	Odds Ratio (OR) (95% CI)	p-value	Black vs. White OR (95% CI)[1]	Hispanic vs. White OR (95% CI)[1]	Score Assigned
Base Model (age, gender adjusted)			**2.86 (1.96, 4.19)**	**1.98 (1.34, 2.94)**	
Genetic Influences					
West African Ancestry	1.02 (0.92, 1.14)	0.658	**2.44 (1.09, 5.46)**	**2.10 (1.18, 3.76)**	N/A[2]
Native American Ancestry	0.94 (0.79, 1.10)	0.428	**2.44 (1.09, 5.46)**	**2.10 (1.18, 3.76)**	N/A[2]
Family History of Diabetes	2.11 (1.54, 2.90)	<0.001	**2.51 (1.71, 3.69)**	**1.80 (1.21, 2.69)**	N/A[2]
Socio-economic Influences					
Income			**2.30 (1.56, 3.39)**	**1.34 (0.87, 2.06)**	
<$20,000	3.13 (2.08, 4.71)	< 0.001			2
$20,000-$49,999	1.63 (1.06, 2.51)				1
≥ $50,000	Reference				0
Education			**1.94 (1.30, 2.88)**	**1.06 (0.68, 1.65)**	
Less than high school	4.56 (2.74, 7.61)	< 0.001			2
High school or GED	2.60 (1.75, 3.86)				1
Some college	1.93 (1.22, 3.05)				1
College or advanced degree	Reference				0
Occupation			**2.59 (1.77, 3.80)**	**1.54 (1.01, 2.35)**	
Professional	Reference	0.005			0
Service	1.34 (0.91, 1.99)				0
Manual labour	1.78 (1.15, 2.76)				1
Never worked	2.23 (1.28, 3.89)				1
Discrimination (log transformed)	1.03 (0.89, 1.21)	0.667	2.82 (1.92, 4.16)	2.00 (1.35, 2.96)	--
Born in US (Yes vs. No)	1.10 (0.68, 1.76)	0.705	2.89 (1.95, 4.27)	**2.14 (1.20, 3.79)**	1*
Acculturation			2.88 (1.96, 4.21)	**1.68 (0.94, 2.99)**	
Low	Ref	0.396			0
High/Bicultural	1.35 (0.67, 2.72)				1*

	Odds Ratio (OR) (95% CI)	p-value	Black vs. White OR (95% CI)[1]	Hispanic vs. White OR (95% CI)[1]	Score Assigned
Health Literacy			**2.46 (1.67, 3.63**)	**1.40 (0.90, 2.18)**	
Inadequate	2.06 (1.33, 3.19)	0.002			1
Marginal	1.81 (1.10, 2.96)				1
Adequate	Ref				0
Access to/Use of health care					
Insurance Status			**2.56 (1.74, 3.77)**	**1.71 (1.14, 2.56)**	
Private	0.87 (0.33, 2.29)	0.004			0
Public	1.69 (0.63, 4.54)				1
Other	Ref				0
Visits to HCP in the past year			2.94 (2.00, 4.33)	2.06 (1.39, 3.06)	
0-1	0.37 (0.23, 0.62)	< 0.001			0
2-6	0.62 (0.45, 0.86)				0
7+	Ref				1
Environmental Influences (random intercept models)			**2.89 (2.08, 4.01)**	**2.53 (1.86, 3.45)**	
CT SES			2.71 (1.91, 3.83)	2.39 (1.72, 3.30)	
Low	1.27 (0.89, 1.82)	*0.193*			--
Middle	1.18 (0.83, 1.68)	*0.356*			--
High	*Reference*				--
CT Poverty			**2.63 (1.84, 3.75)**	**2.29 (1.65, 3.19)**	
< 5%	*Reference*				0
5-9.9%	1.73 (0.88, 3.39)	*0.109*			0
10-19.9%	1.15 (0.62, 2.13)	0.648			0
≥ 20%	1.72 (0.93, 3.18)	0.086			1
CT Racial Composition					
% Black (log transformed)	1.04 (0.92, 1.18)	0.494	2.73 (1.86, 4.02)	2.45 (1.76, 3.41)	--
% White (log transformed)	0.95 (0.82, 1.10)	0.484	2.74 (1.87, 4.00)	2.45 (1.77, 3.40)	--

	Odds Ratio (OR) (95% CI)	**p-value**	**Black vs. White OR (95% CI)[1]**	**Hispanic vs. White OR (95% CI)[1]**	Score Assigned
% Hispanic (log transformed)	1.09 (0.92, 1.29)	0.324	2.82 (2.02, 3.92)	2.42 (1.75, 3.35)	--
Property crime (log transformed)	1.11 (0.86, 1.43)	0.419	2.82 (2.02, 3.94)	2.48 (1.81, 3.40)	--
Violent crime (log transformed)	1.16 (0.94, 1.43)	0.169	2.72 (1.93, 3.82)	2.42 (1.76, 3.33)	--
Access to Supermarkets			2.91 (2.10, 4.03)	2.53 (1.86, 3.45)	--
Low Access (> 0.5 miles)	0.76 (0.53, 1.08)	0.169			--
Medium Access (0.25-0.5 miles)	0.77 (0.52, 1.12)	0.169			--
High Access (< 0.25 miles)	*Reference*				--
Access to Grocery Stores			2.90 (2.09, 4.03)	2.50 (1.83, 3.41)	--
Low Access (> 0.5 miles)	0.69 (0.43, 1.10)	0.121			--
Medium Access (0.25-0.5 miles)	0.88 (0.68, 1.14)	0.331			--
High Access (< 0.25 miles)	*Reference*				--
Access to Convenience Stores			2.89 (2.08, 4.01)	2.50 (1.83, 3.42)	--
Low Access (> 0.5 miles)	0.94 (0.56, 1.56)	0.804			--
Medium Access (0.25-0.5 miles)	0.81 (0.60, 1.09)	0.159			--
High Access (< 0.25 miles)	*Reference*				--
Access to Fast Food			2.93 (2.11, 4.06)	2.54 (1.87, 3.45)	--
Low Access (> 0.5 miles)	0.80 (0.59, 1.08)	0.15			--
Medium Access (0.25-0.5 miles)	0.95 (0.72, 1.26)	0.739			--
High Access (< 0.25 miles)	*Reference*				--
CT % Open Space			2.85 (2.05, 3.95)	2.52 (1.85, 3.43)	--
≤ 5%	1.14 (0.73, 1.78)	0.57			--
5.1-10%	0.94 (0.57, 1.53)	0.798			--
10.1-20%	1.11 (0.67, 1.85)	0.678			--
> 20%	*Reference*				--
Neighbourhood Disorder			2.78 (2.00, 3.87)	2.45 (1.80, 3.35)	
Social (log transformed)	1.09 (0.58, 2.05)	0.79			--
Physical (log transformed)	1.37 (0.79, 2.38)	0.26			--

	Odds Ratio (OR) (95% CI)	p-value	Black vs. White OR (95% CI)[1]	Hispanic vs. White OR (95% CI)[1]	Score Assigned
Years Lived at Current Address (log transformed)	0.90 (0.78, 1.04)	0.16	2.79 (2.01, 3.88)	2.39 (1.74, 3.29)	--
Access to Community Health Centre (miles)	0.96 (0.66, 1.41)	0.851	2.84 (1.94, 4.15)	1.97 (1.32, 2.93)	--
Psychosocial Influences					
Sleep Duration			**2.57 (1.74, 3.80)**	**1.83 (1.21, 2.76)**	
< 6	2.07 (1.45, 2.96)	< 0.001			1
6-9	Ref				0
> 9	3.32 (0.92, 11.95)				2
Major Life Events (log transformed)	1.18 (0.83, 1.69)	0.349	2.82 (1.93, 4.11)	1.97 (1.32, 2.92)	1 (> 1 MLE)
Sense of Control	0.63 (0.45, 0.87)	0.006	2.83 (1.93, 4.14)	**1.68 (1.10, 2.56)**	1 (< 1.0), 2 (< 0.43)
Lifestyle/Behavioural Influences					
Dietary Influences[2]					
< 1500 mg Sodium	0.91 (0.55, 1.51)	0.702	2.84 (1.93, 4.17)	1.94 (1.30, 2.88)	--
3-4 Servings of Vegetables	0.72 (0.39, 1.33)	0.293	2.80 (1.91, 4.12)	**1.87 (1.25, 2.79)**	--
2-3 Servings of Fruit	0.96 (0.61, 1.51)	0.845	2.81 (1.90, 4.14)	1.91 (1.28, 2.84)	--
2-3 Servings of Meat/Beans	0.87 (0.58, 1.28)	0.470	2.81 (1.91, 4.13)	1.92 (1.30, 2.85)	--
6-11 Servings of Grain	0.77 (0.47, 1.27)	0.301	2.78 (1.88, 4.10)	1.91 (1.28, 2.85)	--
25-30 g of Fibre	0.82 (0.44, 1.53)	0.529	2.80 (1.91, 4.11)	1.92 (1.29, 2.85)	--
< 14 g Saturated Fat	0.84 (0.55, 1.28)	0.422	2.84 (1.93, 4.18)	1.96 (1.33, 2.90)	--
FFQ Score (log)	0.70 (0.48, 1.03)	0.068	2.80 (1.90, 4.11)	1.97 (1.33, 2.91)	--
Total Kcal (log)	0.87 (0.65, 1.17)	0.357	2.82 (1.92, 4.14)	1.92 (1.29, 2.85)	--
Physical activity			2.83 (1.92, 4.15)	1.91 (1.28, 2.84)	
Low	1.77 (0.99, 3.17)	0.004			1
Medium	1.00 (0.59, 1.72)				0

	Odds Ratio (OR) (95% CI)	p-value	Black vs. White OR (95% CI)[1]	Hispanic vs. White OR (95% CI)[1]	Score Assigned
High	Ref				0
Smoking status			2.73 (1.87, 3.99)	1.96 (1.32, 2.91)	
Never	Ref	0.014			0
Former	1.03 (0.73, 1.47)				0
Current	1.81 (1.19, 2.75)				1
BMI (log transformed)	31.42 (14.07, 70.15)	< 0.001	**2.51 (1.68, 3.77)**	**1.88 (1.25, 2.84)**	1 (25-29), 2 (30-39), 3 (> 40)
Waist Circumference	1.05 (1.04, 1.06)	< 0.001	2.78 (1.86, 4.15)	**2.54 (1.66, 3.87)**	1 (≥ 102 cm, men; ≥ 88 cm, women)
Body Fat %	1.06 (1.04, 1.09)	< 0.001	**2.54 (1.70, 3.80)**	1.91 (1.28, 2.87)	1 (> 25%, men; > 35% women), 2 (> 33%, men; > 42%, women)
Biophysiological Influences					
SBP	1.02 (1.01, 1.03)	< 0.001	**2.50 (1.70, 3.70)**	1.92 (1.29, 2.87)	1 (SBP ≥ 130)
DBP	1.01 (1.00, 1.03)	0.101	2.73 (1.86, 4.00)	1.97 (1.33, 2.93)	1 (DBP ≥ 85)
Total Cholesterol	0.99 (0.98, 0.99)	< 0.001	3.01 (2.05, 4.41)	2.05 (1.37, 3.06)	1 (≥ 200 mg/dL)
HDL Cholesterol	0.97 (0.96, 0.99)	< 0.001	3.00 (2.04, 4.41)	**1.83 (1.22, 2.75)**	1 (< 40 mg/dL, men; < 50 mg/dL women)
Triglycerides	1.00 (1.00, 1.00)	< 0.001	**3.12 (2.14, 4.55)**	1.97 (1.31, 2.95)	1 (≥ 150)
Hypertension	3.21 (1.98, 5.19)	< 0.001	**2.41 (1.64, 3.55)**	1.90 (1.26, 2.85)	1
Cardiovascular Disease	2.86 (1.99, 4.12)	< 0.001	2.72 (1.84, 4.01)	1.92 (1.28, 2.88)	2
Women Only			**3.09 (1.88, 5.09)**	**2.46 (1.48, 4.10)**	
Menopausal Status			**2.83 (1.71, 4.70)**	2.34 (1.39, 3.93)	
Pre/Peri	Reference	0.017			0

	Odds Ratio (OR) (95% CI)	p-value	Black vs. White OR (95% CI)[1]	Hispanic vs. White OR (95% CI)[1]	Score Assigned
Post	2.14 (0.95-4.81)				1
Undetermined/Unknown	3.11 (1.36-7.11)				2
Gestational Diabetes	8.46 (4.03-17.74)	<0.001	**3.34 (1.99, 5.62)**	**2.28 (1.32, 3.93)**	2

[1] **Bold** indicates racial/ethnic effect was reduced by ≥ 10%

[2] Genetic factors were treated as exogenous (not predicted by any other variables in the model) variables and therefore not incorporated into the mediating risk scores

[3] All dietary influences are also adjusted for total kcal

[*] Point was added to risk score due to mediation of the effect of race/ethnicity rather than a direct effect on T2DM

7.3.2.2 Structural Equation Model – Full Results

Standardized coefficients (StdYX and StdY) are presented in the main body of the paper. However, unstandardized coefficients may be useful as well. All standardized and unstandardized coefficients are available in **Table 7-4**, below. The unstandardized coefficients may be interpreted in the typical manner: as a logistic regression coefficient for a binary outcome (environmental risk and T2DM) or as a linear regression coefficient for a continuous outcome (all other outcomes). For example, the unstandardized coefficients suggest that for every one unit increase in the lifestyle/behavioural risk score the odds of T2DM increase 35% (OR=1.35) and for every one unit increase in the biophysiological risk score the odds increase 29% (OR=1.29).

Table 7-4 Final Structural Equation Model of Factors in the Pathway from Race/Ethnicity to T2DM (full standardized and non-standardized results)

Predictor	Outcome	Standardized Coefficient	Unstandardized Coefficient	*p*-value
Black vs. White	Socioeconomic Risk	0.226	0.969	0.003
Hispanic vs. White	Socioeconomic Risk	0.173	0.900	<0.001
West African ancestry	Socioeconomic Risk	0.105	0.057	0.135
Native American ancestry	Socioeconomic Risk	0.008	0.013	0.801
% Black participants[1]	Environmental Risk	0.140	0.269	0.001
% Hispanic participants[1]	Environmental Risk	0.289	0.689	<0.001
West African ancestry	Environmental Risk	ND[2]		
Native American ancestry	Environmental Risk	ND[2]		
Socioeconomic Risk	Environmental Risk	0.410	0.225	<0.001
Black vs. White	Psychosocial Risk	0.003	0.006	0.965
Hispanic vs. White	Psychosocial Risk	0.173	0.496	<0.001

Predictor	Outcome	Standardized Coefficient	Unstandardized Coefficient	*p*-value
West African ancestry	Psychosocial Risk	0.031	0.009	0.653
Native American ancestry	Psychosocial Risk	0.023	0.019	0.477
Socioeconomic Risk	Psychosocial Risk	0.391	0.207	<0.001
Environmental Risk	Psychosocial Risk	0.009	0.008	0.903
Black vs. White	Lifestyle/behavioural Risk	0.113	0.451	0.081
Hispanic vs. White	Lifestyle/behavioural Risk	0.037	0.178	0.369
West African ancestry	Lifestyle/behavioural Risk	-0.034	-0.017	0.605
Native American ancestry	Lifestyle/behavioural Risk	-0.034	-0.051	0.312
Socioeconomic Risk	Lifestyle/behavioural Risk	0.312	0.291	<0.001
Environmental Risk	Lifestyle/behavioural Risk	0.114	0.165	0.178
Psychosocial Risk	Lifestyle/behavioural Risk	0.008	0.014	0.785
Black vs. White	Biophysiologic Risk	0.069	0.259	0.264
Hispanic vs. White	Biophysiologic Risk	0.044	0.200	0.283
West African ancestry	Biophysiologic Risk	-0.072	-0.034	0.218
Native American ancestry	Biophysiologic Risk	0.015	0.021	0.602
Socioeconomic Risk	Biophysiologic Risk	0.136	0.120	<0.001
Environmental Risk	Biophysiologic Risk	0.083	0.116	0.297
Psychosocial Risk	Biophysiologic Risk	0.049	0.082	0.069
Lifestyle/behavioural risk	Biophysiologic Risk	0.205	0.194	<0.001
Family history	Biophysiologic Risk	0.047	0.169	0.056
Black vs. White	T2DM	0.177	0.875	0.054
Hispanic vs. White	T2DM	0.100	0.600	0.069
West African ancestry	T2DM	-0.003	-0.002	0.976
Native American ancestry	T2DM	-0.016	-0.029	0.725
Socioeconomic Risk	T2DM	0.132	0.152	0.003
Environmental Risk	T2DM	-0.022	-0.037	0.861
Psychosocial Risk	T2DM	0.039	0.085	0.283
Lifestyle/behavioural risk	T2DM	0.248	0.306	<0.001
Family history	T2DM	0.102	0.485	0.005
Biophysiologic Risk	T2DM	0.192	0.251	<0.001

[1] The % of Black and Hispanic participants within each census tract were used to predict neighbourhood-level outcomes

[2] ND = Not determined, model would not converge with this path present

7.3.2.3 Alternative Modelling Techniques

The conceptual model presented in **Figure 7-1** would ideally be modelled as a structural equation model using latent constructs to represent the conceptual mediating domains.

The latent variable specification in SEM is typically based on a confirmatory factor analysis (CFA).[573] The use of CFA modelling in SEM encourages the use of validated instruments with simple measurement structures in an *a priori* specified model. Despite the use of validated instruments an *a priori* conceptual model, it was unknown how the measures included in this study would harmonize. For example, could the measures included in the socioeconomic domain be summarized by a single latent factor?

Despite the fact that CFA procedures are often used for exploratory purposes, there are a number of critiques of using these techniques.[574] Therefore, rather than relying on traditional CFA models, we used the exploratory structural equation modelling (ESEM) approach. In the ESEM approach, exploratory factor measurement models with factor loading matrix rotations can be used.[573]

In order to optimize the number of latent constructs within each mediating domain of interest, ESEMs were formulated for a measurement model. Each domain was explored separately, with varying factor sizes, and using geomin rotation.

For the socioeconomic domain ESEMs with one, two, or three latent constructs were explored. The analyses indicated a three-factor exploratory structure fit the data well (**Table 7-5**). The comparative fit index (CFI) = 1.000 and the root mean squared error of approximation (RMSEA) =

0.005. As described in **Section 5.3**, models are said to fit the data well if the RMSEA is 0.08 or less.

Table 7-5. Exploratory Factor Analysis Estimates for the Socioeconomic Domain

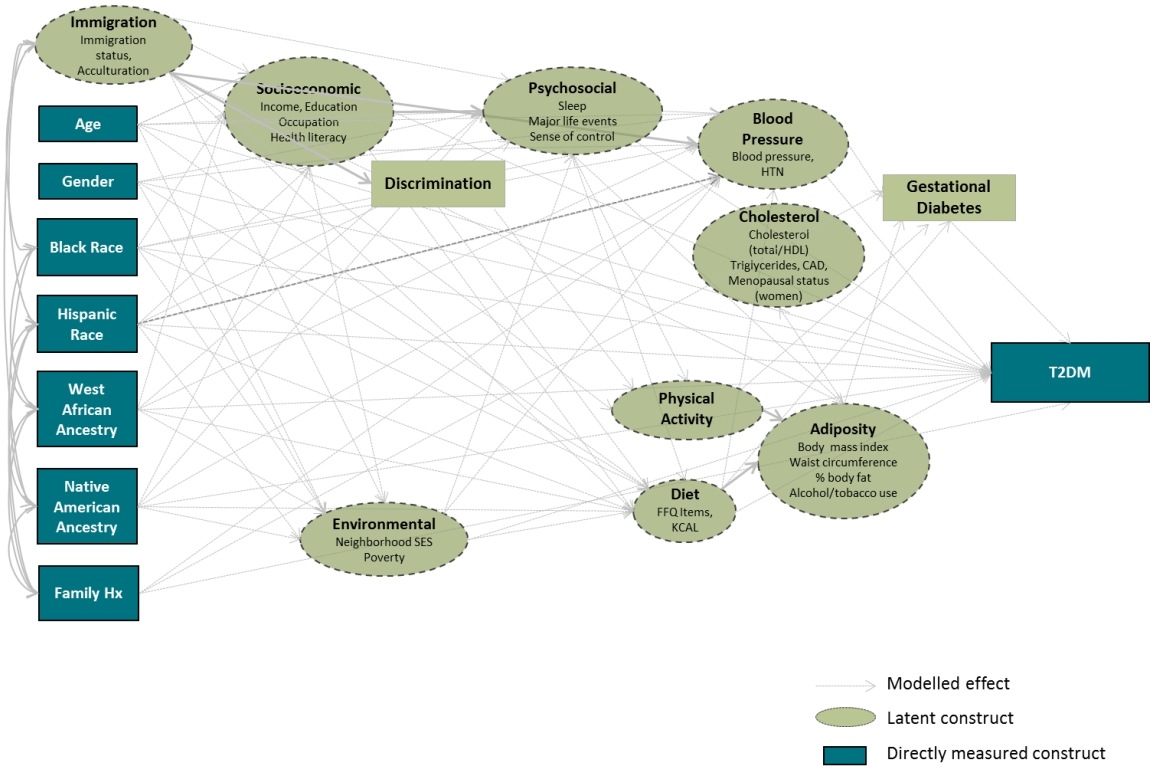
Items	Factor 1 *"Socio-economic"*	Factor 2 *"Immigration"*	Factor 3 *"Discrimination"*
Income	**0.729**	-0.064	0.026
Education	**0.868**	-0.068	-0.031
Occupation*	**0.698**	0.021	0.041
Discrimination	0.000	0.294	**1.150**
Immigration Status	0.000	**1.439**	-0.660
Acculturation*	**0.591**	**0.453**	0.017
Health Literacy	**0.687**	0.111	-0.093

* Reverse coded

The factor loadings presented in **Table 7-5** suggest potential interpretation of the factors in terms of socioeconomic-, immigration-, and discrimination related factors. There was only one notable cross-loading. Acculturation could factor with either the socioeconomic or the immigration domains. In an ESEM the loading estimates are not standardized to item variances and the variances are allowed to vary across items.

The factor loadings and model indices across the other domains indicated: a one factor model for the psychosocial domain (two or higher factor models would not converge), a three factor model for the lifestyle/behavioural domain, a three factor model for the biophysiological domain for women, and a two factor model for men. Given these results the model was revised to accommodate these findings (**Figure 7-3**).

Figure 7-3. Revised Conceptual Model



The full conceptual model as presented in **Figure 7-3** would not converge using structural equation modelling with latent constructs predicted by our measured mediating influences. The following models were attempted in order of decreasing complexity:

- 1-level model removing the environmental influences
- Constructs with low factor loadings were removed
- Psychosocial domain was removed
- SEM with just the socioeconomic and lifestyle/behavioural domains (converged)
- SEM with just the socioeconomic and biophysiologic domains (converged)
- SEM with just the lifestyle/behavioural domains and biophysiologic domains (did not converge)
- SEM with one latent factor for each remaining domain of influence (socioeconomic, lifestyle/behavioural, and biophysiologic) (did not converge)

In conclusion, even greatly simplified models would not converge. This limited the ability to make conclusions regarding the relative contributions of the relevant domains of interest. Therefore, my co-author S.V. Subramanian and I developed the risk score model approach presented in the paper (**Section 7.2**).

There are limitations to the risk score method we developed. The largest limitation is that the risk score approach likely introduces measurement error into the mediating domains in our model. Non-differential measurement error (for a mediator non-differential measurement error is defined as error that is neither associated with the outcome of interest nor the exposure of interest)[575] typically biases estimates towards the null (no association). Therefore, it is likely that the risk score method underestimates the true degree of mediation by the socioeconomic, environmental, psychosocial, lifestyle/behavioural, and biophysiologic domains of interest.

Despite this limitation, there are also benefits to using the risk score approach. The risk scores developed could prove to be useful and intuitive to clinicians. The method used to develop the risk scores mirrors the construction of the American Diabetes Association self-assessment tool[563] and the American Diabetes Association's criteria for testing for diabetes in asymptomatic adults.[21]

To examine the potential impact of our risk score development, I conducted several sensitivity analyses. The outcomes of these sensitivity analyses are presented in **Table 7-6. Sub-table A** demonstrates the standardized coefficient of our risk scores (as described and used in the manuscript) on T2DM directly (each modelled singly) in the column titled **StdYX on T2DM**. The direct effect of Black race and Hispanic race on each risk score, each modelled singly, are

presented in the columns **StdY Black on Domain** and **StdY Hispanic on Domain**. Finally, the direct effect of Black race and Hispanic race on T2DM while the mediating pathway for that risk score, each modelled singly, was controlled are presented (**StdY Black on T2DM** and **StdY Hispanic on T2DM**).

In **Sub-table B**, I developed greatly simplified structural equation models, using only one mediating latent construct at a time. I used the StdY and StdYX for each measured construct on the latent variable (e.g. socioeconomic risk) to create a "risk score." These resulting risk scores were then used in a full structural equation model similar to the model presented in **Figure 7-2**. This allowed for a head-to-head comparison with our results presented in the paper (**Table 7-7**). The greatest differences seen between the risk scores developed in the paper and those developed for the sensitivity analyses are for the psychosocial domain. The latent variable/risk score hybrid approach indicates a greater role for psychosocial influences. This may indicate that our model as presented in the paper may underestimate the true influence of psychosocial risk factors. Despite these results, we proceeded with our initial risk score methodology, as the development of these risk scores may be more valuable to clinicians, since they were based on clinically accepted criteria, and may be more readily interpretable.

In **Sub-table c**, I again developed greatly simplified structural equation models, using only one mediating latent construct at a time. However, no risk construct was created. The results presented indicate the findings using a single latent variable to represent the domain of interest. The results were similar to those demonstrated in **Sub-table B**. And the overall direction and significance of the estimates were in line with **Sub-table A**. The full model would not converge

using latent constructs to represent all domains of interest. Therefore these results are not directly compared to those in **Figure 7-2**.

Table 7-6. Sensitivity analyses comparing risk score methodology to latent variable methodology

a. Method 1 for the development of the risk scores (as described in the manuscript)

	StdYX on T2DM (p-value)	StdY Black on Domain (p-value)	StdY Black on T2DM (p-value)	StdY Hispanic on Domain (p-value)	StdY Hispanic on T2DM (p-value)	R^2
Socioeconomic	0.24 (< 0.001)	0.22 (0.002)	0.24 (0.01)	0.41 (<0.001)	0.08 (0.18)	0.27
Environmental[1]	0.17 (0.09)	0.41[2] (<0.001)	0.24 (0.009)	0.48[2] (<0.001)	0.14 (0.01)	0.24
Psychosocial	0.14 (0.001)	0.09 (0.22)	0.29 (0.001)	0.26 (<0.001)	0.15 (0.006)	0.26
Lifestyle/ Behaviour	0.40 (<0.001)	0.21 (0.001)	0.25 (0.005)	0.12 (0.004)	0.15 (0.003)	0.38
Biophysiologic	0.31 (<0.001)	0.15 (0.02)	0.22 (0.01)	0.11 (0.004)	0.13 (0.02)	0.33

b. Method 2 for the development of the risk scores (hybrid method uses the results of factor analysis of underlying latent construct to create the risk score)

	StdYX on T2DM (p-value)	StdY Black on Domain (p-value)	StdY Black on T2DM (p-value)	StdY Hispanic on Domain (p-value)	StdY Hispanic on T2DM (p-value)	R^2
Socioeconomic	0.25 (< 0.001)	0.18 (0.02)	0.21 (0.01)	0.64 (<0.001)	-0.01 (0.88)	0.28
Environmental[1]	0.17 (0.09)	0.41[2] (<0.001)	0.24 (0.009)	0.48[2] (<0.001)	0.14 (0.01)	0.24
Psychosocial	0.14 (0.001)	0.13 (0.07)	0.24 (0.007)	0.23 (<0.001)	0.13 (0.02)	0.27
Lifestyle/ Behaviour	0.34 (<0.001)	0.18 (0.01)	0.24 (0.008)	0.03 (0.55)	0.17 (0.001)	0.37
Biophysiologic						
Men	0.12 (0.01)	0.15 (0.13)	0.19 (0.14)	0.05 (0.45)	0.13 (0.10)	0.24
Women	0.22 (<0.001)	0.12 (0.26)	0.30 (0.004)	0.15 (0.01)	0.17 (0.02)	0.33

c. Method 3 latent variable method

	StdYX on T2DM (p-value)	StdY Black on Domain (p-value)	StdY Black on T2DM (p-value)	StdY Hispanic on Domain (p-value)	StdY Hispanic on T2DM (p-value)	R^2
Socioeconomic	0.45 (<0.001)	0.26 (<0.001)	0.14 (0.15)	0.71 (<0.001)	-0.16 (0.11)	0.31
Environmental[1]	0.17 (0.09)	0.41[2] (<0.001)	0.24 (0.009)	0.48[2] (<0.001)	0.14 (0.01)	0.24
Psychosocial	0.27 (0.20)	0.07 (0.69)	0.25 (0.02)	0.47 (<0.001)	0.04 (0.78)	0.30
Lifestyle/ Behaviour	0.39 (<0.001)	0.21 (0.002)	0.20 (0.11)	0.08 (0.07)	0.13 (0.03)	0.34
Biophysiologic						
Men	0.02 (0.86)	0.18 (0.29)	0.21 (0.12)	-0.01 (0.95)	0.12 (0.14)	0.23
Women	0.39 (0.36)	0.38 (0.05)	0.19 (0.42)	0.20 (0.08)	0.14 (0.37)	0.38

[1] Estimates for environmental domain are the same because they are parameterized the same. Only one variable predicted this domain.

[2] Estimate for cluster level mean of Black/Hispanic race/ethnicity

Table 7-7. Final Structural Equation Model of Factors in the Pathway from Race/Ethnicity to T2DM (full standardized and non-standardized results) – Compare risk models

		Risk scores based on standard method (Method a)		Risk scores based on latent variable results (Method b)	
Predictor	Outcome	Standard-ized Coefficient	*p*-value	Standard-ized Coefficient	*p*-value
Black vs. White	Socioeconomic Risk	0.22	0.002	0.177	0.003
Hispanic vs. White	Socioeconomic Risk	0.41	<0.001	0.641	<0.001
West African ancestry	Socioeconomic Risk	-0.003	0.977	0.075	0.224
Native American ancestry	Socioeconomic Risk	-0.018	0.693	0.044	0.109
Black vs. White	Environmental Risk	0.149	<0.001	0.168	<0.001
Hispanic vs. White	Environmental Risk	0.153	0.004	0.040	0.609
West African ancestry	Environmental Risk	ND[1]		ND[1]	
Native American ancestry	Environmental Risk	ND[1]		ND[1]	
Socioeconomic Risk	Environmental Risk	0.448	<0.001	0.498	<0.001
Black vs. White	Psychosocial Risk	0.001	0.992	0.055	0.424
Hispanic vs. White	Psychosocial Risk	0.082	0.044	-0.030	0.552
West African ancestry	Psychosocial Risk	0.031	0.665	0.02	0.783
Native American ancestry	Psychosocial Risk	0.015	0.624	-0.001	0.968
Socioeconomic Risk	Psychosocial Risk	0.402	<0.001	0.377	<0.001
Environmental Risk	Psychosocial Risk	0.050	0.505	0.065	0.415
Black vs. White	Lifestyle/ behavioural Risk	0.120	0.065	0.114	0.121
Hispanic vs. White	Lifestyle/ behavioural Risk	-0.028	0.516	-0.049	0.405
West African ancestry	Lifestyle/ behavioural Risk	-0.032	0.621	-0.024	0.752
Native American ancestry	Lifestyle/ behavioural Risk	-0.040	0.259	-0.025	0.471
Socioeconomic Risk	Lifestyle/ behavioural Risk	0.268	0.000	0.009	0.858

		Risk scores based on standard method (Method a)		Risk scores based on latent variable results (Method b)	
Predictor	Outcome	Standard-ized Coefficient	*p*-value	Standard-ized Coefficient	*p*-value
Environmental Risk	Lifestyle/ behavioural Risk	0.164	0.041	0.172	0.018
Psychosocial Risk	Lifestyle/ behavioural Risk	0.026	0.392	0.087	0.003
Black vs. White	Biophysiologic Risk	0.067	0.274	0.029	0.532
Hispanic vs. White	Biophysiologic Risk	0.010	0.803	0.007	0.857
West African ancestry	Biophysiologic Risk	-0.071	0.221	-0.124	0.012
Native American ancestry	Biophysiologic Risk	0.013	0.654	0.023	0.311
Socioeconomic Risk	Biophysiologic Risk	0.131	0.000	0.055	0.070
Environmental Risk	Biophysiologic Risk	0.117	0.142	0.078	0.209
Psychosocial Risk	Biophysiologic Risk	0.054	0.050	0.019	0.394
Lifestyle/behavioural risk	Biophysiologic Risk	0.211	<0.001	0.159	<0.001
Family history	Biophysiologic Risk	0.050	0.032	0.012	0.588
Black vs. White	T2DM	0.181	0.049	0.19	0.045
Hispanic vs. White	T2DM	0.075	0.201	0.024	0.721
West African ancestry	T2DM	-0.003	0.977	-0.009	0.924
Native American ancestry	T2DM	-0.018	0.693	-0.020	0.655
Socioeconomic Risk	T2DM	0.100	0.029	0.200	<0.001
Environmental Risk	T2DM	0.001	0.993	0.047	0.661
Psychosocial Risk	T2DM	0.048	0.197	0.072	0.042
Lifestyle/behavioural risk	T2DM	0.257	0.000	0.283	<0.001
Family history	T2DM	0.098	0.003	0.119	<0.001
Biophysiologic Risk	T2DM	0.197	<0.001	0.105	0.007

[1] ND = Not determined, model would not converge with this path present

[2] N/A = Not applicable, cluster means were used to predict neighbourhood-level outcomes, unstandardized outcome is not directly interpretable

8 Discussion

The purpose of this thesis was to quantify the relative contribution of (i) social and economic, (ii) contextual/neighbourhood, (iii) psychosocial, (iv) lifestyle/behavioural, (v) biophysiologic, and (vi) genetic/ancestral factors to racial/ethnic disparities in T2DM. This aim was addressed through a series of papers with the following objectives:

1. To quantify the contributions of genetic biogeographic ancestry versus socioeconomic factors to racial/ethnic disparities in T2DM incidence.
2. To identify and estimate the contributions of specific aspects of contextual environments/neighbourhoods to racial/ethnic disparities in T2DM prevalence.
3. To quantify the relative contributions of (i) social and economic, (ii) contextual/neighbourhood, (iii) psychosocial, (iv) lifestyle/behavioural, (v) biophysiologic, and (vi) genetic/ancestral factors to racial/ethnic disparities in prevalent T2DM.

In the following section (**Section 8.1**), the results from each manuscript will be discussed briefly and then the findings of these different papers will be synthesized. The strengths and limitations of my overall research findings will then be briefly discussed in **Section 8.2**. The strengths and limitations of each paper have been presented in the submitted papers presented in previous chapters. Therefore, those details will not be repeated here. The implications of my research findings for policy and practice are discussed in **Section 8.3** followed by recommendations for

future research in **Section 8.4**. Finally, an overview of my dissemination activities is provided in **Section 8.5**.

8.1 Summary and synthesis of the research findings

The objective of the first paper with substantive findings (**Chapter 5**) was to quantify the contribution of genetic biogeographic ancestry versus socioeconomic factors to racial/ethnic disparities in T2DM incidence. In these analyses I used longitudinal data from the BACH Study to examine the effects of race/ethnicity, biogeographic ancestry, and socioeconomic factors on the cumulative incidence of diagnosed T2DM. These analyses were supplemented with cross-sectional data examining the prevalence of both diagnosed and undiagnosed T2DM. The results demonstrated that racial/ethnic disparities in the incidence of T2DM were potentially mediated by SES, whereas biogeographic ancestry appeared to have no effect on this association. The results also demonstrated that while African ancestry is significantly associated with T2DM incidence, a large proportion of this association was mediated by self-identified race/ethnicity and socioeconomic factors.

The findings from the supplementary cross-sectional analyses (**Section 5.4**) were similar. However, the association between biogeographic ancestry and T2DM was not eliminated when self-identified race/ethnicity and socioeconomic factors were taken into account.

The objective of the second paper with substantive findings (**Chapter 6**) was to identify and estimate the contribution of specific aspects of contextual environments/neighbourhoods to racial/ethnic disparities in T2DM prevalence. There was a large variation in the prevalence of T2DM by neighbourhood. This geographic variation was not explained by the composition of the neighbourhood (i.e. individual-level factors) in the BACH Study. This geographic variation was also not explained by the contextual variables collected in this study including measures of: (1) built environment (proximity to supermarkets, grocery stores, convenience stores, fast food

outlets, and open recreational space), (2) neighbourhood socioeconomics (composite SES measure, poverty), (3) racial composition, (4) safety (property and violent crime), or neighbourhood disorder (physical and social). More importantly, none of these contextual elements, singly or in combination, attenuated the measured racial/ethnic disparities in T2DM.

The objective of the third paper with substantive findings (**Chapter 7**) was to quantify the relative contribution of (i) social and economic, (ii) contextual/neighbourhood, (iii) psychosocial, (iv) lifestyle/behavioural, (v) biophysiologic, and (vi) genetic/ancestral factors to racial/ethnic disparities in prevalent T2DM. The results indicated that that much of the excess odds of T2DM among Black (61%) and Hispanic (54%) participants could not be explained by the constructs measured in the BACH Study. The socioeconomic risk score developed, which was a composite of household income, education, occupation, immigration status, acculturation, health literacy, insurance status and utilization of health care, explained 22% of the excess odds of T2DM among Black and 26% of the excess odds among Hispanic participants. The environmental risk score explained only 1% and 4% of the excess odds of diabetes among Black and Hispanic participants, respectively; psychosocial factors explained 0% and 5%; lifestyle/behavioural 11% and 6%; and biophysiologic factors 5% and 5%. Finally biogeographic ancestry was included in the final model as a confounder and significant associations with neither T2DM nor with any of the mediating risk domains were found.

The latter result further bolsters the results from the first results-driven paper on biogeographic ancestry. Both the longitudinal and cross-sectional findings demonstrated that self-identified race/ethnicity and socioeconomic factors may explain much of the excess risk of T2DM thought to be associated with biogeographic ancestry. These analyses indicate that while genetic factors, including biogeographic ancestry, may play a role in T2DM, it is likely that the social, cultural, and economic facets of race/ethnicity better explain T2DM disparities in the US. Specifically, the

lower average SES of Blacks and Hispanics in the US, compared with that of Whites, provides a plausible explanation for a large proportion of the excess risk of T2DM.

General conclusions regarding the total contribution of "genetic factors" to racial/ethnic disparities in T2DM cannot be made, since the BACH Study only collected markers relating to biogeographic ancestry. However, review of the literature indicates that genetic variation does not explain a substantial proportion of variation in T2DM risk, even though genetic polymorphisms linked to T2DM have been identified. This suggests that other contributors, including gene-environment interactions, are more likely to play a major role. [576] Furthermore, the presence of disparities in multiple unrelated health outcomes as well as the presence of heterogeneity in racial/ethnic differences over time and across contexts suggests that genetic factors alone are unlikely to explain racial/ethnic disparities in T2DM.

The findings from all three papers underscore the importance of social and economic factors in racial/ethnic disparities in T2DM. The results from the biogeographic ancestry analyses, as well as the relative contributions analyses, indicate that social and economic factors, particularly income, education, and occupation are mediators in the relationship between self-identified race/ethnicity and T2DM incidence and prevalence. Estimates of this indirect effect ranged from 64% and 100% of the total effect for Blacks and Hispanics in the longitudinal analyses to 46% and 100% in the cross-sectional analyses. The cross-sectional findings from both manuscripts indicate that social and economic factors may have an indirect effect on T2DM through lifestyle/behavioural risk factors and body mass. Even after accounting for environmental, psychosocial, lifestyle/behavioural, and biophysiologic risk factors, social and economic risk factors were estimated to account for 22% and 26% of the total relationship between Black race and Hispanic ethnicity and the odds of T2DM.

Lifestyle/behavioural factors also appear to play an important role in development of disparities in T2DM. There is a plethora of research on the impact of diet and exercise on T2DM and these

findings also demonstrate a significant direct effect of lifestyle/behavioural risk factors on T2DM. In the final structural equation model (**Figure 7-2**), the lifestyle/behavioural risk domain had the largest direct effect on T2DM prevalence. However, it is important to note that the results indicated no direct effect between race/ethnicity and lifestyle/behavioural risk. Furthermore, lifestyle/behavioural risk factors (i.e. physical activity, smoking history, BMI, waist circumference, and body fat percentage) appeared to explain only 11% and 6% of the excess odds of T2DM among Blacks and Hispanics, respectively.

Although race/ethnicity had no direct effect on lifestyle/behavioural risk, it is important to note that socioeconomic risk, which was highly associated with race/ethnicity, did have a significant direct effect on lifestyle/behavioural risk. Overall, lifestyle/behavioural risk explained 43.3% of the association between socioeconomic status and T2DM. Other studies have found similar results.[373] These results indicate a complex relationship between race/ethnicity, adverse socioeconomic conditions and lifestyle/behavioural risk factors. While there are many pathways and mechanisms by which race/ethnicity and SES can combine to affect the development of diabetes (see **Section 2.6**) including early life exposures, environmental conditions and opportunities, as well as psychosocial stress, these results appear to emphasize the contribution of adult lifestyle/behavioural risk factors. However, it is important to note that early life exposures were not captured in this study.

Contextual features of residential neighbourhood are one potential pathway by which race/ethnicity and socioeconomic factors may influence lifestyle/behavioural factors and subsequent T2DM risk. People with limited socioeconomic means are more likely to live in neighbourhoods that are more segregated, have fewer places to purchase healthy food, more places to purchase unhealthy food, are less walkable, have less open space, have higher crime and that have a greater perceived lack of safety. Several studies have demonstrated that the contextual elements of the local environment may affect obesity and T2DM.[54129,524 244, 270, 271, 543

Furthermore, the largest randomized experiment examining the effect of spatial mobility found that offering vouchers to move to a lower poverty neighbourhood had a significant impact on the prevalence of obesity and diabetes.[273] However, researchers could not attribute the reduction in obesity to specific environmental factors.[577] My analyses also could not identify specific contextual factors responsible for the neighbourhood variability in T2DM. In addition, I found that racial/ethnic disparities could not be explained by the contextual factors examined. For this particular result, it is very important to note the limitation of this study region to the city of Boston, Massachusetts.

In summary, these research papers indicate that socioeconomic factors contribute to the development and/or amplification of racial/ethnic disparities in T2DM. According to the conceptual model, socioeconomic factors were considered distal to lifestyle/behavioural and biophysiologic risk factors. While these proximal risk factors were found to be direct risk factors for T2DM, they only impacted racial/ethnic disparities through social and economic influences. As highlighted in the study's conceptual framework (**Figure 3-1**), the pathways by which race and ethnicity may impact T2DM risk are complex. Considering these complex pathways, and how they influence each other, can help to identify interventions that might promise reductions in racial/ethnic disparities.

8.2 Strengths and Limitations

Individual limitations of the methodologies used in each manuscript were noted. In addition, there are further considerations that are presented below.

8.2.1 General Strengths

The strengths of this study stem from the BACH Study's community-based stratified random sample design. The BACH Study, by design, includes both sexes, a wide age range (30–79 years) and includes a large number of minority participants, representative of Black and Hispanic

populations. Key strengths of the BACH Survey that were utilized in these analyses include: (1) the wide range of measurements covering six theoretical domains, that (2) allow for both individual-level and neighbourhood-level (multi-level) analyses and (3) the multi-disciplinary approach measures the prevalence of disease through both self-report and physiologic measurements (i.e. fasting glucose and HbA1c to capture undiagnosed cases).

8.2.2 General Weaknesses

A notable limitation of this study is the cross-sectional nature of the majority of the analyses which prevent causal inferences and limit the ability to determine temporality. The bulk of the analyses used BACH III data only. This was done for several reasons. First, the objective measures of diabetes status (fasting glucose, HbA1c and fasting insulin) were only captured at BACH III. This limited potential longitudinal analyses to the cumulative incidence of diagnosed T2DM which affects study power (small number of events) and is also a more subjective measure of diabetes status that may underestimate the true magnitude of racial/ethnic disparities. This was demonstrated in **Section 5.4**. Second, while some measures addressing the six domains of interest were captured at BACH I and BACH II, many were not (see **Table 4-3** for a full list of available measures). This limited the ability to examine the full contribution of certain domains of interest, particularly the environmental and psychosocial domains, longitudinally. A further limitation to using cross-sectional data is that it is likely that one-time measurement of health behaviours may underestimate their contribution. Sensitivity analyses conducted by others have indicated that life-course[331, 332] and repeated measures[373] designs increase the proportion of social inequalities that can be explained by potential mediating risk factors.

Another limitation of this study is that it is geographically limited to Boston, Massachusetts. The BACH Survey sample has been compared to other large regional (Behavioral Risk Factor Surveillance System) and national (the National Health and Nutrition Examination Survey) on a number of socio-demographic and health-related variables[437] and the results indicate that the

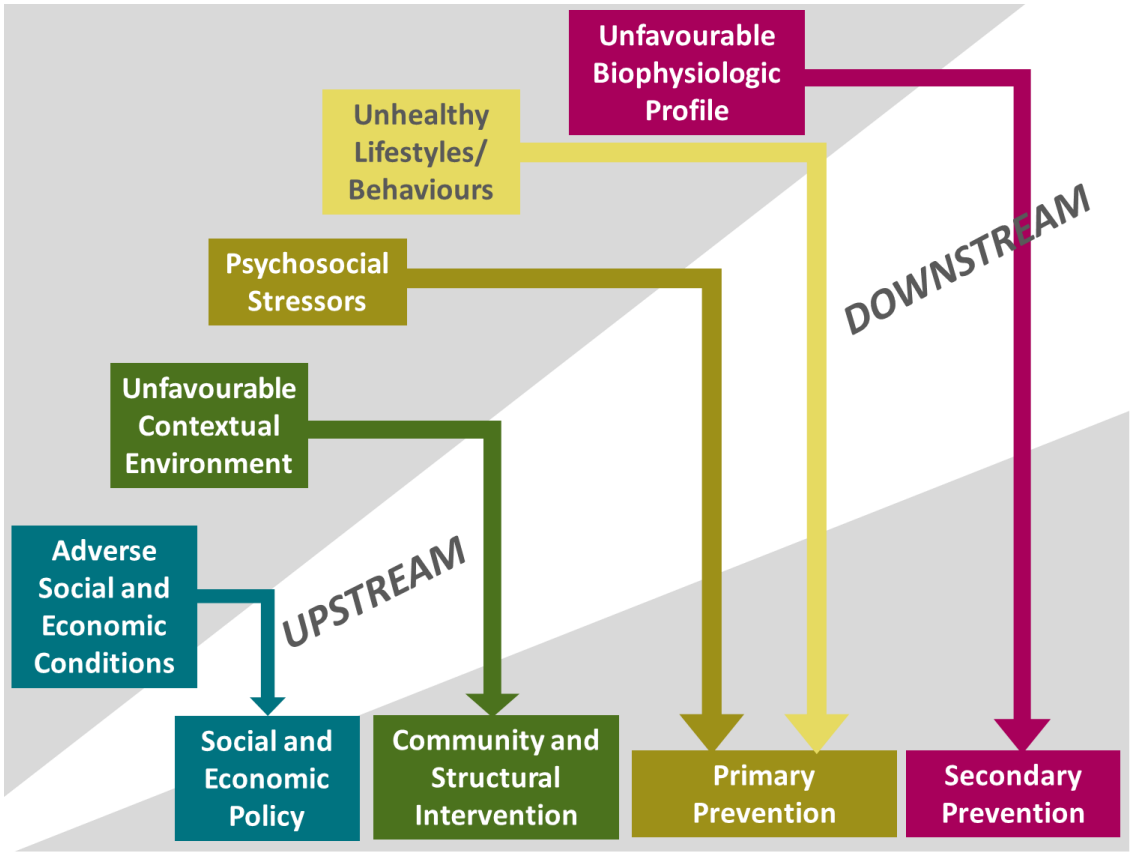
BACH Survey estimates of key health conditions are comparable with national trends. However, the macro-economic influences of living in this urban, northeast environment may not be generalizable to other contexts or to the conditions in which racial/ethnic disparities in T2DM are fostered in the US at large. This limitation particularly affects the estimates regarding the neighbourhood/environmental contributors to racial/ethnic disparities in T2DM.

Finally, although biogeographic ancestry markers were measured, which are thought to estimate the genetic contribution to increased diabetes prevalence in certain populations, the BACH Survey did not include comprehensive markers of genetic risk. Therefore conclusions regarding genetic contributors to racial/ethnic disparities in T2DM cannot be made.

8.3 Implications/Recommendations for Policy and Practice

Each domain of the conceptual framework for this research evokes a particular structural intervention (**Figure 8-1**). The roles of adverse social and economic conditions suggest policy interventions affecting social conditions. Unfavourable built and social environment characteristics suggest community level intervention. Increased psychosocial stressors could be alleviated with primary prevention tactics aimed at reducing psychological strain and increasing coping mechanisms. Unhealthy lifestyles would suggest primary prevention directed at increasing healthy behaviours and decreasing unhealthy behaviours. Secondary prevention efforts aimed at stopping/slowing the progression of disease would be the proposed intervention for individuals with unfavourable biophysiologic profiles.

Figure 8-1. Each domain of influence suggests a specific level of intervention



In many of these analyses and indeed in the following sections we adopted this simplified framework that suggests each domain of has its own specific proposed intervention. However, this may be overly simplistic given the complex interplay between these potential causes as is shown in the conceptual model, (**Figure 3-1**, **p. 53**). For example, there are situations in which a genetic cause may have an environmental solution and vice-versa.[578, 579]

Finally, it is important to note that the risk factors identified as the main causes of T2DM may not necessarily be causes of racial/ethnic disparities.[580] It follows that interventions that may reduce the incidence of T2DM may not necessarily reduce disparities. While many overlaps may exist it is an important epidemiologic distinction to note.[579]

8.3.1 Lifestyle/Behavioural Interventions

One of the most common interventions to prevent or delay the onset of type 2 diabetes is to prescribe physical activity and/or dietary intervention. The results of trials examining lifestyle/behaviour interventions have proved promising. A meta-analysis of nine randomized controlled trials demonstrated that lifestyle modification based on physical activity, dietary interventions, or both is associated with improvements in glucose levels and tolerance levels in participants at risk for T2DM.[581] The Diabetes Prevention Program, the largest major randomized controlled trial of prediabetic adults to date, found that lifestyle modification was just as efficacious in preventing or delaying T2DM as metformin.[582] The results indicated that the lifestyle intervention prevented one case of diabetes per each three treated person-years. However, it is important to note that the efficacy of this lifestyle intervention was a consequence of an intensive regimen. The goal was to attain a weight loss of at least 7% using a low-calorie diet, and increasing physical activity to at least 150 minutes per week. These lifestyle changes were guided by a case manager who provided monthly support sessions and a 16-lesson curriculum.

There are challenges to replicating these types of prevention programs in a widespread setting and particularly in underserved areas. The infrastructure necessary to establish these programs including a suitable setting, and staffing that would be available for the requisite period of time, are difficult to obtain and sustain. Disadvantaged communities in particular lack the requisite resources and community organization necessary to develop such T2DM prevention programs. However, it has been established that these disadvantaged communities have the highest rates of T2DM, thus having the greatest needs for such programs. Accordingly, a major public health challenge for many minority and underserved communities is to acquire resources and the supportive infrastructure to implement intensive diabetes prevention programs.[403]

In addition to these challenges, it is worth mentioning that concentrating on individual behavioural risk factors may not result in change to racial/ethnic and socio-economic inequalities in health outcomes. It is critical to consider how people come to be exposed to individually-based risk factors such as poor diet and lack of exercise, for example by living in a neighbourhood with few healthy food options with low walkability/low greenspace.[324] If the upstream generators of these inequalities are not considered, population-wide intervention to improve health behaviours may result in greater uptake of the message in socially advantaged groups, potentially increasing social inequalities in health.[583] Therefore, solutions to redressing racial/ethnic disparities in T2DM may also lie outside the health sector (see **Section 8.3.3**).

The results of these analyses indicated that lifestyle/behavioural factors contributed to racial/ethnic disparities in T2DM indirectly. Socioeconomic factors were identified as a more fundamental cause of these disparities. As a fundamental cause of disparities, adverse socioeconomic conditions were associated with T2DM through a variety of mechanisms (directly and indirectly). This indicates that even if one effectively modifies an intervening mechanism, such as lifestyle/behaviour, an association between a fundamental cause and disease will likely re-emerge.[212] Therefore, focusing solely on lifestyle/behaviour as a mediating mechanism may

fail to eliminate racial and ethnic disparities because the fundamental cause, social and economic disparities, is not being addressed.

In conclusion, the results of these analyses, as well as the results of several trials,[568] suggest that interventions targeting lifestyle/behavioural and biophysiologic risk may reduce T2DM risk overall. However, the results presented here demonstrate that interventions aimed at reducing disparities may need to target socioeconomic risk factors in order to lessen the racial/ethnic divide.

8.3.2 Contextual/Neighbourhood Interventions

Community-based nutritional health and activity interventions have the potential to make a modest public health impact.[584, 585] Examples of these types of interventions include opening farmers' markets, promoting safe bike and walking paths, community gardens, and community shared agriculture programs. Many of these programs are gaining traction nationally, and several have been implemented in the BACH study area under the Urban Agriculture program initiated in 2010.[586]

However, these initiatives do not address the underlying inequitable distribution of certain neighbourhood amenities. The liberalization of urban and density zoning laws and the investment of business in disadvantaged communities may influence disparities in the built environment. [587] Such infrastructure developments in communities can also improve population health, in addition to reducing disparities.[588]

The implementation of health impact assessments (HIAs) have been promising in minimizing the adverse health impacts of residential segregation.[589, 590] HIAs are used to evaluate the impact of policies and projects in community design and other areas (i.e. transportation planning) on public health.[591] However, there is still a need for rigorous evaluation of the impact of various interventions.

It is important to note that disparities in neighbourhoods or across areas result from specific policies, or absence of policies. Neighbourhood contexts are mutable and can be responsive to economic and social policy interventions. This makes the local social and built environmental policy a particularly suitable target for disparities reduction.[304]

Interventions like the MTO initiative, which provided vouchers for individuals and families to move to lower poverty, lower crime neighbourhoods, offer the potential to diminish racial and ethnic disparities in obesity and T2DM.[273] The increase in US residential segregation, both racially and socioeconomically, in recent decades may expose populations to concentrated poverty.[592] Mobility programs, like the MTO, result in families living in lower poverty neighbourhoods and having better health outcomes. Housing mobility is a platform for positive outcomes. However, it is likely that a more comprehensive approach is needed to reduce T2DM disparities.

8.3.3 Social and Economic Interventions

The results of this study, and others, indicate that lower socioeconomic status is central to explaining why racial/ethnic minorities have a higher prevalence and incidence of T2DM. Variations in the distribution of income are associated with disparities in the distribution of a large number of health outcomes including mortality. These disparities parallel relative investments in human and social capital. Social and economic policies that influence income and wealth inequality may have an important impact on health outcomes.[310]

Despite abundant work describing health disparities, little progress has been made in identifying or implementing policies or interventions to eliminate inequalities. One possible explanation is that the underlying and structural causes of disparities have not been identified. A fast-growing body of research is investigating the many potential causes of socioeconomic disparities in health and are attempting to disentangle multiple potential causal pathways.[15] A primary focus

is investigating how adverse socioeconomic conditions shape exposure to T2DM across the lifespan. The research presented in this thesis contributes to this knowledge base. We attempted to disentangle several potential causes of racial/ethnic disparities in T2DM. The findings indicate that social conditions are a fundamental cause that exerts both direct and indirect effects on T2DM.

Another reason why interventions on macroeconomic, cultural, and environmental conditions have rarely been used to date is that the macroeconomic, cultural, and environmental causes for health disparities are distal and may be quite distant in space and time from health outcomes. [593] The consequences of intervening on these distal and structural causes can be very difficult to convincingly identify in observational or experimental studies. Social and economic factors affect disease outcomes through multiple mechanisms and therefore may maintain an association with disease even when intervening mechanisms change.

The political climate of the US and other Western cultures also shapes the focus on proximate risk factors for targeted intervention (e.g. lifestyles/behaviours **Section 8.3.1**). US culture emphasizes the ability of the individual to control his or her own personal fate and the importance of doing so (i.e. "personal responsibility").[211, 212] These cultural values contribute to the level of public and policy interest in T2DM research findings, and influence funding priorities as well.

Nonetheless, action at the federal level in the US is starting to occur. The Centers for Disease Control and Prevention (CDC) have partnered with the Federal Bureau of Primary Care and Institute for Healthcare Improvement to engage with community health centres. The resulting Health Disparities Collaborative, which focuses on diabetes and several other conditions, work to link patients with community resources to promote health education and lifestyle changes to diet and exercise.[11, 594, 595] However, these collaboratives tend to focus on downstream health

outcomes of already diagnosed disease and early results appear to be disappointing for diabetes outcomes.[596]

Focusing on risk factors further upstream, childhood obesity is also a target for this model. Obesity experts have long advocated for the development and application of multi-level, multi-sector prevention strategies that invoke change at the environment and policy level.[597] Evidence for the effectiveness of some of these obesity prevention interventions is mounting, with the most promising approaches being changes in environments and policies.[598] A recent national effort to prevent childhood obesity is the Let's Move! campaign. Let's Move! focuses on early childhood obesity prevention, parent and caregiver empowerment, healthier food in schools, access to healthy, affordable foods, and increased physical activity. Despite these promising strides towards structural and policy intervention, resistance towards policy changes remain, and strategies to overcome such resistance are elusive.

As mentioned in the section above, one of the most promising social and environmental interventions to date was the "Moving to Opportunity" program in the U.S.[273] Implemented under the U.S. Department of Housing and Urban Development, this social experiment offered more than 4,000 low-income families the chance to move to a low-poverty neighbourhood. Long-term results indicated that the mobility program resulted in families living in lower poverty, safer neighbourhoods. The study demonstrated that participants who moved to lower poverty neighbourhoods had better health outcomes including extreme obesity and diabetes, as well as decreased psychological distress and major depression. However, families in the experimental group did not experience better employment or income outcomes, nor did their children experience better educational achievement.

In summary a comprehensive public health perspective is likely needed to reduce racial/ethnic disparities in T2DM addressing the multiple levels of influence and the complex pathways that were demonstrated in these findings. Coordinated interventions presented at two or more

ecological levels are likely needed to produce, population-wide, comprehensive, and efficacious reductions in any given health disparity.[403] Such interventions can range from the macrolevel (e.g., changing social policy, social institutions, cultural norms and practices) to the microlevel (e.g. individualized lifestyle/behavioural diabetes prevention interventions).

8.4 Research Recommendations

This study has drawn attention to the complex interplay of factors leading to the racial/ethnic disparities manifest in T2DM.

As discussed in **Section 8.2.2**, there were several limitations to this research that should be remediated in future research. First, a true longitudinal design with repeated measures of objective diabetes status are needed and over a longer follow-up period. It is likely that the one-time measurement of health behaviours may underestimate their contribution. Other longitudinal studies indicate that life-course[331, 332] and repeated measures[373] designs have shown to increase the proportion of social inequalities that can be explained by potential mediating risk factors.

Second, future studies should include comprehensive measures of not just adult, but also pre-natal and childhood, exposures. While there are several cohort studies that have generational data in addition to T2DM measures,[599] studies that are driven by a comprehensive conceptual framework are generally lacking.

Racial/ethnic disparities in T2DM arise from a complex interplay of social and economic, local environmental, psychosocial, lifestyle/behavioural, biophysiologic, and genetic factors. Given this complexity, it is likely that conclusive evidence will not necessarily flow from a single study or with increasing methodological sophistication within a single type of study. Rather, consensus will likely emerge from the work of multiple disciplines, often with diverse methodological

approaches. Partnership between health researchers, communities, and policy experts, will be crucial.

8.5 Dissemination

Research of this nature carries a responsibility to disseminate findings to try to create positive change. Dissemination efforts to date have focused on (1) the scientific community, (2) local and national policy leaders, and (3) the Boston community.

8.5.1 Scientific Community

My findings from this research have been published in several top tier epidemiology journals including: the International Journal of Epidemiology, Annals of Epidemiology, and Social Science and Medicine. In addition, I applied the methodological techniques I mastered over the course of my doctoral training to several other manuscripts published in peer reviewed journals. A complete list of publications relevant to this thesis is provided below.

1. Goonesekera SD, Fang SC, **Piccolo RS**, Florez JC, McKinlay JB. Biogeographic ancestry is associated with higher total body adiposity among African-American females: the Boston Area Community Health Survey. **PLoS ONE.** In press.
2. **Piccolo RS**, Duncan D, Pearce N, McKinlay, JB. The role of neighborhood characteristics in racial/ethnic disparities in type 2 diabetes: Results from the Boston Area Community Health (BACH) Survey. **Social Science in Medicine**, Apr 2015; 130: 79-90.
3. Yang MH, Hall SA, **Piccolo RS**, Maserejian NN, McKinlay JB. Do Behavioral Risk Factors for Prediabetes and Insulin Resistance Differ Across the Socioeconomic Gradient? Results from a Community-Based Epidemiologic Survey. **International Journal of Endocrinology**, in press.
4. **Piccolo RS**, Pearce N, Araujo AB, McKinlay, JB. The contribution of biogeographic ancestry and socioeconomic status to racial/ethnic disparities in type 2 diabetes: Results

from the Boston Area Community Health (BACH) Survey. **Annals of Epidemiology**, Sep 2014; 24(9): 648-654.

5. Meigs JB, Grant RW, **Piccolo R**, Lopez L, Florez JC, Porneala B, Marceau L, McKinlay JB. Association of African Genetic Ancestry with Fasting Glucose and Hemoglobin A1c Levels in Non-Diabetic Individuals: The Boston Area Community Health (BACH) Prediabetes Study. **Diabetologia**, Sept 2014; 57 (9): 1850-1858.
6. **Piccolo RS**, Araujo AB, Pearce, N, McKinlay JB. Cohort Profile: The Boston Area Community Health (BACH) Survey. **International Journal of Epidemiology**. Feb 2014; 43 (1): 42-51.

Preliminary and final findings were presented at a number of scientific conferences from June 2012- November 2013.

American Public Health Association (Boston, MA) November 2013

- *Does Genetic Ancestry Explain Racial/Ethnic Disparities in Diabetes? Results from a Longitudinal Study* (Piccolo RS)
- *Racial/Ethnic Disparities in Type 2 Diabetes: The Role of Neighborhood* (Piccolo RS)

AcademyHealth (Baltimore, MD) June 2013

- *Are Racial/Ethnic Disparities in Diabetes Explained by Ancestry or by Socioeconomic Differences? Results from a Longitudinal Study* (Piccolo RS)
- *The Role of Neighborhood Socioeconomic Status in Racial/Ethnic Disparities in Type 2 Diabetes* (Piccolo RS)

American Diabetes Association (Chicago, IL) June 2013

- *The Role of Neighborhood Socioeconomic Status in Racial/Ethnic Disparities in Type 2 Diabetes* (Piccolo RS)
- *Is Genetic Ancestry Associated with Incident Type 2 Diabetes?* (Piccolo RS)

Society for Social Medicine (London, UK) September 2012

- *A Profile of Undiagnosed Diabetics in the Community: Results from the Boston Area Community Health (BACH) Pre-Diabetes Survey* (Piccolo RS)

American Diabetes Association (Philadelphia, PA) June 2012

- *A Profile of Undiagnosed Diabetics in the Community: Results from the Boston Area Community Health (BACH) Pre-Diabetes Survey* (Piccolo RS)
- *Does Limited Health Literacy Explain Racial/Ethnic Disparities in Diabetes Control?* (Piccolo RS)

AcademyHealth (Orlando, FL) June 2012

- *Does Limited Health Literacy Explain Racial/Ethnic Disparities in Diabetes Control?* (Piccolo RS)

8.5.2 Policy Leaders

In an effort to reach relevant local and national policy leaders, I presented my findings at two summits focusing on racial/ethnic disparities. While attending and presenting at these national summits, I took the opportunity to meet and discuss with National Institutes of Health officials, including program officers.

2013 Reducing Health Disparities in Type 2 Diabetes Mellitus Summit (Baltimore, MD) March 2013

- *The Role of Neighborhood Socioeconomic Status in Racial/Ethnic Disparities in Type 2 Diabetes* (Piccolo RS)

2012 Science of Eliminating Health Disparities Summit (Washington D.C.) December 2012

- *Does Limited Health Literacy Explain Racial/Ethnic Disparities in Diabetes Control?* (Piccolo RS)

In addition, I provided the BACH funding organization, the National Institute of Diabetes and Digestive and Kidney Diseases, with regular updates on our findings through official progress reports and personal emails.

Finally, new results are posted regularly the New England Research Institutes (NERI) website and twitter accounts.

8.5.3 Boston Community

The BACH research team regularly reaches out to the Boston area and the BACH participants, specifically, with updates on the study findings. We compiled a one page summary of the findings summarizing the major findings from the study including findings from this research. This summary is sent to all BACH participants and to several community leaders within the Boston area.

8.6 Conclusion

This study presents, to my knowledge, the first examination of a multidisciplinary, multilevel risk model aimed at explaining racial/ethnic disparities in T2DM. This research highlighted the complexity in the causation and amplification of racial/ethnic disparities in T2DM. Guided by the conceptual model, I conclude that social and economic factors are fundamental in the creation and amplification of these disparities. The evidence did not indicate a fundamental role of

biogeographic ancestry, contextual environmental factors, or psychosocial factors in the manifestation of these disparities. Lifestyle/behavioural and biophysiologic risk factors appeared to be heavily influenced by socioeconomic parameters. These results have national and local policy implications as they suggest that in order to reduce disparities, either wide-scale social and economic policy shifts need to occur, or interventions need to be targeted toward racial/ethnic minorities and the socially and economically disadvantaged.

It is inaction that cannot be afforded, for the human and economic costs are too high

Sir Michael Marmot,[1] p. 35

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Appendix A: Ethics Approval

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636
www.lshtm.ac.uk

Observational / Interventions Research Ethics Committee

Rebecca Piccolo
Research student
MSD/EPH
LSHTM

3 August 2012

Dear Ms Piccolo,

Study Title: **Multilevel Modelling of Social Disparities in Type-2 Diabetes**
LSHTM ethics ref: **6243**

Thank you for your application of 30 July 2012 for the above research, which has now been considered by the Chair on behalf of the Observational Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

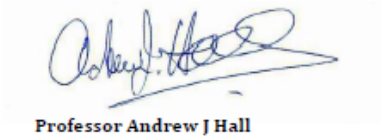
The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
LSHTM ethics application	n/a	30/07/2012
Protocol		28/12/2009
Information Sheet		14/01/2010
Consent form		14/01/2010

After ethical review

Any subsequent changes to the application must be submitted to the Committee via an E2 amendment form. All studies are also required to notify the ethics committee of any serious adverse events which occur during the project via form E4. At the end of the study, please notify the committee via form E5.

Yours sincerely,



Professor Andrew J Hall
Chair
ethics@lshtm.ac.uk
http://intra.lshtm.ac.uk/management/committees/ethics/

Appendix B: Study Questionnaires

9.1 Physical Measures

SECTION A: KEY IDENTIFYING INFORMATION

A1. Subject identification number

A2. Date of physical measurements

M M / D D / Y Y Y Y

A3. Start time (24 hour clock)

H H : M M

A4. Data collector ID number

SECTION B: BODY MEASUREMENTS

SCRIPT: Now I'd like to take some measurements of your body. These should not cause you any pain and will take only a few seconds each.

INSTRUCTION: ASK SUBJECT TO TAKE OFF SHOES FOR HEIGHT AND WEIGHT MEASUREMENT.

B1. Height (cm)

a. Self-reported height

1. Feet

2. Inches

B2. Do you have a pacemaker, implanted cardiac defibrillator, other implanted electrical medical devices or an artificial limb?

YES..... 1 **(B4)**

NO 2

NOT SURE..... 3 **(B4)**

INSTRUCTION: THE TANITA ULTIMA SCALE PASSES A LOW-LEVEL ELECTRICAL CURRENT THROUGH THE BODY THAT MAY INTERFERE WITH THE OPERATION OF MEDICAL DEVICES. IF THE SUBJECT HAS, OR MAY HAVE, SUCH A DEVICE, SKIP THE BODY FAT ASSESSMENT (B3) AND USE THE WEIGHT-ONLY PROTOCOL

B3. Body fat percentage | | |

B4. Weight (kg) | | | | . | |

a. Self-reported weight (lbs) | | | |

B5. What was your approximate birth weight?

a. Pounds | | |

b. Ounces | | |

B6. Waist circumference (cm) | | | | . | |

a. Measurement taken in LIGHT CLOTHING 1

UNDERGARMENTS 2

B7. Hip circumference (cm) | | | | . | |

a. Measurement taken in LIGHT CLOTHING 1

UNDERGARMENTS 2

SECTION C: PULSE AND BLOOD PRESSURE

SCRIPT: I am now going to begin taking your pulse and blood pressure. Please keep your legs uncrossed while I check your blood pressure.

INSTRUCTION: ENCOURAGE SUBJECT TO SIT QUIETLY DURING MEASUREMENTS AND REFRAIN FROM TALKING.

C1. Arm circumference (cm) | | | . | |

a. Arm LEFT .....1 RIGHT 2

C2. Cuff size PEDIATRIC 1

ADULT 2

LARGE ADULT..... 3

THIGH..... 4

C3. Heart rate (beats/60 seconds)

C4. Systolic blood pressure (mmHg)

C5. Diastolic blood pressure (mmHg)

C6. End time (24 hour clock)

		:		
H	H	:	M	M

9.2 Phlebotomy Form

SECTION A: KEY IDENTIFYING INFORMATION

A1. Subject identification number

A2. Date of phlebotomy

M M / D D / Y Y Y Y

A3. Start time (24 hour clock)

H H : M M

A4. Phlebotomist ID number

SECTION B: INTERVIEW

SCRIPT: Now I am going to draw your blood. First I need to ask you some questions:

B1. Do you currently take blood thinners (Warfarin or Coumadin) or do you have hemophilia?

YES.....1 **(END)** NO..... 2

B2. What time did you wake up? (24 hour clock)

H H : M M

B3. Have you fasted for at least 8 hours? YES.....1 NO..... 2

B4. Have you had anything alcoholic in the past 8 hours?

YES ..... 1 NO 2

B5. Have you had anything with caffeine in the past 8 hours?

YES ..... 1 NO 2

B6. At what time did you last have any food or beverage?

		:		
H	H	:	M	M

SECTION C: BLOOD DRAW

C1. Time of 1st attempt (24 hour clock)

		:		
H	H	:	M	M

a. Arm for first attempt LEFT ..... 1 RIGHT 2

b. Was first attempt successful? YES .....1 **(C3)** NO 2

C2. Time of 2nd attempt (24 hour clock)

		:		
H	H	:	M	M

a. Arm for second attempt LEFT ..... 1 RIGHT 2

C3. List the specimens collected

Response		1.						
YES	**NO**	Volume drawn						
a. SST 1	1	2				.		mL
b. SST 2	1	2				.		mL
c. Red Top 1	1	2				.		mL
d. Lavender Top 1	1	2				.		mL
e. Lavender Top 2	1	2				.		mL

C4. Was draw completed?

YES……..1 NO 2**(C4a)**

a. Why was draw not completed?

UNSUCCESSFUL ATTEMPTS……..1

SUBJECT REFUSAL……..2

OTHER……99 **(C4a1)**

a1. Specify other reason why blood draw was not completed:

_____

_____

SECTION D: RESULTS

D1. HemoCue 201 (mg/dL) | | | |

a. Was the HemoCue measurement taken using venous blood (from blood draw) or capillary blood (finger stick)?

VENOUS BLOOD.....1

CAPILLARY BLOOD.....2

D2. VeraLight (mg/dL) | | | |

D3. Comments: please note if there were any unusual circumstances:

_____

_____

D4. End time (24 hour clock) | | | : | | |

H H : M M

SECTION E: FOLLOW-UP

E1. Is a blood re-draw needed? YES.....1 NO.....2 **(END)**

E2. Did subject consent to a blood re-draw? YES.....1 NO.....2

9.3 Interviewer Administered Questionnaire

SECTION A: INTERVIEW SUMMARY

A1. SUBJECT ID:

A2. BACHSUBS SURVEY EVENT | | | | |

A3. FORM COMPLETION DATE: | | | / | | | / | | | | |
M M D D Y Y Y Y

A4. DATA COLLECTOR ID: | | | |

A5. SEX OF SUBJECT:
MALE 1
FEMALE 2

A6. LANGUAGE:
ENGLISH.....1
SPANISH 2

A7. START TIME OF INTERVIEW: | | | : | | | 24 HR CLOCK
H H M M

SECTION B: Self Assessed Health Status

This interview will ask questions about your overall health, some specific health conditions, your lifestyle, and your typical daily activities. Remember, we are interested in how you feel about your health. Many of these questions may seem familiar to you. We are interested in how your health may or may not have changed since we last spoke with you. Today I am also going to ask you some questions about things that may or may not have an affect on your day-to-day life, such as work, friends and family and how you feel about certain situations. Finally I will give you a short form to fill out yourself.

Once again, I would like to remind you that all the information you provide is completely confidential. If you feel uncomfortable answering a question, you should feel free to tell me and we can skip it. Also, there are no right or wrong answers. If you don't know the answer to something, just tell me and we'll move on.

If you need to take a break at any time, just let me know. Are you ready? Let's begin.

B1. In general, would you say your health is:

Excellent	1
Very good	2
Good	3
Fair	4
Poor	5

SECTION C: HEALTH AND HEALTH CARE

Now I have some questions about whether a health care provider has ever told you that you have a particular health condition. As you consider your answer, please keep in mind that a health care provider can be a general doctor, a specialist doctor, a nurse practitioner, a physician assistant, a nurse or anyone else you would see for health care.

C1		***Have you ever been told by a health care provider that you now have or previously had:**	**YES**	**NO**	**RF**	**DK**	i: **IF YES:** How old were you when you were first told **OR** at the time of the first event **OR** when you had surgery?
*a.		Insulin-dependent or juvenile-onset diabetes Type I	1	2 **(C1b)**	-7	-8	
	a1.	**IF YES**: Are you treating your diabetes by…..					
	i.	No treatment	1 **(C1a2)**	2	-7	-8	
	ii.	Modifying your diet	1	2	-7	-8	
	iii.	Medications taken by mouth	1	2	-7	-8	
	iv.	Insulin injection	1	2	-7	-8	
	a2.	**IF YES**: Has the diabetes caused:					
	i.	Problems with your kidneys	1	2	-7	-8	
	ii.	Problems with your eyes treated by an ophthalmologist?	1	2	-7	-8	

C1	***Have you ever been told by a health care provider that you now have or previously had:**	**YES**	**NO**	**RF**	**DK**	i: **IF YES:** How old were you when you were first told **OR** at the time <u>of the first event</u> **OR** when you had surgery?
*b.	Non-insulin dependent or adult-onset diabetes Type II	1	2 **(C1c)**	-7	-8	| | |
	b1 **IF YES**: Are you treating your diabetes by…..					
	i. No treatment	1 **(C1b2)**	2	-7	-8	
	ii. Modifying your diet	1	2	-7	-8	
	iii. Medications taken by mouth	1	2	-7	-8	
	iv. Insulin injection	1	2	-7	-8	
	b2. **IF YES**: Has the diabetes caused:					
	i. Problems with your kidneys	1	2	-7	-8	| | |
	ii. Problems with your eyes treated by an ophthalmologist or optometrist?	1	2	-7	-8	| | |
*c.	Elevated blood sugar (hyperglycemia) IF FEMALE: excluding when you were pregnant (gestational diabetes)	1	2	-7	-8	| | |
d.	**WOMEN ONLY:** Gestational diabetes	1	2	-7	-8	| | |

C1		***Have you ever been told by a health care provider that you now have or previously had:**	**YES**	**NO**	**RF**	**DK**	i: **IF YES:** How old were you when you were first told **OR** at the time <u>of the first event</u> **OR** when you had surgery?
e.		Kidney disease or poor kidney function (blood tests show high creatinine)	1	2 **(C1f)**	-7	-8	| | |
	e1.	**IF YES**: Have you ever used hemodialysis or peritoneal dialysis?	1	2 **(C1f)**	-7	-8	| | |
	e2.	**IF YES**: Have you ever received kidney transplantation?	1	2	-7	-8	| | |

C1.	*** Have you ever been told by a health care provider that you now have or previously had:**	**YES**	**NO**	**RF**	**DK**	i: **IF YES:** How old were you when you were first told **OR** at the time <u>of the first event</u> **OR** when you had surgery?
*f.	A heart attack (myocardial infarction or MI)	1	2	-7	-8	☐☐
*g.	Congestive heart failure (CHF) (you may have been short of breath and the doctor may have told you that you had fluid in your lungs or that your heart was not pumping well)	1	2 **(C1h)**	-7	-8	☐☐
	g1. **IF YES**: Were you treated for this?	1	2	-7	-8	
*h.	Surgery or angioplasty for arterial disease of the leg (an operation to unclog or bypass arteries in your leg)	1	2	-7	-8	☐☐
i.	A TIA or mild stroke (Transient Ischemic Attack, mini stroke)	1	2	-7	-8	☐☐
j.	A Stroke (CVA, cerebrovascular accident, blood clot or bleeding in the brain)	1	2 **(C1k)**	-7	-8	☐☐
	j1. **IF YES**: Do you have difficulty moving an arm or leg as a result of the stroke or cerebrovascular accident?	1	2	-7	-8	
*k.	Angina pectoris, chest pain	1	2	-7	-8	☐☐

C1.	*** Have you ever been told by a health care provider that you now have or previously had:**	**YES**	**NO**	**RF**	**DK**	i: **IF YES:** How old were you when you were first told **OR** at the time <u>of the first event</u> **OR** when you had surgery?
l.	Carotid artery surgery (on artery in neck)	1	2	-7	-8	
*m.	Heart-rhythm disturbance	1	2	-7	-8	

C1	***Have you ever been told by a health care provider that you now have or previously had:**	**YES**	**NO**	**RF**	**DK**	i: **IF YES:** How old were you when you were first told **OR** at the time <u>of the first event</u> **OR** when you had surgery?
n.	Peripheral vascular disease	1	2	-7	-8	☐☐
o.	High cholesterol	1	2	-7	-8	☐☐
p.	High blood pressure (hypertension)	1	2	-7	-8	☐☐
q.	Surgery of the stomach for weight loss purposes (i.e. stomach band, gastric bypass)	1	2	-7	-8	☐☐

WOMEN ONLY. MALE SUBJECTS SKIP TO C6.

Now I have some questions about your reproductive health history. I know that these may be quite personal, but we ask them of everyone. Please remember that all information you provide is confidential.

C2. *Have you ever had:

			YES	NO
*a.	A hysterectomy, an operation to remove your uterus or womb?		1	2 (C2b)
	a1. IF YES: Was this surgery done through the abdomen or vagina (birth canal)?	ABDOMINALLY ..... 1 VAGINALLY ..... 2 DK ..... -8		
*b	An ovary removed?		1	2
	b1. IF YESWere one or two ovaries removed?	ONE ..... 1 TWO ..... 2 DK ..... -8		

C3. Have you had a menstrual period in the past 12 months?

YES.....1	**(C4)**	RF.....-7	**(C4)**
NO.....2		DK.....-8	**(C4)**

a. Did they stop because of:

		YES	NO	RF	DK
1.	Medication, chemotherapy or radiation treatment	1	2	-7	-8
2.	Pregnancy or breastfeeding	1	2	-7	-8
3.	Menopause	1	2	-7	-8
4.	Severe weight loss or another reason	1	2	-7	-8

b. Can you tell me approximately what year your periods stopped?

Y	Y	Y	Y

RF .....-7 **(C6)**

DK.....-8 **(C6)**

C4. Compared to a year ago, has the number of days between the start of one menstrual period and the start of your next menstrual period become less predictable?

YES 1

NO..... 2

C5. Have you had a menstrual period in the past 3 months?

YES 1

NO.....2

SECTION C3. FAMILY MEDICAL HISTORY

Next, I am going to ask you a question about the health of your primary blood relatives, including your parents, siblings and any children you might have.

[IF MORE THAN ONE SISTER/BROTHER/CHILD HAS DIABETES RECORD AGES FOR EACH SISTER/BROTHER/CHILD UNTIL ALL ARE ACCOUNTED FOR]

C6	* Please tell me if any of the following people has or had Diabetes: Do not include adopted, step or half relatives.	YES	NO	N/A	RF	DK	i: IF YES: At what age was ___ diagnosed with diabetes?
a.	Your biological mother?	1	2	-1	-7	-8	
b.	Your biological father?	1	2	-1	-7	-8	

C6	* Please tell me if any of the following people has or had Diabetes: Do not include adopted, step or half relatives.	YES	NO	N/A	RF	DK	i: IF YES: At what age was ___ diagnosed with diabetes?
c.	Your biological sister?	1	2	-1	-7	-8	
d.	Your biological brother?	1	2	-1	-7	-8	
e.	Your biological child?	1	2	-1	-7	-8	

SECTION C4: MEDICATIONS

Now I am going to ask you questions about your medications. Think about the pills or medicines you are currently taking or have taken within the last 4 weeks, which are prescribed by your health care provider. I will read off a list of medications, please let me know if you are taking any in the groups I mention.

IF YES, GO ACROSS. IF NO, GO TO NEXT ITEM

C7	i. *In the last four weeks have you taken:	YES	NO	RF	DK	ii. What is the name of that medication ? Any others?	iii. What do you take it for?	iv. Amount per dose (include units)	v. Doses per day	vi. How long have you been on this medicine? vi_i. MONTHS YEARS
*a.	Insulin or pills for sugar in your blood? (NPH, regular insulin,	1	2	-7	-8					1 2

C7	i. *In the last four weeks have you taken:	YES	NO	RF	DK	ii. What is the name of that medication ? Any others?	iii. What do you take it for?	iv. Amount per dose (include units)	v. Doses per day	vi. How long have you been on this medicine? vi_i. MONTHS YEARS	
	Glucophage, Micronase, Glucotrol, Avandia)										1 2
*b.	Anything for your heart or heart beat including pills, paste or patches? (Digoxin, Nitrodur,	1	2	-7	-8						1 2
											1

C7	i. *In the last four weeks have you taken:	YES	NO	RF	DK	ii. What is the name of that medication ? Any others?	iii. What do you take it for?	iv. Amount per dose (include units)	v. Doses per day	vi. How long have you been on this medicine? vi_i. MONTHS YEARS	
	Nitroglycerin, Inderal)										2
*c.	Any medications for cholesterol or fats in your blood? (Lipitor, Zocor, Mevacor, Pravachol)	1	2	-7	-8						1 2
											1 2

C7	i. *In the last four weeks have you taken:	YES	NO	RF	DK	ii. What is the name of that medication ? Any others?	iii. What do you take it for?	iv. Amount per dose (include units)	v. Doses per day	vi. How long have you been on this medicine? vi_i. MONTHS YEARS _____

C7. Continued

C7	i. *In the last four weeks have you taken:	YES	NO	RF	DK	ii. What is the name of that medication? Any others?	iii. What do you take it for?	iv. Amount per dose (include units)	v. Doses per day	vi. How long have you been on this medicine? vi_i. MONTHS YEARS	
d.	Blood pressure or fluid pills (Norvasc, Vasotec, Aldomet, Nifedipine, Captopril, Atenolol, Lasix, HCTZ, Spironolactone)?	1	2	-7	-8						1 2
											1 2
*e.	IF FEMALE: Any female hormones	1	2	-7	-8						1

C7	i. *In the last four weeks have you taken:	YES	NO	RF	DK	ii. What is the name of that medication? Any others?	iii. What do you take it for?	iv. Amount per dose (include units)	v. Doses per day	vi. How long have you been on this medicine? vi_i. MONTHS YEARS
	including for birth control, including pills, creams, patches, implants or injectables? (Premarin, Provera, Prempro, Estrace)									2 1 2

SECTION D. HEALTH CARE

Now I am going to ask you a few questions about your use of health care services.

D1. In the last year, how many times did you go to see a health care provider for yourself? (This would include visits for routine health care, emergency, mental health care, dental, vision, physical therapy, etc).

 # VISITS **IF ZERO, GO TO D3.**

D2. What was (were) the major reason(s) for your visit(s)? Was it (Were they) for:		**YES**	**NO**
a.	An urgent (acute) problem	1	2
b.	A routine visit for an ongoing problem	1	2
c.	A flare-up of an ongoing problem	1	2
d.	Pre- or post-surgery/injury care	1	2
e.	Non-illness care (e.g., routine prenatal, general exam)	1	2

D3. When did you last see a health care provider for your own health? Was it…

6 months ago or less 1

More than 6 months ago, but less than a year ago ... 2

More than 1 year ago, but less than 2 years ago..... 3

More than 2 years ago, but less than 5 years ago 4

5 years ago or more 5

Now I'd like to find out more about your usual health care. By usual we mean whatever it means to you.

D4. Is there a particular doctor's office, clinic, health center, or other place that you usually go if you are sick or need advice about your health?

Would you say…

Yes	1	(D6)
No, or	2	
More than one place	3	(D6)

D5. What is the **main** reason you do not have a usual source of health care?

(Pick only one)

You seldom or never get sick	1	(D14)
You recently moved into area	2	(D14)
You don't know where to go for care	3	(D14)
Your usual source of medical care in this area is no longer available	4	(D14)
You can't find a provider who speaks your language	5	(D14)
You like to go to different places for different health needs	6	(D14)
You just changed insurance plans	7	(D14)
You don't use doctors/ you treat yourself	8	(D14)
The cost of medical care, or	9	(D14)
Another reason	99	↓

Can you tell me more? _____

D6. Where do you usually go for health care?		YES	NO
a.	An outpatient clinic or doctor's office	1	2
b.	A hospital emergency room	1	2
c.	A hospital outpatient clinic	1	2
d.	A health center	1	2
e.	A free clinic	1	2
f.	Retail clinic i.e. CVS Minute Clinic	1	2

D7. How do you usually get to your usual provider? PROBE: Whatever a usual provider means to you.		YES	NO
a.	Drive	1	2
b.	Someone drives you	1	2
c.	Taxi, cab, The Ride, bus, train, other public transportation	1	2
d.	Walk	1	2

D8. How long does it take you to get to your usual provider? (From wherever you usually leave from whether it is home, work, or some place else.)

MINUTES.....1

HOURS.....2

DAYS.....3

D9. How difficult is it for you to get to your usual provider?

Would you say it is….

Very difficult 1

Somewhat difficult 2

Not too difficult or..... 3

Not at all difficult..... 4

D10. Using any number from 0 to 10, where 0 is the worst doctor possible and 10 is the best doctor possible, what number would you use to rate your usual provider?

0 1 2 3 4 5 6 7 8 9 10

Worst Doctor Possible

Best Doctor Possible

D11.	In the last 12 months, were the explanations your usual provider gave you about each of the following hard to understand? *Was the explanation of [ITEM] hard to understand?	YES	NO	DOES NOT APPLY
*a.	What was wrong with you?	1	2	3
*b.	The reason for a treatment?	1	2	3
c.	What a medicine was for?	1	2	3
d.	How to take a medicine?	1	2	3
*e.	Results of a blood test, x-ray or other test?	1	2	3
f.	What to do if a condition got worse or came back?	1	2	3
*g.	Something else?	1↓	2	3

D11g1. Please specify: _____

D12. What language do you speak to your usual health care provider in?

SPECIFY: _____

D13. In the last 12 months, were any of the explanations your usual provider gave you hard to understand because of an accent or the way the doctor spoke [LANGUAGE ABOVE]?

YES 1

NO 2

Now I am going to ask you a few questions about your health insurance.

D14.	What is your current health insurance? You might have more than one type of insurance. *Do you have…	YES	NO
*a.	Private insurance from your or your partner's employer	1	2
*b.	Private insurance that you purchased (you pay the entire premium)	1	2
c.	Medicare	1	2
d.	Medicaid or Mass Health	1	2
e.	TriCare Military Health (Champus or ChampVA)	1	2
f.	Worker's compensation (a current injury is covered by worker's comp.)	1	2
g.	Free care at a particular clinic or hospital	1	2
h.	COBRA	1	2
i.	Some other type of insurance	1 ↓	2
	i1. SPECIFY: _____		
*j.	IF NO TO ALL: Do you currently have any type of health insurance?	1 ↓	2
	i1. SPECIFY: _____		

D15.	**IF NONE:** How long have you been uninsured?
	MONTHS 1 **YEARS 2**

I am going to ask you a few more questions about health care, particularly the cost of care. When answering the next few questions, do not include dental care, vision care, and prescription medicines.

D16. In the last 12 months, did you or a doctor believe you needed any medical care, tests, or treatment?

Yes..... 1

No..... 2 **(D20)**

D17. In the last 12 months, were you unable to get medical care, tests, or treatments you or a doctor believed necessary?

Yes..... 1

No..... 2 **(D20)**

D18.	In the last 12 months, why were you unable to get medical care, tests, or treatments you or a doctor believed necessary? Was it because….	YES	NO
a.	You couldn't afford care	1	2
b.	The insurance company wouldn't approve, cover, or pay for care.....	1	2
c.	The doctor refused to accept family's insurance plan	1	2
d.	Problems getting to doctor's office	1	2
e.	Different language	1	2
f.	You couldn't get time off work	1	2
g.	You didn't know where to go to get care	1	2
h.	You were refused services	1	2
i.	You couldn't get child care	1	2

D18.	In the last 12 months, why were you unable to get medical care, tests, or treatments you or a doctor believed necessary?		
	Was it because….	YES	NO
j.	You didn't have time or took too long.....	1	2
k.	Another reason.....	1 ↓	2
	k.i. SPECIFY:		

D19. How much of a problem was it that you did not get **medical** care, tests, or treatments you or a doctor believed necessary?

Would you say…

A big problem, ... 1

A small problem, or 2

Not a problem?..... 3

INCLINATION TO SEEK CARE

People seek medical care for many different reasons. An important reason for one person may be not at all important for another. We are interested in what would cause you to seek medical care. **For these questions we are interested in chronic experiences, that is, experiences that occur over a period of 3 months or more.**

D20.	[**SHOW RESPONSE CARD 'D20'**] *How important to you would it be for you to seek medical care if / to (USE EITHER WORK AS APPLICABLE)….	**EXTREMELY UNIMPORTANT**	**UNINMORTANT**	**NEITHER UN-IMPORTANT NOR IMPORTANT**	**IMPORTANT**	**EXTREMELY IMPORTANT**
*a.	you had a suspicious mole/growth on your skin	1	2	3	4	5
*b.	you were told that a sibling (brother or sister) had been diagnosed with diabetes	1	2	3	4	5
*c.	you had chest pains	1	2	3	4	5
d.	get a flu shot	1	2	3	4	5
e.	get your blood pressure or cholesterol checked	1	2	3	4	5

TAKE BACK RESPONSE CARD

E. DIABETES RISK

Now I would like to ask you a few questions about Diabetes.

E1. Please answer this question as true or false. Diabetes is an illness in which you have more than normal sugar in your blood.

TRUE	1	
FALSE	2	

E2. Do you consider diabetes to be:

Not a serious disease	1	
A moderately serious disease.....	2	
A serious disease	3	
A very serious disease	4	
No Opinion	5	

E3. Do you think your personal risk for diabetes is:

I have diabetes	1	**(F1)**
Almost no risk	2	
Slight risk	3	
Moderate risk	4	
High risk	5	

E4.	*In the past month, did you ever have:	YES	NO
*a.	Increased thirst?	1	2
b.	Increased need to urinate?	1	2
*c.	Increased fatigue?	1	2
*d.	Weight loss without decreasing your food intake or increasing exercise?	1	2

F. SLEEP (Sleep Quality Questionnaire and Berlin Sleep Questionnaire)

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

[SHOW RESPONSE CARD 'F1']

F1.	*Thinking about the past month…	Almost never or never	A few times	Sometimes	Most times	Almost always or always
*a.	Do you have difficulties falling asleep?	1	2	3	4	5
*b.	After getting up in the morning, can you fall asleep again?	1	2	3	4	5
*c.	Do you use sleeping pills?	1	2	3	4	5
d.	Are you tired during wake time?	1	2	3	4	5
e.	Are you tired after sleeping?	1	2	3	4	5
f.	Are you restless during the night (moving your legs and arms)?	1	2	3	4	5
g.	Do you get up during the night?	1	2	3	4	5
*h.	Do you suffer from headaches first thing in the morning?	1	2	3	4	5
i.	Do you feel exhausted for no obvious reasons?	1	2	3	4	5
*j.	How often have you been told that you quit breathing during your sleep?	1	2	3	4	5
k.	How often have you nodded off or fallen asleep while driving a vehicle?	1	2	3	4	5
*l.	How frequently have you been told that you snore?	1	2	3	4	5

[TAKE BACK RESPONSE CARD]

F2. How many hours of actual sleep do you usually get during the night?

(This may be different than the number of hours you spend in bed)

		.		HOURS

F3. How long does it usually take you to fall asleep at bedtime?

			MINUTES

SECTION G: PHYSICAL ACTIVITY (PASE)

Now I am going to ask you about your activities in the last seven days not including today. Your answers should reflect how you actually behaved. There are no right or wrong responses.

G1. **[SHOW RESPONSE CARD 'G1']** *In the last 7 days, how often did you:		**[SHOW RESPONSE CARD 'G1i']** **i. IF EVER**: On average, how many hours per day did you engage in these activities?
*a. Participate in sitting activities such as reading, watching TV or doing handcrafts. Would you say:	Never ..... 0 Seldom (1-2 days) ..... 1 Sometimes (3-4 days) ..... 2 Often (5-7 days) 3	Less than 1 hour ..... 1 1 but less than 2 hours ..... 2 2-4 hours ..... 3 More than 4 hours..... 4
*b. Take a walk outside your home or yard for any reason? For example, for fun or exercise, walking to work, walking the dog, etc. Would you say:	Never ..... 0 Seldom (1-2 days) ..... 1 Sometimes (3-4 days) ..... 2 Often (5-7 days) 3	Less than 1 hour ..... 1 1 but less than 2 hours ..... 2 2-4 hours ..... 3 More than 4 hours..... 4
*c. Engage in light sport or recreational activities such as catch, darts, bocci, golf with a cart, fishing from a boat or pier or other similar activities. Would you say:	Never ..... 0 Seldom (1-2 days) ..... 1 Sometimes (3-4 days) ..... 2 Often (5-7 days) 3	Less than 1 hour ..... 1 1 but less than 2 hours ..... 2 2-4 hours ..... 3 More than 4 hours..... 4
*d. Engage in moderate sport and recreational activities		

G1. **[SHOW RESPONSE CARD 'G1']** *In the last 7 days, how often did you:		**[SHOW RESPONSE CARD 'G1i']** **i. IF EVER**: On average, how many hours per day did you engage in these activities?
such as doubles tennis, dancing, hunting, ice skating, golf w/o a cart, softball, skating or other similar activities. Would you say:	Never ..... 0 Seldom (1-2 days) ..... 1 Sometimes (3-4 days) ..... 2 Often (5-7 days) 3	Less than 1 hour ..... 1 1 but less than 2 hours ..... 2 2-4 hours ..... 3 More than 4 hours..... 4
*e. Engage in strenuous sport and recreational activities such as jogging, swimming, cycling, singles tennis, basketball, skiing or other activities. Would you say:	Never ..... 0 Seldom (1-2 days) ..... 1 Sometimes (3-4 days) ..... 2 Often (5-7 days) 3	Less than 1 hour ..... 1 1 but less than 2 hours ..... 2 2-4 hours ..... 3 More than 4 hours..... 4
*f. Do any exercises specifically to increase muscle strength and endurance, such as lifting weights or push-ups, etc. Would you say:	Never ..... 0 Seldom (1-2 days) ..... 1 Sometimes (3-4 days) ..... 2 Often (5-7 days) 3	Less than 1 hour ..... 1 1 but less than 2 hours ..... 2 2-4 hours ..... 3 More than 4 hours..... 4

[TAKE BACK RESPONSE CARD FOR 'G1' AND 'G1i']

	*In the last 7 days, have you done any:	YES	NO
G2.	Light housework, such as dusting or washing dishes?	1	2
*G3.	Heavy housework or chores, such as vacuuming, scrubbing floors, washing windows, or carrying wood?	1	2
G4a.	Home repairs like painting, wallpapering, electrical work, etc.	1	2
*b.	Lawn work or yard care, including snow or leaf removal, wood chopping, etc.	1	2
c.	Outdoor gardening	1	2
*d.	Caretaking of another person, such as children, dependent spouse, or another adult	1	2

G5. In the last 7 days, did you work, including work as a volunteer?

YES..... 1

NO ..... 2 **(SECTION G6)**

a. How many hours per week did you work, including work as a volunteer, in the last 7 days?

			HOURS

b. Which of the following categories best describes the amount of physical activity required on your job or in your volunteer work?

Mainly sitting with slight arm movements 1

Sitting or standing with some walking 2

Walking, with some handling of materials weighing less than 50 pounds 3

Walking and heavy manual work often requiring handling of materials weighing over 50 pounds 4

G6. In the last year, did you work, including work as a volunteer?

YES 1

NO ..... 2 **(SECTION H)**

ASK OF SUBJECTS WHO HAVE WORKED IN THE LAST 12 MONTHS ONLY

At this point in the interview, the style of the questions changes; up until now, the questions have been more specifically health related (your health history, health care, etc.). Now I want to find out more about different feelings and social situations that you may or may not experience, as sometimes these can affect a person's health. Please be patient as we go through these next few sections. We ask everyone the same questions so that we can get an overall idea of the lives of our study participants.

Since we were just talking about work, I'm going to start with that. Here are some situations that might arise at work. Please tell me how often you have had these things happen to you during the past 12 months.

[IF SUBJECT IS SELF-EMPLOYMED INSTRUCT THEM TO THINK ABOUT THEIR CLIENTS OR PEOPLE THEY WORK WITH ON A REGULAR BASIS]

[SHOW RESPONSE CARD G7]

G7.	***During the past 12 months...**	**Almost everyday**	**At least once a week**	**A few times a month**	**A few times a year**	**Less than once a year**	**Never**
*a.	How often do you feel that you have to work twice as hard as others to get the same treatment or evaluation?	1	2	3	4	5	6
*b.	How often are you watched more closely than other workers?	1	2	3	4	5	6
c.	How often are you unfairly humiliated in front of others at work?	1	2	3	4	5	6
*d.	How often does your supervisor or coworkers make slurs or jokes about	1	2	3	4	5	6

G7.	*During the past 12 months...	Almost everyday	At least once a week	A few times a month	A few times a year	Less than once a year	Never
	racial or ethnic groups?						
e.	How often does your supervisor or coworkers make slurs or jokes about women?	1	2	3	4	5	6
f.	How often does your supervisor or co-workers make slurs or jokes about gays or lesbians?	1	2	3	4	5	6

TAKE BACK RESPONSE CARD.

SECTION H. DISCRIMINATION

Next please tell me how often, in your day-to-day life the following things have happened to you.

[SHOW RESPONSE CARD H1 / H3.]

H1.	***In your day-to-day life how often ...**	**Almost everyday**	**At least once a week**	**A few times a month**	**A few times a year**	**Less than once a year**	**Never**
*a.	are you treated with less courtesy or respect than other people	1	2	3	4	5	6
*b.	Do you receive poorer service than other people at restaurants or stores.	1	2	3	4	5	6
c.	Do people act as if they think you are not smart.	1	2	3	4	5	6
d.	Do people act as if they are afraid of you.	1	2	3	4	5	6
e.	Are you threatened or harassed.	1	2	3	4	5	6

IF <u>NEVER</u> TO ALL GO TO H3.

H2. Thinking about the experiences we just discussed [PROBE AS NECESSARY TO REMEMBER WHICH.], what do you think was the **main** reason why these happened to you? Please choose only one response.

Your ancestry or national origin	1
Your gender	2
Your race	3
Your age	4
Your height	5
Your weight	6
Some other aspect of your physical appearance	7
Your sexual orientation	8
Something else?	9 ↓

Can you tell me more? _____

Vigilance

Next please tell me how often, in your day-to-day life you do the following things.

[SHOW RESPONSE CARD H1 / H3.]

H3.	***In your day-to-day life, how often do you …**	**Almost everyday**	**At least once a week**	**A few times a month**	**A few times a year**	**Less than once a year**	**Never**
*a.	try to prepare for possible insults from other people before leaving home	1	2	3	4	5	6
*b.	feel that you always have to be very careful about your appearance to get good service or avoid being harassed.	1	2	3	4	5	6
c.	watch carefully what you say and how you say it.	1	2	3	4	5	6
d.	try to avoid certain social situations and places	1	2	3	4	5	6

TAKE BACK RESPONSE CARD.

SECTION I: PSYCHOSOCIAL FACTORS

Major Life Events [557]

Next, I'm going to read you events that may or may not have happened to you over the past year. Think about the last year and the events that have happened in your life. Please answer Yes, it happened to me or No, it did not happen to me to each statement that I read.

I1.	***In the past year have you…?**	**YES**	**NO**
*a.	Experienced the death of a spouse?	1	2
*b.	Gone through a divorce?	1	2
*c.	Gone through a marital separation?	1	2
d.	Been detained in jail or in another institution?	1	2
*e.	Experienced the death of a close family member (other than a spouse)?	1	2
f.	Had a major injury or illness?	1	2
g.	Gotten married?	1	2
*h.	Been fired at work?	1	2
i.	Had a marital reconciliation?	1	2
j.	Retired from work?	1	2

SECTION J. SENSE OF CONTROL AND ALIENATION [182]

Next, I'm going to read you several statements describing how people sometimes feel. Think about yourself and the feelings you may have experienced. Please tell me how much you agree or disagree with each statement that I read, keeping in mind that the "I" in each statement refers to you.

[SHOW RESPONSE CARD J1]

J1.	*How much do you agree or disagree….	**Strongly Disagree**	**Disagree**	**Neither Agree nor Disagree**	**Agree**	**Strongly Agree**
*a.	I am responsible for my own successes.	1	2	3	4	5
*b.	I can do just about anything I really set my mind to.	1	2	3	4	5
*c.	My misfortunes are the result of mistakes I have made	1	2	3	4	5
d.	I am responsible for my failures.	1	2	3	4	5
e.	The really good things that happen to me are mostly luck	1	2	3	4	5
*f.	There is no sense in planning a lot—if something good is going to happen it will.	1	2	3	4	5
g.	Most of my problems are due to bad breaks	1	2	3	4	5
*h.	I have little control over the bad things that happen to me	1	2	3	4	5
i.	Most people are honest because they are afraid of being caught.	1	2	3	4	5
j.	In order to get ahead people don't always do what's right	1	2	3	4	5
*k.	In order to get ahead you have to take everything you can get.	1	2	3	4	5

J1.	*How much do you agree or disagree….	**Strongly Disagree**	**Disagree**	**Neither Agree nor Disagree**	**Agree**	**Strongly Agree**
l.	For some people to succeed others must fail	1	2	3	4	5
*m.	I feel it is not safe to trust anyone	1	2	3	4	5
n.	I feel suspicious	1	2	3	4	5
*o.	I feel sure that everyone is against me.	1	2	3	4	5
p.	I have someone I can turn to for support and understanding when things get rough	1	2	3	4	5
q.	I have someone I can really talk to	1	2	3	4	5
r.	I have someone who would help me out with things like give me a ride, watch the kids or house, or fix something	1	2	3	4	5
s.	I have someone who would take care of me if I were sick	1	2	3	4	5

TAKE BACK RESPONSE CARD.

SECTION K: TOBACCO AND ALCOHOL CONSUMPTION (NHANES III)

Now I'd like to ask you about any past or present tobacco and alcohol use.

K1. For the purposes of this question we consider a "smoker" as someone who has smoked at least 100 cigarettes (about 5 packs) in their entire life. Are you now or have you ever been a smoker (smoked at least 100 cigarettes in your entire life)?

YES CURRENT	1	
YES PAST	2	
NO I HAVE NOT SMOKED 100 OR MORE CIGARETTES	3	

Now I would like to ask you a few questions about drinking alcoholic beverages.

K2. Have you <u>ever</u> had an alcoholic drink?

YES	1	
NO	2	**(L1)**

K3. Have you had an alcoholic drink in the last 30 days?

YES	1	
NO	2	**(K6)**

K4. Considering all the types of alcoholic beverages, how many times during the last 30 days did you have 5 or more drinks within a 24-hour period?

		# TIMES

K5. Now, thinking about the occasions or days that you drink, how many drinks on average do you have during those occasions (at one sitting or session)?

		# DRINKS

K6. In the past 10 years, has your use of alcoholic beverages…….

Increased 1

Decreased..... 2

Not changed..... 3

SECTION L: LANGUAGE AND ACCULTURATION

Now I'd like to ask you questions about the languages that you might speak since some survey participants speak more than one language.

L1. Can you please tell me which language was the first you learned to speak?

English ..... 1 **(L5)**

Spanish 2

Portuguese 3

French..... 4

Italian..... 5

Russian 6

German..... 7

Or something else 99

a. SPECIFY: _____

Language Use Subscale

[SHOW RESPONSE CARD L2/L4]

L2	Almost never	Sometimes	Often	Almost Always
a. How often do you speak English?	1	2	3	4
b. How often do you speak in English with your friends?	1	2	3	4
c. How often do you think in English?	1	2	3	4
d. How often do you speak [FIRST LANGUAGE]?	1	2	3	4
e. How often do you speak in [FIRST LANGUAGE] with your friends?	1	2	3	4
f. How often do you think in [FIRST LANGUAGE]?	1	2	3	4

TAKE BACK RESPONSE CARD.

Language Use Subscale

[SHOW RESPONSE CARD L3]

L3	Very Poorly	Poorly	Well	Very Well
a. How well do you speak English?	1	2	3	4
b. How well do you read in English?	1	2	3	4
c. How well do you understand television programs in English?	1	2	3	4
d. How well do you understand radio programs in English?	1	2	3	4
e. How well do you write in English?	1	2	3	4
f. How well do you understand music in English?	1	2	3	4
g. How well do you speak [FIRST LANGUAGE]?	1	2	3	4
h. How well do you read in [FIRST LANGUAGE]?	1	2	3	4
i. How well do you understand television programs in [FIRST LANGUAGE]?	1	2	3	4
j. How well do you understand radio programs in [FIRST LANGUAGE]?	1	2	3	4
k. How well do you write in [FIRST LANGUAGE]?	1	2	3	4
l. How well do you understand music in [FIRST LANGUAGE]??	1	2	3	4

TAKE BACK RESPONSE CARD.

Electronic Media Subscale

[SHOW RESPONSE CARD L2/L4]

L4	Almost never	Sometimes	Often	Almost Always
a. How often do you watch television programs in English?	1	2	3	4
b. How often do you listen to radio programs in English?	1	2	3	4
c. How often do you listen to music in English?	1	2	3	4
d. How often do you watch television programs in [FIRST LANGUAGE]??	1	2	3	4
e. How often do you listen to radio programs in [FIRST LANGUAGE]?	1	2	3	4
f. How often do you listen to music in [FIRST LANGUAGE]?	1	2	3	4

TAKE BACK RESPONSE CARD.

Let's talk a little about technology and items you may or may not have.

L5	As I read the following list of items, please tell me if you happen to have each one, or not. *Do you have...	YES	NO
*a.	A desktop computer?	1	2
*b.	A laptop computer?	1	2
*c.	A cell phone?	1	2
d.	A Blackberry, iPhone or other similar device?	1	2
e.	A PDA or other personal data device	1	2

IF NO TO **A** AND **B** GO TO L7.

IF NO TO ALL, GO TO L8.

L6. Do you have an internet connection on your home computer? For example, dial-up, cable, or DSL?

YES 1

NO ..... 2 **(L7)**

L6a.	How are you connected to the internet	YES	NO
a.	Dial-up	1	2
b.	Fiber Optic	1	2
c.	DSL	1	2
d.	Cable	1	2
e.	Satellite Wireless	1	2
f.	Other	1	2

L7	*Do you ever use your cell phone, Blackberry or other device to [ITEM]?	YES	NO
*a.	Send or receive email?	1	2
b.	Send or receive text messages?	1	2
*c.	Access the internet?	1	2

L8. Do you have access to a computer somewhere other than home ?

YES 1

NO .....2 (**SECTION M**)

L9.	Other than home, where do you use a computer?	YES	NO
a.	Work	1	2
b.	Local Library	1	2
c.	Friends	1	2
d.	Family outside household	1	2
e.	Other	1	2

SECTION M: SOCIO-DEMOGRAPHIC INFORMATION

Now I am going to ask you some questions about your background and about where you live.

M1. What is your current marital status?

Married	1
Living with a partner	2
Divorced/separated	3
Widowed	4
Single, never married	5
OTHER	99

[SHOW RESPONSE CARD M2]

M2. What is the highest grade/degree you have completed?

LESS THAN 8TH GRADE	1
8TH GRADE	2
9TH THROUGH 11TH GRADE	3
HIGH SCHOOL DIPLOMA/GED	4
TECHNICAL TRAINING	5
ASSOCIATES DEGREE	6
BACHELORS DEGREE	7
MASTERS DEGREE	8
DOCTORATE DEGREE (E.G. MD, PHD, JD)	9

TAKE BACK RESPONSE CARD.

M3. How many years of school have you completed altogether?

		YEARS

Now I would like to ask you a few questions about your current work situation.

M4. Which of the following categories best describes your current work situation?

Working for pay	1	
Unemployed and looking for work	2	**(M8)**
Temporarily laid off; On sick or other leave	3	**(M8)**
Disabled	4	**(M8)**
Retired	5	**(M8)**
Homemaker	6	**(M8)**
Full-Time Student	7	**(M8)**
Other (INCLUDING VOLUNTEER)	99	

a. SPECIFY: _____

M5. How many jobs do you currently have? NUMBER: ____

M6. Are you currently working 35 hours or more each week (full time) or less than 35 hours?

35 HRS OR MORE/WK	1
LESS THAN 35 HRS/WK	2

M7. How many <u>days</u> per week do you work? NUMBER: _____

M8. What is (was) your usual occupation? SPECIFY: _____

[SHOW RESPONSE CARD M9]

M9. Income is important in analyzing the health information we collect. Including income from wages, salaries, Social Security or retirement benefits, help from relatives, veteran's benefits, real estate, investments, and other sources, about how much was your total household income in the last 12 months? Please look at this card and tell me which category best describes the amount.

LESS THAN $5,000	1
$5,000 - $9,999	2
$10,000 - $19,999	3
$20,000 - $29,999	4
$30,000 - $39,999	5
$40,000 - $49,999	6
$50,000 - $59,999	7
$60,000 - $69,999	8
$70,000 - $79,999	9
$80,000 - $89,999	10
$90,000 - $99,999	11
$100,000 - $109,999	12
$110,000 - $119,999	13
$120,000 - $149,999	14
$150,000 - $199,999	15
$200,000 - $299,999	16
$300,000 - $499,999	17
$500,000 - $999,999	18
$1,000,000 OR MORE	19
RF	-7
DK	-8

TAKE BACK RESPONSE CARD.

SECTION N: NEIGHBORHOOD

Now I am going to ask about your neighborhood. Please think about the area that you currently live in and answer how much you agree or disagree. The word neighborhood in these questions is whatever it means to you.

[SHOW RESPONSE CARD N1.]

N1.	*How much do you agree or disagree...	**Strongly Disagree**	**Disagree**	**Neither Agree nor Disagree**	**Agree**	**Strongly Agree**
*a.	There is a lot of graffiti in my neighborhood	1	2	3	4	5
*b.	My neighborhood is noisy	1	2	3	4	5
*c.	Vandalism is common in my neighborhood	1	2	3	4	5
d.	There are a lot of abandoned buildings in my neighborhood	1	2	3	4	5
e.	My neighborhood is clean	1	2	3	4	5
*f.	People in my neighborhood take good care of their houses and apartments.	1	2	3	4	5
g.	There are too many people hanging around on the streets near my home.	1	2	3	4	5
*h.	There is a lot of crime in my neighborhood.	1	2	3	4	5
i.	There is too much drug use in my neighborhood.	1	2	3	4	5
j.	There is too much alcohol use in my neighborhood.	1	2	3	4	5
*k.	I'm always having trouble with my neighbors.	1	2	3	4	5
l.	My neighborhood is safe.	1	2	3	4	5

[TAKE BACK RESPONSE CARD]

SECTION O: CONTACT INFORMATION

I am going to ask you several questions about where you live. Please tell me about where you currently live.

O1. Do you own or rent your home?

Own..... 1

Rent..... 2

Other..... 99 ↓

SPECIFY_____

O2. Which of the following <u>best</u> describes your home. Please choose only one.

Single Family House..... 1

Multi-Family House or unit in a Multi-Family House 2

Unit in an Apartment Building..... 3

Townhouse/Brownstone..... 4

Other..... 99 ↓

SPECIFY_____

O3. How long have you lived at your current address?

DAYS.....1

MONTHS.....2

YEARS.....3

BEGIN TEAR OFF SHEET – PRIVATE PROTECTED INFORMATION

O4.	What is your current primary address?	# AND STREET APT # CITY, STATE ZIPCODE
O5.	What are the two nearest cross streets to your home?	STREET 1 STREET 2

O6. In how many different places have you lived in the past 5 years?

THE FOLLOWING SECTION WILL BE PULLED FROM BACH II

PROMPT THE PARTICIPANT TO CONFIRM THE FOLLOWING INFORMATION

P1. What is your home telephone number? _____

P2. What is your work telephone number? _____

P3. What is your cell phone number? _____

P4. Do you have an email address where we could contact you? _____

P5. **IF MARRIED/PARTNERED**: What is your spouse/partner's first and last name?

a. FIRST NAME: _____

b. LAST NAME: _____

Before I give you the last form to complete it would also be helpful to have the name and phone number of a contact person for you. This would be someone who does <u>not</u> live in your household but who would know how to contact you. We will only contact this person if we cannot contact you. This information, as with all of the other information that you have provided, will remain strictly confidential.

P6. What is the name of a reliable contact person for you? Can you spell the first and last name?

a. FIRST NAME: _____

b. LAST NAME: _____

c. What is (his/her) address?

c1. ADDRESS _____

c2. CITY _____

c3. STATE _____

c4. ZIP _____

d. What is (his/her) home, work, and cell phone numbers?

d1. HOME: _____

d2. WORK: _____

d3. CELL: _____

P7. What is the name of a second reliable contact person for you? Can you spell the first and last name?

a. FIRST NAME: _____

b. LAST NAME: _____

c. What is (his/her) address?

c1. ADDRESS _____

c2. CITY _____

c3. STATE _____

c4. ZIP _____

d. What is (his/her) home, work, and cell phone numbers?

d1. HOME: _____

d2. WORK: _____

d3. CELL: _____

P9. END TIME OF INTERVIEW: | | | : | | | 24 HR CLOCK

H H M M

SECTION Q. HEALTH LITERACY

Here are some medical instructions that people sometimes see around a hospital.

Each instruction has some of the words missing. There are four possible choices that might work with each sentence. TURN PAGES TO SHOW EXAMPLES.

For each instruction, please look at each of the four choices and decide which makes the most sense to fill in the blank. Then circle the letter and go on to the next until you have finished all the questions.

GIVE THE PARTICIPANT THE HEALTH LITERACY PACKET. ALLOW THE PARTICIPANT 7 MINUTES TO COMPLETE THE SURVEY**. DO NOT TELL THEM IT IS TIMED.** WHEN SEVEN MINUTES HAVE ELAPSED TELL THE PARTICIPANT THAT "THAT SHOULD GIVE US WHAT WE ARE LOOKING FOR. THANK YOU FOR YOUR COOPERATION" AND REMOVE THE TEST MATERIAL.

Q1. WHAT IS THE SUBJECT'S HEALTH LITERACY SCORE?

Appendix C: Relevant Presentations and Publications

9.4 Publications

Publications relevant to this thesis that I have either produced or contributed to over the course of my education are listed below:

7. Goonesekera SD, Fang SC, **Piccolo RS**, Florez JC, McKinlay JB. Biogeographic ancestry is associated with higher total body adiposity among African-American females: the Boston Area Community Health Survey. **PLoS ONE.** In press.
8. **Piccolo RS**, Duncan D, Pearce N, McKinlay, JB. The role of neighborhood characteristics in racial/ethnic disparities in type 2 diabetes: Results from the Boston Area Community Health (BACH) Survey. **Social Science in Medicine**, Apr 2015; 130: 79-90.
9. Yang MH, Hall SA, **Piccolo RS**, Maserejian NN, McKinlay JB. Do Behavioral Risk Factors for Prediabetes and Insulin Resistance Differ Across the Socioeconomic Gradient? Results from a Community-Based Epidemiologic Survey. **International Journal of Endocrinology**, In press.
10. **Piccolo RS**, Pearce N, Araujo AB, McKinlay, JB. The contribution of biogeographic ancestry and socioeconomic status to racial/ethnic disparities in type 2 diabetes: Results from the Boston Area Community Health (BACH) Survey. **Annals of Epidemiology**, Sep 2014; 24(9): 648-654.
11. Meigs JB, Grant RW, **Piccolo R**, Lopez L, Florez JC, Porneala B, Marceau L, McKinlay JB. Association of African Genetic Ancestry with Fasting Glucose and Hemoglobin A1c Levels in Non-Diabetic Individuals: The Boston Area Community Health (BACH) Prediabetes Study. **Diabetologia**, Sept 2014; 57 (9): 1850-1858.
12. McKinlay J, **Piccolo R**, Marceau L. An additional cause of health care disparities: the variable clinical decisions of primary care doctors. **Journal of Evaluation in Clinical Practice**. Aug 2013; 19 (4) 664-73.
13. **Piccolo RS**, Araujo AB, Pearce, N, McKinlay JB. Cohort Profile: The Boston Area Community Health (BACH) Survey. **International Journal of Epidemiology**. Feb 2014; 43 (1): 42-51.

9.5 Papers in Progress

An additional six papers are under review or in process.

1. **Piccolo RS**, Subramanian SV, Pearce N, McKinlay JB. The Relative Contributions of Socioeconomic, Local Environmental, Psychosocial, Lifestyle/Behavioral, Biophysiologic, and Ancestral Factors to Racial/Ethnic Disparities in Type 2 Diabetes. To be submitted.
2. Goonesekera SD, Yang MH, Hall SA, Fang SC, **Piccolo RS**, McKinlay JB. Racial ethnic differences in type II diabetes treatment patterns and glycemic control in the Boston Area Community Health Survey. BMJ Open. Under Revision.
3. Lagisetty PA, **Piccolo R**, Yang M, Marceau LD, Grant R, Lopez L, Meigs JB, McKinlay JB. Food Environment, Diet Behavior and Weight Gain in a Multi-Ethnic Urban Cohort. Preventing Chronic Disease . Under Review.

4. Lopez L, Grant RW, Marceau LD, **Piccolo RS**, McKinlay JB, Meigs JB. Association of Accultration and Health Literacy with Prevalent Dysglycemia and Diabetes Control among Latinos in the Boston Area Community Health (BACH) Survey. Journal of Immigrant and Minority Health. Under Review.

9.6 Abstracts/Presentations

American Public Health Association (Boston, MA) November 2013

- *Does Genetic Ancestry Explain Racial/Ethnic Disparities in Diabetes? Results from a Longitudinal Study* (Piccolo RS)
- *Racial/Ethnic Disparities in Type 2 Diabetes: The Role of Neighborhood* (Piccolo RS)

AcademyHealth (Baltimore, MD) June 2013

- *Are Racial/Ethnic Disparities in Diabetes Explained by Ancestry or by Socioeconomic Differences? Results from a Longitudinal Study* (Piccolo RS)
- *The Role of Neighborhood Socioeconomic Status in Racial/Ethnic Disparities in Type 2 Diabetes* (Piccolo RS)

American Diabetes Association (Chicago, IL) June 2013

- *The Role of Neighborhood Socioeconomic Status in Racial/Ethnic Disparities in Type 2 Diabetes* (Piccolo RS)
- *Is Genetic Ancestry Associated with Incident Type 2 Diabetes?* (Piccolo RS)

2013 Reducing Health Disparities in Type 2 Diabetes Mellitus Summit (Baltimore, MD) March 2013

- *The Role of Neighborhood Socioeconomic Status in Racial/Ethnic Disparities in Type 2 Diabetes* (Piccolo RS)

2012 Science of Eliminating Health Disparities Summit (Washington D.C.) December 2012

- *Does Limited Health Literacy Explain Racial/Ethnic Disparities in Diabetes Control?* (Piccolo RS)

Society for Social Medicine (London, UK) September 2012

- *A Profile of Undiagnosed Diabetics in the Community: Results from the Boston Area Community Health (BACH) Pre-Diabetes Survey* (Piccolo RS)

American Diabetes Association (Philadelphia, PA) June 2012

- *A Profile of Undiagnosed Diabetics in the Community: Results from the Boston Area Community Health (BACH) Pre-Diabetes Survey* (Piccolo RS)
- *Does Limited Health Literacy Explain Racial/Ethnic Disparities in Diabetes Control?* (Piccolo RS)

AcademyHealth (Orlando, FL) June 2012

- *Does Limited Health Literacy Explain Racial/Ethnic Disparities in Diabetes Control?* (Piccolo RS)