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**Title**

The Impact of Neighborhoods on CV Risk

**Permalink**

<https://escholarship.org/uc/item/8ww8538t>

**Journal**

Global Heart, 11(3)

**ISSN**

2211-8160

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**Publication Date**

2016-09-01

**DOI**

10.1016/j.gheart.2016.08.002

Peer reviewed



# HHS Public Access

Author manuscript

*Glob Heart*. Author manuscript; available in PMC 2017 September 01.

Published in final edited form as:

*Glob Heart*. 2016 September ; 11(3): 353–363. doi:10.1016/j.ghert.2016.08.002.

## The impact of neighborhoods on cardiovascular risk: the MESA Neighborhood Study

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### Abstract

Cardiovascular disease (CVD) continues to be the leading cause of death and a major source of health disparities in the United States and globally. Efforts to reduce CVD risk and eliminate cardiovascular health disparities have increasingly emphasized the importance of the social determinants of health. Neighborhood environments have emerged as a possible target for prevention and policy efforts. Hence there is a need to better understand the role of neighborhood environments in shaping cardiovascular risk. The Multi-Ethnic Study of Atherosclerosis Neighborhood Study provided a unique opportunity to build a comprehensive place-based resource for investigations of associations between specific features of neighborhood physical and social environments and cardiovascular risk factors and outcomes. This manuscript summarizes the approaches used to characterize residential neighborhood environments in the MESA cohort, provides an overview of key findings to date, and discusses challenges and opportunities in neighborhood health effects research. Results to date suggest that neighborhood physical and social environments are related to behavioral and biomedical risk factors for CVD and that cardiovascular prevention efforts might benefit from taking neighborhood context into account.

### Keywords

cardiovascular disease; health disparities; neighborhoods; social determinants

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Despite overall declines in cardiovascular disease (CVD) mortality since the 1970s, it remains the leading cause of death in the U.S.[1] and a major cause of health disparities in

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The authors have no conflicts of interest or financial disclosures.

morbidity and mortality. Compared to non-Hispanic whites, African Americans and other racial/ethnic minorities have a higher incidence and prevalence of CVD [2, 3] and CVD mortality[2], and these differences have persisted over-time.[4] There also continue to be large and persistent differences in cardiovascular risk by socioeconomic position.[5] A great deal of research over the past fifty years has emerged to improve understanding of the genetic, biological, and behavioral factors that contribute to the development of cardiovascular disease.[6] However, there has also been increasing recognition of the need to investigate the upstream causes of these more proximal risk factors not only to better understand the drivers of disparities by socioeconomic position and race/ethnicity but also to develop more effective prevention strategies for the population as a whole.[7]

Efforts to reduce CVD risk and eliminate cardiovascular health disparities have increasingly emphasized the importance of the social determinants of health, defined as factors related to the social circumstances in which people are born, grow, live and age.[8] Signaling the growing awareness of this topic in the cardiovascular health community, a recent statement by the American Heart Association noted that “at present, the most significant opportunities for reducing death and disability from CVD in the United States lie within addressing the social determinants of cardiovascular outcomes”.[5]

There is a long history in CVD epidemiology of efforts to understand how context broadly defined influences the distribution of cardiovascular disease. A seminal paper in this area is “Sick individuals and sick populations” by Geoffrey Rose,[9] in which Rose makes a strong case for the need to examine not only the drivers of inter-individual variability within populations (the “causes of cases” as he calls it) but also the causes of differences in the distribution of cardiovascular risk across populations (“the causes of incidence” in Rose’s terminology). However, traditionally CVD epidemiology has been focused primarily on individual-level risk factors such as behaviors, biomedical risks factors (like blood lipids, obesity, diabetes and hypertension), and more recently genetic factors, often divorced from their social and environmental contexts.

The Multi-Ethnic Study of Atherosclerosis (MESA) with its wealth of longitudinal behavioral, biomedical, and subclinical risk factor data collected across six diverse geographic sites and in a large multi-ethnic sample, presented a unique opportunity to link this rich individual-level information to broader social and environmental contexts. This paper summarizes the approaches used to characterize residential neighborhood environments in the MESA cohort and highlights some of the key findings to date on the links between neighborhoods and cardiovascular risk that have emerged from the MESA Neighborhood Study. Challenges in identifying the health impact of neighborhood factors and ideas for future work are also discussed.

## **EARLY STUDIES OF NEIGHBORHOODS AND CARDIOVASCULAR DISEASE**

Neighborhoods are certainly not the only social and environmental contexts potentially relevant to the development and prognosis of cardiovascular disease. Family contexts, work contexts, school contexts, and peer-group contexts among others are all likely to be relevant. Broader macro-level factors that characterize societies themselves (like the reliance on

processed foods, the dependence on the automobile for transportation, the marketing of less healthy foods or tobacco, and the presence of regulations or taxation of tobacco products) also likely play a key role. However, the “meso” level of neighborhoods is of interest for three important reasons. First, many of these broader social determinants are manifested, and directly affect individuals, through neighborhood social and physical environments. Thus the study of neighborhoods provides an opportunity to understand the processes linking these broader social and economic factors to CVD in very concrete ways. Second, the strong residential segregation by race and class that is present in the United States (and in many other countries) suggests that these neighborhood differences could be important contributors to disparities in cardiovascular disease. Last but not least, differences across neighborhoods are not “natural” but are the result of the impact of policies (or the absence of policies) and are hence directly amenable to intervention.

In one of the earliest studies of neighborhood health effects, Haan et al.[10] used data from the Alameda County study to show that individuals living in federally designated poverty areas had a 50% higher all-cause mortality rate compared to individuals residing in non-poor areas. Subsequent studies used a similar approach to attempt to isolate the impact of “neighborhood socioeconomic context” on a range of outcomes including cardiovascular disease. For example, Diez Roux et al.[11] used data from the Atherosclerosis Risk in Communities Study to show that living in disadvantaged neighborhoods, as measured by an index derived from census measures, was associated with a higher risk of coronary heart disease, independent of individual-level characteristics. Other studies have documented that living in socioeconomically disadvantaged neighborhoods is associated with a higher prevalence and incidence of CVD risk factors, [12, 13] outcomes, [11, 14, 15] and mortality. [16–18]

Although intriguing, these types of studies cannot be used to draw firm conclusions regarding causation. First they present methodologic challenges regarding the ability to isolate contextual factors from compositional factors (especially because the neighborhood measure used is itself an aggregate of the socioeconomic characteristics of residents). Second, and most importantly, they do not allow identification of what neighborhood factors are the true causal factors. Neighborhood disadvantage indices are used as crude proxies for a range of social and physical environment factors that could be related to cardiovascular disease. Strengthening causal inference requires identifying the specific factors that might be relevant. This is also critical for the development (and subsequent testing) of policies and interventions aimed at modifying neighborhood factors.

## THE CHARACTERIZATION OF NEIGHBORHOOD ENVIRONMENTS IN MESA

The MESA Neighborhood Study was designed to investigate the impact of a set of specific features of neighborhood physical and social environments on CVD risk and the contributions of these specific features to disparities in CVD risk by race/ethnicity and socioeconomic position. Critical elements of the study design included the measurement of time-varying neighborhood environments and the ability to link these measures to rich longitudinal risk factor and outcome data collected as part of the MESA parent study.

The hypotheses investigated in the MESA Neighborhood Study and the neighborhood assessments performed were guided by a conceptual framework (figure 1) that provides an overview of the aspects of neighborhood environments that may be relevant and the potential pathways linking these features to clinical cardiovascular disease. A major emphasis of the MESA Neighborhood Study was the development and operationalization of a diverse set of strategies to characterize the neighborhood environments of MESA participants over time. This required a careful tracking of the residential locations of MESA participants as well as the periodic measurement of features of neighborhood social and physical environments. This allowed the study to characterize exposure to neighborhood environments not only at the study baseline, but also cumulative exposure over time, as well as changes in exposures (resulting from residential mobility or from changes in specific neighborhoods over time). The ability to track neighborhood exposures longitudinally was critical to many study hypotheses and specifically to the ability to strengthen causal inferences by linking changes in exposures to changes in outcomes.

At the time of the inception of the MESA Neighborhood Study, the measurement of neighborhood exposures was in its infancy. The vast majority of studies of neighborhoods and health relied on information from the U.S. census and indicators of neighborhood disadvantage that could be linked to health study participants using home address information. A major contribution of the MESA Neighborhood Study has therefore been the development and testing of a diverse set of measurement strategies to characterize environmental contexts. Given the heterogeneous nature of the constructs that needed to be assessed, a combination of measurement strategies was necessary, including survey-based measures, measures based on linking various resources to study participants using geographic information systems (GIS), and audit-type measures. [19] All three types of measures were used to characterize MESA neighborhood environments to varying degrees and in some cases measures were created that combined strategies.

Flexibility in the spatial definition of “neighborhoods” was important given that the appropriate definition of “neighborhood” could vary based on the process being investigated (e.g. for some causal process the immediate neighborhood may be important but for others a broader area, perhaps not even identified as a neighborhood by residents, might be more causally relevant). In addition for some data sources, such as census data, only certain definitions (e.g. census tracts) would be possible based on availability. Hence some measures were created for census tracts (originally defined to be socioeconomically homogeneous and used as proxies for neighborhoods in much prior work) and others were created for buffers of varying size around a person's home in order to allow flexibility in the size of the area investigated, as well as sensitivity analyses using varying buffer sizes.

### **Survey-based Measures**

Surveys can be used to assess each individual's perception of his or her neighborhood or aggregated across multiple respondents (who serve as neighborhood “informants”) in order to derive more valid and reliable measures of the objective features of neighborhoods by averaging across individual subjectivities. The use of measures based on aggregating multiple respondents also avoids “same source bias” which may arise in using individual

neighborhood perceptions when an underlying factor affects both the individual's perceptions of the neighborhood (e.g. whether it is safe or not) as well as self-reported health outcomes (e.g. depression) creating spurious associations. Both approaches were used in MESA. MESA participants themselves were queried about their neighborhoods at several visits and a separate random sample of residents of MESA neighborhoods was surveyed via phone or mail at varying time points at various sites over the course of the study.

A series of scales were used to capture a range of neighborhood constructs including aesthetic quality, walking/physical activity environment, availability of healthy foods, safety, violent crime, social cohesion, activities with neighborhoods, neighborhood problems, and social and physical disorder.[20–23] Survey items were based on prior work when possible. [24–26] Survey respondents were asked to refer to an area about 1-mile (or a 20 minute walk) surrounding their home.[20] An important contribution of the MESA Neighborhood Study was the investigation of not only the psychometric but also the “ecometric” properties of these scales, i.e. the extent to which they reliably capture group level constructs and the extent to which respondents within a neighborhood agree in their assessments. All scales, excluding activities with neighborhoods, had good psychometric and ecometric properties and good convergent validity.[20] Another important methodologic innovation was the use of empirical Bayes estimation to derive estimates of neighborhood-level constructs for individual census tracts.[27] This approach improves the reliability of the estimates as a whole by shrinking estimates for neighborhoods with small numbers of respondents to an overall or conditional mean.[28] It also allows estimates to be adjusted for the age and gender of respondents when reporting differs systematically across these characteristics (independently of true neighborhood conditions).

### Geographic Information (GIS)-based Measures

**Built environment and access to food, recreational resources and social destinations**—An important strength of the MESA Neighborhood Study is the breadth and depth of measures of the neighborhood built environment, including both detailed metrics and composite measures. We also gathered GIS layers and processed them using ArcGIS, (ESRI, Redlands, CA) to produce a multitude of measures on density, placement of land-uses, street network, and access to destinations around MESA participants' homes. Specific measures were tailored to investigate environmental domains that city and regional planners might be able to influence (e.g. street connectivity, land-use mix, public transportation), as well as, population density. Population density was measured using population counts from the US Census. Land-use parcel files were obtained from local planning departments, city governments, and regional entities. Two investigators independently classified parcels into 2 mutually exclusive land-use categories (retail and residential) based on land-use codes. Areas with higher percentages of land zoned for retail use and lower percentages zoned for residential use were considered to have a higher land-use mix. Land-use mix was also measured as entropy, which was calculated using an established formula[29] to quantify the similarity in the proportion of the area in parcels devoted to different land uses.

Files containing data on bus routes were obtained from local planning departments, city governments, and regional entities and used to create distance to nearest bus route. Street calculations were performed using StreetMap and StreetMap Premium for ArcGIS (Esri). StreetMap files may be less accurate than data provided by municipalities, [30] but they are uniform across cities. Street connectivity was characterized by the network ratio, which is the proportion of a buffer created using Euclidean distance that is covered by a buffer created using network distance. Composite measures include Walk Score™ and Transit Score™, two commercial measures of neighborhood walkability and transportation access (Front Seat Management, LLC). These measures are useful because they allow investigation of the combined impact of many elements of the built environment, and are also easily accessible to the public and practitioners.

GIS-based measures of access to food stores, alcohol outlets, physical activity resources, walking destinations, and social engagement destinations were created using data obtained from the National Establishment Time Series (NETS) database from Walls and Associates for the years 2000–2010. [31] This data includes time-series data on establishments derived from Dun and Bradstreet (D&B) archival establishment data, which provides annual information on stores in business. We used Standard Industrial Classification (SIC) codes to identify supermarkets and grocery stores, and fruit and vegetable markets, which we classified as healthy food stores. [32] Additional supermarket data was obtained from Nielsen/TDLinx to enhance the supermarket list[33]. We identified supermarkets as grocery stores with at least \$2 million in annual sales or at least 25 employees. Additionally, we included supermarkets that had a standard chain name based on a list derived from the Nielsen/TDLinx data. [34] Alcohol outlets were derived from SIC codes for food stores, and sub-codes representing liquor stores and drinking places (consumption on-site) were selected.

For physical activity resources, 114 SIC codes were selected to represent establishments with indoor conditioning, dance, bowling, golf, team and racquet sports, and water activities derived from lists used in previous studies. [35, 36] Walking destinations were defined as locations that are common place to walk to. [37] Social engagement destinations were defined as locations that facilitate social interaction and promote social engagement. [37] Simple (unweighted) and kernel[38] (weighted) densities per square mile were created for a range of buffer sizes (1/2- 1-, 3-, 5-miles) around each residential address using ArcGIS 9.3 (ArcGIS, version 9.3; Esri). Kernel densities assign greater weight to resources closer to the participants' homes. Densities were matched to participants annually such that changes over time occurred whenever neighborhood resources changed or a participant moved.

Data on parks, including the total number of: parks, unique types of amenities within parks, and total number of amenities within parks, was also collected using data from municipal or county planning, parks, and recreation departments, the ESRI (ESRI, Redlands, CA) and TeleAtlas.[39] Access to parks was characterized by the percentage of Euclidean buffer devoted to parkland and by densities of types of amenities available within the parks for the range of buffer sizes.

**Other GIS-based measures**—Additional GIS-based measures included data on crime and foreclosures. Police-recorded crime data for years 1999–2012 were available for the Chicago MESA site from the Chicago Police department. Measures for the total number of incidents within crime categories for buffer sizes of ¼-, ½, and 1-mile around participants' addresses were created using ArcGIS v9.1.[40, 41] Geocoded foreclosure data was obtained from RealtyTrac for the years 2005–2012. [42, 43] We defined foreclosures as residential properties with mortgages in default that were issued a Notice of Trustee's Sale or a Notice of Foreclosure Sale indicating the upcoming auction of the property (i.e. properties in the foreclosure process). [44, 45] A count of the number of foreclosures within a ¼-mile Euclidean buffer around each MESA participant's residence was calculated for each year between exams 4 and 5 using ESRI ArcGIS 10.1 (Redlands, CA).

### Census-based Measures

Neighborhood-level racial/ethnic residential segregation was measured separately for non-Hispanic blacks and whites, and Hispanics by using the local  $G_i^*$  statistic[46], based on US Census data. The  $G_i^*$  statistic returns a  $Z$  score for each neighborhood (census tract), indicating the extent to which the racial/ethnic composition in the focal tract and neighboring tracts deviates from the mean racial composition of some larger areal unit surrounding the tract (in our case, the set of counties represented in each MESA site).

Summary census based measures of the socioeconomic environment were derived to use for adjustment purposes or for questions related to neighborhood socioeconomic context generally. Census-tract measures were obtained from the U.S. Census 2000, [47] American Community Survey (ACS) 2005-2009,[48] and ACS 2007-2011[49]. We conducted principal factor analysis with orthogonal rotation of 21 census variables reflecting race/ethnicity, crowding, foreign born, education, occupation, income and wealth, poverty, employment, and housing. Five factors, capturing 74% of the variance, explained were retained.[50] The scales are linked to MESA participants by census tract using Census 2000 data for years 2000–2004, ACS 2005- 2009 data for years 2005–2007, and ACS 2007-2011 data for years 2008–2012.

In addition, we obtained 20-year residential history information prior to MESA baseline. We derived estimates of tract-level poverty by linking residential history to US census data from 1980, 1990, and 2000 from the Neighborhood Change Data Base (NCDB).[51] The NCDB allows comparison across various census years by recalculating and normalizing past census years to 2000 census tract boundaries. Using this approach we derived a measure of average exposure to neighborhood poverty for the 20-year period for each person.

### Neighborhood Audits

Neighborhood audits and systematic social observation[52] have been proposed as a strategy to characterize important aspects of neighborhoods that cannot be captured using surveys or GIS measures. Extensive systematic social observation was not possible across the six diverse sites of MESA. However a sub study at the Baltimore site did an assessment of healthy food availability using a validated store assessment tool. These data were used to demonstrate variability in healthy food availability across stores located in different types of



neighborhoods [53] and to examine associations of objectively assessed healthy food availability with diet.[54]

## SELECT FINDINGS TO DATE

### Cross-sectional Analyses

Initial analyses focused on investigating the cross-sectional associations between specific neighborhood measures and behaviors or biomedical risk factors.

**Neighborhood environments and diet**—MESA food environment studies were among the first to use complementary measures of the local food environment across an extended geographic area to examine the robustness of associations of the environment on overall dietary quality. Analyses of three different measures of the local food environment (individual perceptions, neighborhood aggregate survey measures, and supermarket densities) indicated that individuals who lived in less supportive environments were less likely to have a healthy diet than those living more supportive local food environments, [55, 56] Other aspects of neighborhood environments, including social cohesion, were also associated with having a healthy diet.[57] Environment measures were positively but not highly correlated suggesting that they may tap into complementary (although related) constructs of the local food environment.[58] Directly measuring the availability of various healthier foods within stores located in the residential areas of the MESA participants also confirmed that less availability of healthy foods was associated with lower dietary quality. [53, 54] MESA has also provided insight into eating out behavior by demonstrating that greater neighborhood exposure to fast food is associated with a poorer diet and greater fast food consumption.[59]

**Neighborhood environments and physical activity**—MESA has provided evidence that participants who live in supportive neighborhood environments report higher levels of physical activity. Overall physical activity level was found to be positively associated with density of recreational resources. [60] Additionally, MESA work suggests that walking may be an important mechanism through which neighborhoods affect physical activity. MESA participants whose residence had higher Walk Scores™ and Transit Scores™, had higher levels of walking for transportation.[61] Analyses of specific neighborhood built environment features found greater walking for transportation to be associated with higher population density,[62] greater land area devoted to retail uses,[62] and greater pedestrian-oriented uses for social interaction such as community centers and other gathering places. [63] Higher perceptions of neighborhood safety and lower levels of neighborhood criminal incivilities were also found to be associated with more walking for transportation and for leisure.[41] Higher neighborhood social cohesion was also associated with more regular physical activity.[57]

**Neighborhood environments and other health-related behaviors**—Neighborhood social environments characterized by less disorder, and higher safety and social cohesion were associated with longer self-reported [64] and objectively measured sleep duration (Johnson DA et al., unpublished). Adverse neighborhood social and physical environments,

and lower neighborhood SES were associated with greater sleepiness, but associations with physical environments were no longer statistically significant after adjustment for sociodemographic characteristics. Residents of neighborhood with worse walking environments also had higher odds of severe sleep apnea, with this relationship being stronger in males and obese individuals.[65] Neighborhood characteristics were not significantly associated with insomnia,[64] sleep efficiency, or sleep fragmentation (Johnson, DA et al., unpublished). Neighborhoods that are more socially cohesive (Mayne SL et al., 2016),[66] and have greater safety and aesthetic quality were associated with lower smoking prevalence (Mayne SL et al., 2016). Findings for alcohol use were more mixed: a greater density of alcohol outlets was found to be associated with greater alcohol use but only among men. [67]

**Neighborhood environments and hypertension, body mass index, and insulin resistance**—One of the first studies investigating associations between neighborhood physical and social environment indicators and hypertension prevalence was conducted in MESA using data from three study sites.[68] Individuals living in neighborhoods with better healthy food availability, opportunities for physical activity, safety, and social cohesion had a lower prevalence of hypertension as compared to individuals living in worse environments, independent of a basic set of confounders (age, gender, education, income).[68] However, it was difficult to disentangle the effects of race and place in this sample. Subsequent analyses showed that racial/ethnic differences in hypertension prevalence and in an ideal cardiovascular health score were reduced after adjusting for neighborhood-level chronic stressors and other measures of neighborhood physical, social, and socioeconomic environments (Mujahid MS et al., unpublished).[69]

Cross-sectional studies conducted in MESA suggest that living in neighborhoods with better physical environments, based on a summary measure of healthy food availability and opportunities for physical activity, was associated with a lower body mass index (BMI) among men and women.[27] The magnitude of the associations were stronger in women than in men. Furthermore, results suggest that these associations may be mediated by diet and physical activity as further control for these variables attenuated the associations. There were no significant associations between neighborhood social environments (a summary measure of safety, social cohesion, and aesthetic quality) and average BMI among women, however, among men, findings were in the unexpected direction. Living in neighborhoods with better social environments was associated with a higher BMI compared to men living in lower social environments, independent of individual-level confounders. Another cross-sectional study in MESA extended these analyses to consider not only the physical and social environment of the residential neighborhood but also the neighborhood environment of the workplaces of employed MESA participants.[70] Associations between neighborhood walkability and BMI were stronger when both residential and work exposures were considered using a weighted average approach (compared to residential exposures alone) suggesting that both contexts may affect behaviors.[70]

MESA analyses showed that living in neighborhoods with better physical activity and healthy food resources was associated with a lower insulin resistance and impaired fasting glucose, independent of sociodemographic confounders and partly mediated by diet,

physical activity and BMI.[71] Other analyses examined the role of resources outside the neighborhood and showed that living further from wealthy areas was associated with higher insulin resistance, independent of the local poverty rate.[72] In an illustration of the potential cumulative impact of neighborhood environments on multiple cardiovascular risk factors, healthy food stores, physical activity resources, walking/physical activity environment, and neighborhood socioeconomic status were individually associated with higher odds of having an ideal cardiovascular health (CVH) score.[73]

### **Neighborhood environments and psychosocial or stress-related measures—**

Neighborhoods may also affect cardiovascular risk through their impact on stress-related processes. Neighborhoods characterized as more stressful (higher poverty, more violence) were found to be associated with lower wakeup cortisol values[21], slower early decline,[21, 74] and flatter wake-to-bed slope.[74] Higher social cohesion and safety were associated with higher wake-up cortisol, steeper early decline and steeper wake-to-bed slope.[74] This flattening of the cortisol curve has been hypothesized to be related to adverse health outcomes.

Several MESA publications focused on the links between neighborhood environments and depression or depressive symptoms. [66, 75–77] Living in neighborhoods with lower levels of social cohesion,[66, 76] lower densities of social engagement destinations, [77] and aesthetic quality, [76] and higher levels of neighborhood problems and violence[66, 76] was found to be associated with higher levels of depressive symptoms. Findings also documented that living in a neighborhood with a higher percentage of residents of the same race/ethnicity was associated with higher Center for Epidemiologic Studies Depression Scale (CES-D) scores in African American men, but with lower CES-D scores in Hispanic men and women, possibly reflecting the different environmental correlates of these compositional characteristics in different race/ethnic groups.[75]

An intriguing body of work has suggested that chronic stress could affect health (including cardiovascular health) through its impact on telomere shortening.[78–80] We used MESA telomere data at baseline to investigate whether neighborhood social environment was associated with telomere length. Respondents who lived in neighborhoods characterized by lower aesthetic quality, safety, and social cohesion had shorter telomeres than those who lived in neighborhoods with a more salutary social environment, even after adjusting for individual-level socioeconomic status and biomedical and lifestyle factors related to telomere length.[81]

### **Longitudinal Analyses**

A major goal of the MESA Neighborhood Study was to capitalize on longitudinal data to investigate not only whether neighborhood factors are related to changes over time in risk factors or incident disease, but also to investigate the impact of cumulative exposures and to examine whether changes in exposures are related to changes in outcomes. Longitudinal analyses are ongoing and will continue as MESA follow-up continues. A few recent examples are described here.

**Behaviors**—Physical activity (including walking) has been the behavior most investigated in relation to neighborhoods in MESA. This is because multiple repeated measures of physical activity are available (in contrast to diet where only baseline and one follow up measure are available) and because changes in neighborhood environments may show relatively quick effects on physical activity behaviors. While overall physical activity decreased over time in MESA, increases in the neighborhood density of recreational resources were associated with a less pronounced decline over time.[82] This association was stronger among the older participants, underscoring the important role neighborhood environments may play to promote physical activity during aging. In econometric fixed effects models,[83] MESA participants who moved to a location with higher Walk Score™ experienced a simultaneous increase in walking for transportation.[84] Moving to an area with higher walkability, however, was not significantly associated with walking for leisure, [84] perhaps because the Walk Score™ measure heavily focuses on access to destinations. When examining specific built environment features, density and street connectivity were the most consistently associated with positive transportation walking trajectories.[85]

Neighborhoods with higher baseline population density, land zoned for retail, density of destinations for social engagement, density of walking destinations, and street connectivity were associated with greater increases in walking for transportation over time.[85] In contrast, higher baseline levels of land zoned for residential uses or being farther from buses at baseline were associated with less pronounced increases (or decreases) in walking for transportation over time.[85] Increases over time in the number of destinations (for both walking and social engagement) and street connectivity were associated with greater increases in walking for transportation.[85] While some baseline features were associated with more positive trajectories of walking for leisure, no associations were observed between change over time in specific environmental features and leisure walking trajectories.[85] No associations were found between changes in perceived safety and changes in either walking for transportation or for leisure.[40] However, residing in a neighborhood that experienced an increase in homicides was associated with decreases in transport walking.[40]

Increases in neighborhood SES were associated with decreases in the probability of current alcohol use. [50] Increases in liquor store densities[50] and neighborhood foreclosures were associated with increases in weekly alcohol consumption. Increases in neighborhood-level foreclosure were associated with decreases in the number of cigarettes smoked (Crawford N et al., unpublished). No association was observed between changes in the social environment and changes in smoking risk or intensity over time.[86] However longitudinal analyses of smoking and alcohol use are limited by the relative stability of these measures over time in MESA.

**Diabetes, obesity, and hypertension**—Two of the first studies to examine associations of neighborhood physical and social environments with incidence of type 2 diabetes were conducted in MESA.[23, 87] The first study found that among those free from type 2 diabetes at baseline, better neighborhood physical activity and healthy food resources at baseline was associated with a lower incidence of type 2 diabetes (38% reduction in resource distribution corresponding to a difference between the 90<sup>th</sup> and 10<sup>th</sup> percentile), with this

association being partly mediated by physical activity, dietary factors, and BMI.[87] These analyses were restricted to individuals at 3 of 6 MESA sites who were followed for an average of 5 years. In a subsequent study, extended to include all MESA sites and both survey and GIS based measures of cumulative exposures, a 1 SD better healthy food availability and a 1 SD better access to physical activity resources were associated with a 12 and 21% lower risk of developing type 2 diabetes, respectively, over an average of 8.9 years of follow-up.[23] In analyses that considered the GIS and survey-based measures separately, the survey-based measures had the most consistent associations with type 2 diabetes. Increases in neighborhood foreclosures were associated with small increases in fasting glucose but hypothesized associations with other risk factors were not observed.[88]

In analyses of MESA participants without obesity at baseline and followed for an average of 5 years, living in neighborhoods with a better healthy food and physical activity environment was associated with a lower incidence of obesity, independent of individual-level confounders.[89] In subsequent analyses extending the follow up and including time-varying neighborhood data over the 10 year follow-up, improvements in the healthy food and physical activity environment were associated with a decrease in BMI among those obese at baseline but associations were in the unexpected direction among persons normal weight at baseline.[90] Changes in the built environment including increases in intensity of developments (e.g. higher density of walking destinations) were associated with less pronounced increases in BMI and waist circumference during a median of 9.1 years of follow-up, but there was no significant association between, changes in connected retail centers (e.g. higher percent retail and street connectivity), or public transportation (e.g. distance to a bus) and changes in BMI or WC.[91] There were also significant associations between moving to a location with a better walking environment and reductions in BMI over time within the subset of 700 MESA participants who moved between 2004 and 2012.[85] Studies investigating associations between the social environment and obesity found that perceptions of improved neighborhood safety were associated with lower adiposity (BMI and WC) over a 10-year follow-up for men but the opposite effect was observed in women. [92] There were no significant associations between police-reported crime and adiposity measures.[92] However, these analyses had limited power because they were restricted to participants within the Chicago site for which there was additional data on police-reported crime.

Among MESA participants free from hypertension at baseline and followed for a median of 10 years, a one-standard deviation higher healthy food availability score was associated with a 12% lower incidence rate of hypertension, independent of other individual and neighborhood-level covariates.[93] There were no significant associations between other neighborhood physical and social environment indicators and incident hypertension. These analyses used both survey-based and GIS measures of neighborhood environments and assessed the associations with cumulative average measures of these constructs.

**Psychosocial and stress factors**—An early MESA report based on 4–5 years of follow up found that adverse neighborhood social environments were associated with incident depression, defined by CES-D 16 or taking an antidepressant medication in women but no association was seen for men, in part because of wide confidence intervals.[76]

Subsequent MESA analyses capitalized on time varying data. Although we found that long-term cumulative exposure to social cohesion, safety, and social engagement destinations were not significantly associated with changes in depressive symptoms over time,[77] there was some evidence that changes to the environment were related to contemporaneous changes in depressive symptoms. Specifically, within-person increases in safety[77] and social cohesion[22, 77] were associated with decreases in CES-D. No significant association was found between changes in social engagement destinations[77] or neighborhood foreclosures and changes in CES-D(Crawford ND et al., unpublished). In other analyses neighborhood poverty and social environments were not consistently related to changes in cortisol over time [74] although these analyses were likely limited by the complexity of measuring changes in cortisol profiles.

**Subclinical atherosclerosis and cardiovascular events**—Relatively few studies have investigated the impact of neighborhoods on subclinical atherosclerosis or incidence of cardiovascular events. Clearly if neighborhoods affect the development of atherosclerosis or the incidence of events they must do so over very long periods limiting the utility of even 10 year cohort studies like MESA to detect such effects. However, the MESA Neighborhood Study has begun to explore some of these associations within the constraints of the data available. Neighborhood poverty, both a contemporaneous measure and a cumulative 20-year long term exposure, was inversely associated with common carotid intimal–medial thickness (IMT) in women but not men.[94, 95] Associations were somewhat reduced after adjustment for cardiovascular risk factors, suggesting that these factors may play a mediating role.[94] Recent analyses using econometric fixed effects models suggest that increases in density of neighborhood healthy food stores may be associated with decreases in CAC (Tomey K et al., unpublished). However changes recreational resources and survey-based availability of healthy food, walking environment, and social environment were not associated with within-person change in CAC (Tomey K et al., unpublished). These findings warrant replication.

It has been hypothesized that residential racial segregation by race may result on differences in neighborhood physical and social environments with important consequences for health. [96] The availability of measures of racial segregation made it possible to investigate this question in MESA. Among non-Hispanic blacks, each standard deviation increase in black segregation was associated with a 12% higher hazard of developing CVD after adjusting for potential confounders (95% confidence interval, 1.02–1.22). For whites, higher white segregation was associated with lower CVD risk after adjusting for demographics (hazard ratio, 0.88; 95% confidence interval, 0.81–0.96), but not after further adjustment for other neighborhood characteristics. Segregation was not significantly associated with CVD risk among Hispanics.[97]

In other preliminary analyses there was a non-linear relationship between neighborhood-level stressors and incident CHD. Participants in the medium category had 49% higher CHD risk (95% CI 1.06 to 2.10) compared with those in the low category; those in the high category had only 27% higher CHD risk (95% CI 0.83 to 1.95). These associations persisted with adjustment for risk factors and individual-level stressors.[98] Analyses linking

neighborhood physical and social environments to CVD incidence are awaiting the compilation of additional events in the MESA cohort.

## STRENGTHS AND LIMITATIONS

The MESA Neighborhood Study has a number of important strengths. The diversity of the cohort in terms of geography, race/ethnicity and socioeconomic characteristics is critical for improving understanding of the role of neighborhoods in shaping cardiovascular health and health disparities. A second major strength is the rich neighborhood-level data that has been linked to the cohort. Creating measures across multiple neighborhood domains using a multiplicity of measurement approaches allows for a rich set of analyses. A third major strength is the time-varying nature of both neighborhood and individual-level data allowing investigation of how changes in neighborhood environments are associated with changes in health outcomes over time. More specifically the design allows the use of econometric fixed effects models to examine how within person change in neighborhood exposures is related to within person change in outcomes while tightly controlling for time invariant characteristics. [99]

However, the MESA Neighborhood experience has also highlighted some challenges in understanding how neighborhoods may affect cardiovascular risk. Despite the intense effort invested in characterizing neighborhoods many of the measures remain crude. For example density of supermarkets is necessarily a very imperfect proxy of access to healthy foods given that the quality of quantity of healthy foods present in supermarkets may vary substantially across places.[53] The time-resolution of some of the data remain limited, for example the survey measures capture only limited time-variability over follow up and diet was only assessed at two time points. Some important measures, such as objectively measured crime could not be obtained with adequate spatial resolution across all sites. Despite many years of research on neighborhood health effects there is still very little theory or evidence on which to base the definition of the appropriate spatial scale for different causal processes. The MESA Neighborhood Study grappled with this question by creating flexible measures (e.g. buffers of different sizes) but this can also introduce multiple testing issues and other methodologic challenges.[100]

Although the ability to employ econometric fixed effects models is an important advance, these models are very inefficient when there is low within person change in exposures or outcomes. This has been a challenge in MESA data because of limited variability in many variables over time linked in part to the age and stability of the cohort. More fundamentally, an older cohort such as MESA may not be the best sample in which to investigate how changes in neighborhoods may relate to changes in behaviors or biomedical risks factors over time. Younger cohorts with more variability and change in both exposures and some behaviors, may be more suited for this purpose. In addition cardiovascular risk factors in older adults are likely to be influenced by lifecourse exposures and may much less responsive to changes in environments than they would be in younger samples.

A major challenge in MESA has been confounding of neighborhood exposures by race/ethnicity and study site. Strong residential segregation by race has sometimes made it

difficult to isolate race differences from neighborhood differences. Although the presence of six sites has added important geographic and neighborhood diversity, there is always the lingering question on whether site is exerting an “independent” effect on the outcomes through mechanisms that do not involve neighborhoods and should therefore be adjusted for. This however may result in site absorbing much of the neighborhood variance and power for within site analyses is often low. Some of the individual-level outcome data have also posed challenges. Repeat measures of physical activity measures have been very useful but objectively measured physical activity would likely have been much more informative. The power for event analyses, a key goal of the study, is still low due to relatively low event rates in the sample.

Despite its many strengths the MESA Neighborhood Study shares some of the limitations of other neighborhood studies. Information on other contexts (work or family) is limited. Even with the use of longitudinal methods causal inference is limited by the observational nature of the study if underlying predispositions linked to the outcomes affect residential location (a matter that should itself be the subject of empirical inquiry). It is often challenging if not impossible to isolate the effects of multiple correlated neighborhood measures, and yet this is critical to identify promising interventions. Although having six diverse geographic sites is a major advance over single site studies, these sites are by no means representative of geographic variability across the US. This may limit the ability to detect important effects and to generalize findings to other contexts.

## CONCLUSIONS AND FUTURE DIRECTIONS

Taken together results from the MESA Neighborhood Study point to the relevance of environmental contexts to cardiovascular risk. The study documented that better food and physical activity environments are generally related to better dietary and physical activity behaviors. Moreover favorable changes in physical activity environments were found to be associated with favorable changes in physical activity behaviors (especially walking). Healthier neighborhood food and physical activity environments were also related to lower incidence of diabetes and hypertension and to favorable changes in BMI over follow up (in some subgroups). Adverse neighborhood social environments (characterized by less safety, more violence, higher disorder or lower social cohesion) were associated with shorter sleep duration altered daily cortisol patterns, and higher levels of depressive symptoms. Living in segregated areas was associated with higher incidence of CVD in African Americans. Preliminary evidence suggests that changes in healthy food environments may be inversely related to changes in coronary calcification.

Additional follow up of the cohort will allow additional longitudinal analyses necessary to strengthen causal inferences. The eventual linkage of the cohort to geographically and time-varying policy data may allow more specific evaluation of the impact of various policies by capitalizing of natural experiments. As in other contexts, there is always a tension between isolating the effects of a very specific intervention and understanding how multifaceted interventions (e.g. that increase walkability and access to health foods) may act synergistically. Future studies will need to consider the interactive effects of policies as well



as potential unintended effects (e.g. increasing walkability resulting in greater exposure to traffic related air pollution). [101]

Analyses examining interactions between neighborhood factors and individual-level variables (e.g. degree of dependence on neighborhoods for various resources, utilization of neighborhood amenities, or genetic factors) may yield additional insights on the circumstances under which neighborhood factors are likely to be most relevant. Ultimately a series of complementary approaches including observational studies like the MESA Neighborhood Study, policy evaluations, and simulation modeling will be necessary to identify effective neighborhood interventions to improve cardiovascular health.[102]

## Acknowledgements

This work is supported by R01 HL071759 and 2P60MD002249 (Diez-Roux). The MESA Study was supported by contracts N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168 and N01-HC-95169 from the National Heart, Lung, and Blood Institute and by grants UL1-TR-000040 and UL1-TR-001079 from NCRR. The authors thank the other MESA Neighborhood investigators including Amy Auchincloss, Kelly Evenson, Daniel Rodriguez, Dan Brown, Shannon Brines, Brisa Sanchez, Lynda Lisabeth, and Sarah Adar and the many students and trainees who made the study possible. We also wish to thank MESA investigators and staff, as well as the participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at <http://www.mesa-nhlbi.org>. The findings and conclusions in this report are those of the authors and do not necessarily represent the official positions of the Centers for Disease Control and Prevention.

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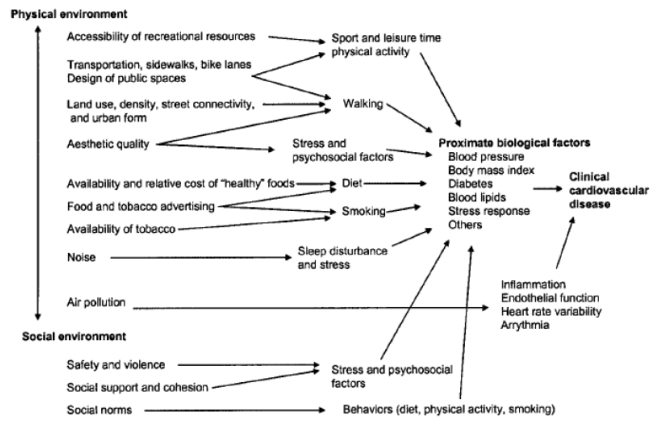
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Source: Diez Roux, A. V. (2003). "Residential environments and cardiovascular risk." *Journal of Urban Health* 80(4): 569-589.

**Figure 1.** Schematic conceptual model of the hypothesized links between neighborhood environments and cardiovascular disease