ORIGINAL RESEARCH

Association Between Neighborhood Walkability and Predicted 10-Year Cardiovascular Disease Risk: The CANHEART (Cardiovascular Health in Ambulatory Care Research Team) Cohort

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***Background*—**Individuals living in unwalkable neighborhoods appear to be less physically active and more likely to develop obesity, diabetes mellitus, and hypertension. It is unclear whether neighborhood walkability is a risk factor for future cardiovascular disease.

***Methods and Results*—**We studied residents living in major urban centers in Ontario, Canada on January 1, 2008, using linked electronic medical record and administrative health data from the CANHEART (Cardiovascular Health in Ambulatory Care Research Team) cohort. Walkability was assessed using a validated index based on population and residential density, street connectivity, and the number of walkable destinations in each neighborhood, divided into quintiles (Q). The primary outcome was a predicted 10-year cardiovascular disease risk of ≥7.5% (recommended threshold for statin use) assessed by the American College of Cardiology/American Heart Association Pooled Cohort Equation. Adjusted associations were estimated using logistic regression models. Secondary outcomes included measured systolic blood pressure, total and high-density lipoprotein cholesterol levels, prior diabetes mellitus diagnosis, and current smoking status. In total, 44 448 individuals were included in our analyses. Fully adjusted analyses found a nonlinear relationship between walkability and predicted 10-year cardiovascular disease risk (least [Q1] versus most [Q5] walkable neighborhood: odds ratio =1.09, 95% CI: 0.98, 1.22), with the greatest difference between Q3 and Q5 (odds ratio=1.33, 95% CI: 1.23, 1.45). Dose–response associations were observed for systolic blood pressure, high-density lipoprotein cholesterol, and diabetes mellitus risk, while an inverse association was observed with smoking status.

***Conclusions*—**In our setting, adults living in less walkable neighborhoods had a higher predicted 10-year cardiovascular disease risk than those living in highly walkable areas. **(*J Am Heart Assoc*. 2019;8:e013146. DOI: 10.1161/JAHA.119.013146.)**

Key Words: built environment • cardiovascular disease risk • diabetes mellitus • smoking • walkability

Cardiovascular disease remains one of the most common causes of morbidity and mortality globally.[1] Regular physical activity is associated with a better cardiometabolic risk profile, including a lower risk of diabetes mellitus, hypertension, and major cardiovascular events.[2–8] The protective relationship between physical activity and cardiovascular risk is likely mediated in large part through effects on body weight and visceral adiposity, leading to improvements in insulin sensitivity and downstream metabolic processes.[9–13] While national guidelines recommend that all adults accumulate a minimum of 150 minutes of moderate to high intensity physical activity each week,[14,15] nearly 1 in 4 American adults do not engage in any form of leisure-time physical activity.[16]

Public policies that make it easier to incorporate physical activity into daily life have the potential to increase participation in physical activity on a broad scale. Urban development practices that create a supportive, walkable

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Accompanying Data S1 and Tables S1 through S3 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013146

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Received July 2, 2019; accepted September 5, 2019.

Clinical Perspective

What Is New?

- Adults residing in less walkable neighborhoods had a higher predicted 10-year risk of cardiovascular disease, a lower high-density lipoprotein cholesterol level, higher systolic blood pressure, and higher likelihood of having diabetes mellitus, but were also less likely to smoke.

What Are the Clinical Implications?

- Living in neighborhoods that make it easier to be physically active is associated with reduced risk of cardiovascular disease.

environment is one such approach. Neighborhood walkability has been positively associated with walking, cycling, and overall physical activity levels, and inversely associated with car use.[17–20] Moreover, residents living in highly walkable neighborhoods appear to have lower rates of overweight and obesity, and less age-related weight gain over time.[18–20] Recently, several studies have suggested that walkability may also be inversely associated with traditional cardiovascular risk factors including diabetes mellitus, hypertension, and dyslipidemia.[21–23] While each of these risk factors is important on their own, cardiovascular risk factors often co-occur and may act synergistically to impact one's overall risk of cardiovascular disease outcomes.[24–26] As such, it is important to globally assess the impact of walkability on cardiovascular risk. In a sample of 3593 people, Coffee and colleagues found a small inverse association between walkability and an aggregate outcome including several cardiovascular disease risk factors (hypertension, abdominal adiposity, reduced high-density lipoprotein [HDL] cholesterol, raised triglycerides, raised low-density lipoprotein cholesterol, and raised fasting plasma glucose).[27] Another study of 5805 individuals by Unger and others identified that individuals who perceived their neighborhood to be more supportive of physical activity were more likely to have ideal cardiovascular health based on various cardiovascular risk factors.[28] However, neither study, nor others in the literature have examined the association between walkability and the likelihood of future cardiovascular disease. Understanding the potential for interventions that promote walkability to reduce the burden of cardiovascular disease in the population is a critical step to guide public policies in this area.

The aim of the current study was to test whether residents living in less walkable neighborhoods have a higher predicted 10-year cardiovascular disease risk compared with those living in highly walkable areas. To do this, we utilized data from a large, population-based sample drawn from 15 municipalities in Ontario, Canada to evaluate the relationship between neighborhood walkability and predicted 10-year cardiovascular risk based on calculated American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equation risk scores. We hypothesized that among community-dwelling adults free of prior cardiovascular disease, residence in less walkable areas would be associated with a higher predicted 10-year cardiovascular risk, compared with residence in high walkability neighborhoods.

Methods

Design, Setting, and Population

A cross-sectional sample was drawn of community-dwelling individuals residing in 15 major urban centers in Ontario, Canada on January 1, 2008. Individuals were selected for inclusion from a cohort created from linked health administrative databases, known as the CANHEART (Cardiovascular Health in Ambulatory Care Research Team) cohort.[29] These data sets were linked using unique encoded identifiers and analyzed at ICES. A full description of each can be found in Data S1. The sample was further restricted to members of the cohort aged 40 to 74 years in whom clinical information from primary care electronic medical records was available. We excluded individuals with prior cardiovascular events (1992–2008), including hospitalization for myocardial infarction, stroke, congestive heart failure, percutaneous coronary intervention, or coronary artery bypass graft surgery. Individuals residing in a long-term care facility within the previous 5 years and individuals who were not residents in Ontario for the entire 2-year period preceding baseline (2006–2007) were also excluded. This study was approved by the Sunnybrook Health Sciences and University of Toronto Research Ethics Boards. No informed consent was required. The data set from this study is held securely in encoded form at ICES.[30] While data-sharing agreements prohibit ICES from making the data set publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full data set creation plan and underlying analytic code are available from the authors upon request, with the understanding that the programs may rely upon coding templates or macros that are unique to ICES.

Walkability

Individuals were assigned a walkability exposure based on their dissemination area of residence, a small unit of geography that corresponds to approximately several city

blocks in major urban centers. Residential walkability was assessed using a validated index developed for Ontario cities, which predicts transportation patterns (walking, cycling, public transit use, car use) and car ownership.[18,19] It consists of 4 equally weighted components: (1) population density, (2) dwelling density, (3) street connectivity, and (4) number of accessible destinations (eg, banks, grocery stores, restaurants) (Data S1). The components were derived based on geographic boundaries that represent the approximate distance one could travel within 10 minutes from the center of each dissemination area (800 m). Each of these components is individually standardized before being totaled to create the final score. For analysis, walkability scores are treated as quintiles (Q1 lowest, Q5 highest) using cut points derived from neighborhoods (dissemination areas) across the entire study area. As such, the number of individuals across quintiles is not equally divided.

Outcomes

The primary outcome in this study was predicted 10-year cardiovascular disease risk measured using ACC/AHA Pooled Cohort Equation risk score.[31] These scores were designed to predict hard atherosclerotic cardiovascular disease end points (nonfatal myocardial infarction, coronary heart disease death, nonfatal and fatal stroke). Scores were generated using sex-stratified models based on age, HDL and total cholesterol, systolic blood pressure (treated or untreated), smoking status, and diabetes mellitus diagnosis. For our main analyses, we dichotomized the predicted 10-year risk derived from the ACC/AHA score at a threshold of 7.5%, which is the threshold used by the ACC/AHA for recommending statin therapy.[32] As a sensitivity analysis, we also used a higher threshold of ≥10%, corresponding to current guidelines by the United States Preventive Services Task Force for use of statins and aspirin among individuals 50 to 59 years of age.[33,34] As secondary outcomes, we further assessed relationships between walkability and the subcomponents of the ACC/AHA score: diagnosis of diabetes mellitus, systolic blood pressure, total cholesterol, HDL cholesterol, and smoking status. Diabetes mellitus status was identified using a validated algorithm with sensitivity and specificity values of 0.87 and 0.97.[35,36] Systolic blood pressures were taken from the Electronic Medical Record Administrative data Linked Database (EMRALD). The closest measurement preceding the baseline date (within 2 years) was used, or within 5 years after the baseline date if no earlier value was available. The closest cholesterol measurement recorded either in EMRALD or a commercial laboratory (Dynacare Medical Laboratories) database was used, with the same criteria regarding proximity of the value to the baseline as used for blood pressure. Current smoking status was ascertained using the EMRALD data.

Covariates

Information on other baseline sociodemographic and clinical confounders were assessed. These included age, sex, ethnicity, immigration history, neighborhood median household income, use of antihypertensive medications, use of statin medications, chronic obstructive pulmonary disease diagnosis, and number of comorbidities assessed using Johns Hopkins Collapsed Aggregated Diagnostic Groups (Johns Hopkins ACG® System Ver. 7.0). Collapsed Aggregated Diagnostic Groups representing pregnancy-related care and preventive care were not included in the counts. Neighborhood income quintile data were derived from the 2006 Canadian Census based on the household income per single person equivalent within the dissemination area (neighborhood) across the general population. Full details are included in Table S1.

Analysis

Descriptive statistics were tabulated by walkability quintile (mean [SD] for continuous variables, percentage for dichotomous/nominal variables). Continuous outcomes were modeled using multiple linear regression with the generalized estimating equations method to account for clustering at the dissemination area level. Binary outcomes were modeled using logistic regression, also estimating cluster-robust standard errors with generalized estimating equations. Influence diagnostics (DFBetas) were checked to assess estimates' sensitivity to the inclusion of individual observations. Covariates included in the model for cardiovascular risk were sex, ethnicity, immigration history, neighborhood income, and number of comorbidities. Covariates for models of diabetes mellitus, systolic blood pressure, HDL, and total cholesterol included the above as well as age, smoking status, and chronic obstructive pulmonary disease. Models for HDL and total cholesterol additionally included whether the individual was prescribed a statin, and models for blood pressure similarly included a variable for the use of antihypertensive medications. Smoking models contained the same sociodemographic variables as for the cholesterol models. However, since smoking may plausibly influence a wide variety of comorbidities, the only collapsed aggregated diagnostic group variables included were markers for use of preventive care and psychosocial comorbidity. To account for missing data, multiple imputation using chained equations was performed using 5 imputation sets (Data S1). Several sensitivity analyses were performed to assess the robustness of the results to

modeling assumptions. We assessed the sensitivity of the results to the use of multiple imputation by presenting results derived from complete case analyses. Additionally, as a post hoc assessment of how smoking may affect associations between neighborhood walkability and predicted 10-year cardiovascular disease risk, we performed analyses stratified by current smoking status. All analyses were performed using SAS Enterprise version 7.1 (SAS Institute, Cary, NC).

Results

Descriptive Analyses

Overall, 44 448 individuals were included in the sample. The sociodemographic profile of individuals living in high versus low walkability neighborhoods were similar for many attributes, with the exception of neighborhood income (Table 1). Whereas only 6.4% of individuals in the least walkable neighborhoods were in the lowest neighborhood income quintile, >20% were in the lowest neighborhood income quintile in the most walkable neighborhoods. The distribution of comorbidities overall was also similar, but individuals living in highly walkable areas were more likely to have a prior diagnosis of chronic obstructive pulmonary disease.

Association Between Neighborhood Walkability and Cardiovascular Disease Risk

The results of regression modeling for ACC/AHA Pooled Cohort Equation risk scores are presented in Table 2. Compared with individuals living in the most walkable neighborhoods (Q5), residents in less walkable areas were 9% to 33% more likely to have a high predicted 10-year cardiovascular risk based on an ACC/AHA score of 7.5% or greater, after adjustment for sociodemographic confounders and comorbidities (Model 3). However, the pattern was nonlinear, with individuals in the third quintile of walkability exposure (Q3) having the greatest increase in predicted risk relative to Q5 and those in the lowest quintile (Q1) the least and with CIs crossing 1.0. Sensitivity analyses showed consistent results, with the likelihood of having a predicted cardiovascular risk of 10% or greater significantly higher in all 4 lower quintiles of walkability (Q1–Q4) relative to Q5 (Table 2).

Table 1. Sample Characteristics by Walkability Quintiles

Characteristic	Walkability Quintiles (Q)				
	Q1 (Lowest) N=5375	Q2 N=5544	Q3 N=5491	Q4 N=8091	Q5 (Highest) N=19 947
Mean age, y (SD)	53.3 (9.1)	53.8 (9.1)	54.0 (9.3)	53.5 (9.2)	52.9 (9.0)
Female (%)	3065 (57.0)	3215 (58.0)	3147 (57.3)	4826 (59.6)	11 254 (56.4)
Ethnicity					
Chinese (%)	171 (3.2)	185 (3.3)	197 (3.6)	263 (3.3)	554 (2.8)
South Asian (%)	99 (1.8)	70 (1.3)	94 (1.7)	108 (1.3)	231 (1.2)
Other (%)	5105 (95.0)	5289 (95.4)	5200 (94.7)	7720 (95.4)	19 162 (96.1)
Immigration history (%)					
0–5 y	71 (1.3)	85 (1.5)	87 (1.6)	169 (2.1)	387 (1.9)
5–10 y	96 (1.8)	112 (2.0)	134 (2.4)	173 (2.1)	352 (1.8)
Long-term resident	5208 (96.9)	5347 (96.4)	5270 (96.0)	7749 (95.8)	19 208 (96.3)
Neighborhood income quintile (%)					
Q1 (low)	343 (6.4)	699 (12.6)	896 (16.3)	1629 (20.2)	4153 (20.9)
Q2	428 (8.0)	747 (13.5)	1107 (20.2)	1501 (18.6)	3342 (16.8)
Q3	860 (16.1)	988 (17.8)	1036 (18.9)	1029 (12.8)	3406 (17.2)
Q4	1332 (25.0)	1329 (24.0)	1139 (20.7)	1146 (14.2)	3212 (16.2)
Q5 (high)	2369 (44.4)	1779 (32.1)	1313 (23.9)	2746 (34.1)	5723 (28.9)
COPD (%)	285 (5.3)	334 (6.0)	375 (6.8)	560 (6.9)	1635 (8.2)
Median number of comorbidities (IQR)	3 (2–5)	3 (2–5)	3 (2–5)	3 (2–5)	3 (2–5)

All values are frequencies unless otherwise stated. All values are rounded to the nearest significant digit. Imputed data were not used in calculation of descriptive statistics. COPD indicates chronic obstructive pulmonary disease; IQR, interquartile range.

Table 2. Association Between Neighborhood Walkability and 10-Year Cardiovascular Disease Risk ≥7.5% and 10%

Variable/Outcome	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
ACC/AHA ≥7.5% Walkability			
Q1 (low)	1.04 (0.93, 1.16)	1.08 (0.97, 1.21)	1.09 (0.98, 1.22)
Q2	1.21 (1.11, 1.32)	1.25 (1.15, 1.37)	1.26 (1.15, 1.38)
Q3	1.29 (1.19, 1.41)	1.32 (1.21, 1.44)	1.33 (1.23, 1.45)
Q4	1.19 (1.10, 1.28)	1.20 (1.11, 1.29)	1.22 (1.13, 1.31)
Q5 (high)	Ref	Ref	Ref
ACC/AHA ≥10.0% Walkability			
Q1 (low)	1.07 (0.96, 1.18)	1.12 (1.01, 1.24)	1.13 (1.02, 1.26)
Q2	1.21 (1.10, 1.33)	1.26 (1.14, 1.38)	1.26 (1.15, 1.39)
Q3	1.31 (1.20, 1.44)	1.34 (1.22, 1.47)	1.36 (1.24, 1.49)
Q4	1.20 (1.10, 1.30)	1.20 (1.10, 1.31)	1.23 (1.13, 1.34)
Q5 (high)	Ref	Ref	Ref

Model 1 associations are adjusted for sex only (n.b., age is a component of ACC/AHA Pooled Cohort Equation risk score). Model 2 associations adjusted for model 1 covariates and ethnicity, immigration history, and neighborhood income. Model 3 associations adjusted for model 2 covariates and number of comorbidities. ACC/AHA indicates American College of Cardiology/American Heart Association; OR, odds ratio; Q, quintile; Ref, reference category.

Association Between Neighborhood Walkability and Traditional Cardiovascular Disease Risk Factors

Figure 1 shows the association between walkability and several individual components of the ACC/AHA Pooled Cohort Equation. After adjustment for sociodemographic covariates, comorbidities, smoking, and medication use, individuals living in the least versus most walkable neighborhoods were found to have significantly higher mean systolic blood pressure (Figure 1A: Q1 versus Q5=2.54 mm Hg, 95% CI: 1.90, 3.19) and lower mean HDL cholesterol (Figure 1B: Q5 versus Q1 −1.67 mg/dL, 95% CI: −2.34, −1.01). Total cholesterol levels did not differ significantly between groups (Figure 1C). Individuals living in the least walkable areas also had a significantly higher adjusted odds of having a prior diagnosis of diabetes mellitus (Figure 2A: Q5 versus Q1 odds ratio=1.22, 95% CI: 1.08, 1.37). For each of these risk factors, the relationship appeared to be dose dependent. Conversely, living in a less walkable neighborhood was associated with a lower likelihood of smoking (Figure 2B: Q1 versus Q5 odds ratio=0.75, 95% CI: 0.67, 0.84).

Sensitivity Analyses

To explore the role of smoking in the nonlinear relationship between walkability and predicted 10-year cardiovascular risk, we performed analyses stratified by smoking status (Table S2). While associations were strengthened among nonsmokers and were generally attenuated among smokers, a nonlinear pattern of association was still present. Models from complete case analyses revealed results comparable to those from multiple imputation models (Table S3).

Discussion

In our sample of 44 448 community-dwelling individuals in Southern Ontario, we found that low neighborhood walkability was associated with a higher predicted 10-year risk of having a cardiovascular disease event. Furthermore, we observed that decreasing walkability follows a dose–response relationship with increasing systolic blood pressure, HDL cholesterol, and likelihood of diabetes mellitus, but conversely, that lower walkability is associated with a lower likelihood of smoking. These results support connections between walkability and overall cardiovascular risk and further highlight its potential as an upstream correlate of many cardiovascular risk factors. However, our findings also suggest that the differences in predicted cardiovascular risk may be partially offset because of higher levels of smoking in highly walkable versus less walkable neighborhoods.

To our knowledge, our results are the first to report that residing in a less walkable neighborhood is associated with a clinically significant elevation in predicted 10-year risk of cardiovascular disease. These findings are broadly consistent with recent research identifying inverse associations between walkability and individual risk factors and positive

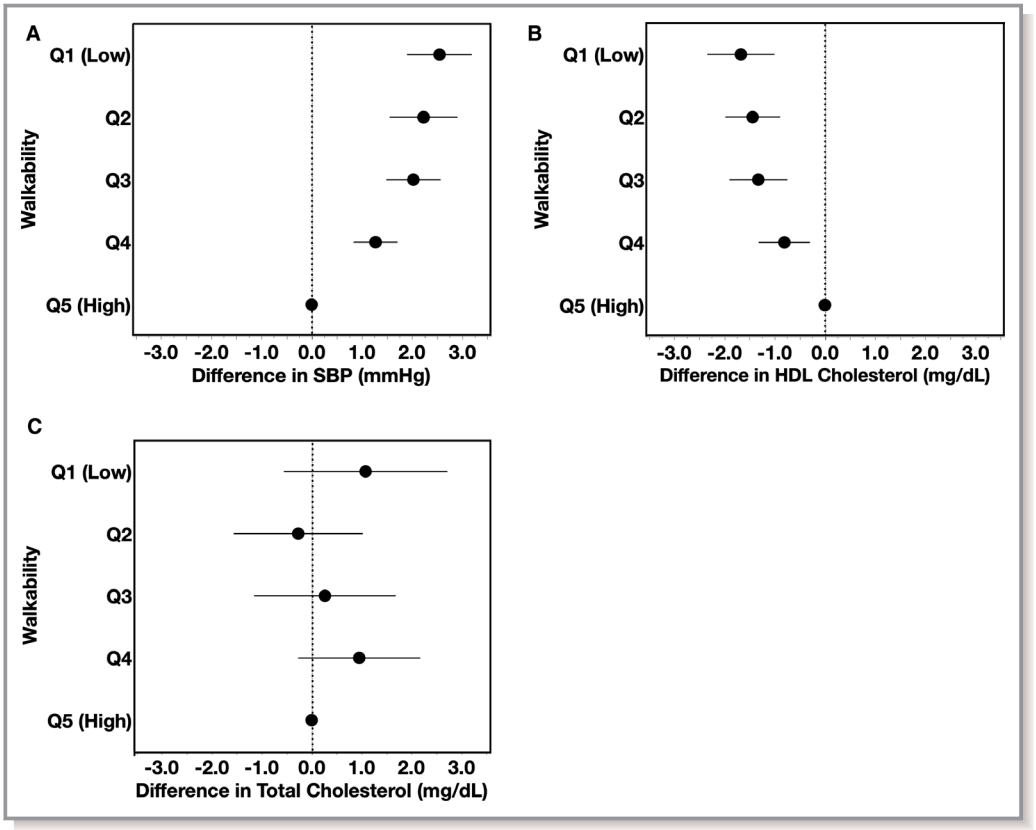

Figure 1. Association between neighborhood walkability, systolic blood pressure, high-density lipoprotein cholesterol, and total cholesterol. Significant associations were identified between walkability and SBP (**A**) and HDL cholesterol (**B**). No statistically significant association was identified between walkability and total cholesterol (**C**). All values were adjusted for age, sex, ethnicity, immigration history, and neighborhood income. Covariates for models of SBP, HDL, and total cholesterol included the above as well as smoking status, COPD, and number of comorbidities. Models for HDL and total cholesterol additionally included whether the individual was prescribed a statin, and models for blood pressure similarly included a variable for the use of antihypertensive medications. COPD indicates chronic obstructive pulmonary disease; HDL, high-density lipoprotein; SBP, systolic blood pressure. Q1 to Q5: Walkability Quintiles (Q1: Low, Q5: High).

associations with population-based indicators of cardiovascular health.[19–21,28,37–39] Recent work by Unger and colleagues found a 20% increase in the odds of having ideal versus poor cardiovascular health for each 1 SD improvement in individuals' "walking/physical activity environment," as assessed using the AHA 2020 Strategic Impact Goals framework.[28] Coffee et al also found that the rates of developing a cardiovascular risk factor decreased 6% for each 10-unit increase in walkability (≈1.5 SD).[27] The magnitude of association is also comparable with those observed contrasting the most versus least walkable neighborhoods and diabetes mellitus and hypertension in other studies.[19,40,41] Conversely, Braun et al did not report any cross-sectional or longitudinal association between Walk Score® and metabolic syndrome among participants in the MESA (Multi-Ethnic Study of Atherosclerosis) cohort.[42] As an upstream determinant of health, walkability is believed to affect cardiovascular disease risk by modifying individuals' participation in physical activity, in particular utilitarian, transportation-related activity such as walking to work or for the purpose of performing errands. Many studies, including an international study drawing participants from 10 countries, have identified that walkability-related variables are associated with increased levels of walking and moderate-to-vigorous physical activity.[19,20,43–45] These increased activity levels may in turn reduce body mass index or slow age-related weight gain, which can have consequences on the metabolic derangements (eg, insulin resistance) that drive cardiovascular risk.[19,46,47]

Unexpectedly, we found that the association between walkability and 10-year predicted cardiovascular disease risk may be nonlinear, with the strongest point estimates observed comparing Q3 to Q5 (most walkable neighborhoods), with a weaker difference observed between Q1 (least walkable) versus Q5 exposures. These patterns were not observed for associations between walkability and the secondary outcomes. We identified different patterns in

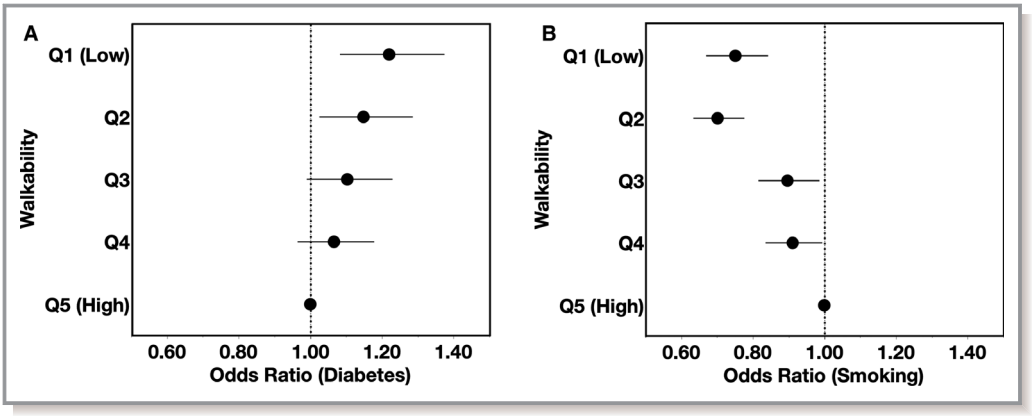

Figure 2. Association between neighborhood walkability, diabetes mellitus, and smoking. Significant associations were identified between walkability and odds of diabetes mellitus (**A**) diagnosis and smoking status (**B**). All values were adjusted for age, sex, ethnicity, immigration history, and neighborhood income. Covariates for the model of diabetes mellitus included the above as well as smoking status, COPD, and number of comorbidities. The model for smoking contained the same sociodemographic variables as for the diabetes mellitus models. However, since smoking may plausibly influence a wide variety of comorbidities, only use of preventive care and psychosocial comorbidity were included and not total number of comorbidities or COPD specifically. COPD, indicates chronic obstructive pulmonary disease; Q1 to Q5: Walkability Quintiles (Q1: Low, Q5: High).

association between walkability and smoking behavior versus walkability and other cardiovascular risk factors, whereby exposure to a less walkable neighborhood was associated with a lower likelihood of being a smoker. This difference likely contributed towards the observed nonlinearity in association between walkability and overall cardiovascular disease risk. However, the nonlinearity in the primary outcome persisted in analyses stratified by individuals' smoking status. It is not immediately clear what may be causing these patterns of point-estimates. It is possible that an unaccounted for compositional (ie individual-level) or contextual (ie neighborhood-level) variable may be driving this pattern. One possibility in this regard may be that the most suburban areas, farther from the urban core are closer to rural areas or outdoor recreation areas that may be independent drivers of physical activity, while intermediate areas may not benefit from either highly dense, walkable areas or more peri-urban greenspace. However, in a previous study we have performed within this study area, we did not identify any nonlinear difference in distance to the nearest major park across levels of walkability.[19] Another possibility is that with recent demographic shifts that have seen urban areas increasingly occupied by wealthier individuals, marginalized individuals have been displaced towards the inner suburbs. In our previous work we found limited evidence for this possibility.[19] The proportion of residents 20 years and older with only a high school education or less appeared to peak in Q3 walkability, paralleling the results we see here, but other markers of socioeconomic status (unemployment rate, poverty rate, proportion of residences in need of major repair) had a more linear trend and indicated that Q5 was most disadvantaged. It is also important to note that the CIs largely overlap across contrasts, so some caution should be used when interpreting the potential nonlinearity of association. Further studies are needed to assess the robustness of this observation and to more deeply explore possible explanations, if replicated.

Our results suggest that neighborhood walkability is associated with clinically relevant differences in predicted cardiovascular disease. This lends support to the idea that neighborhood walkability may serve as an important point for public health intervention to offset risk for atherosclerotic cardiovascular disease. As neighborhoods are created or redeveloped, encouraging cities to permit higher densities and re-think approaches to zoning to allow mixed-used developments combining places to work, live, and engage in recreation may provide benefits to public health for existing and future populations. Doing so would reverse the decades-long trend towards low-density, suburban developments that predominated the latter half of the 20th century. Additionally, enhancing access to public transportation could enable those living in suburban areas to become more physically active by connecting them with more walkable urban areas and reducing dependence on cars.

Our study also demonstrated a novel association between walkability and smoking rates, emphasizing the importance of taking a broader perspective in understanding neighborhood effects on health. Moreover, for upstream policy interventions to have a clinically meaningful impact, they need to consider all aspects of cardiovascular risk. We observed that highly walkable

areas have higher rates of smoking, for reasons that are not entirely clear. It is possible that greater proximity to retail in highly walkable neighborhoods results in more tobacco sellers. This may result in unexpected support for smoking. Previous studies have found that greater distances between home and a tobacco outlet (eg convenience stores) are associated with a higher likelihood of quitting smoking.[48,49] In our study area, highly walkable neighborhoods also had higher levels of poverty, which may have contributed to higher levels of smoking in these areas. While our results persisted after adjustment for sociodemographic characteristics, further adjustment for individual socioeconomic status variables would enhance confidence in this finding. These results may suggest that to reap the full benefit of walkable environments, efforts must be made to curb tobacco availability or target smoking cessation campaigns within areas of higher tobacco availability. However, further studies designed to focus on this question are needed.

Several major strengths of this study are its use of a large population-based sample, representation from several distinct urban regions, and focus on a clinically meaningful outcome designed to predict hard atherosclerotic cardiovascular disease and guide use of statin medication.[31–34] However, there are some important limitations to the current findings that should be highlighted. Our analyses were cross-sectional, and so we cannot establish a temporal relationship between walkability and cardiovascular risk. Confounding by neighborhood self-selection is also possible and could lead to systematic differences in healthy behaviors between populations. Nevertheless, previous studies generally noted that associations between the built environment, risk factors, and health behaviors remain after addressing residential self-selection, by design or adjustment for neighborhood preference.[39,44,50] Furthermore, in ours and other samples, walkability is often inversely associated with measures of individual and area-level socioeconomic status, suggesting that residual confounding may be biasing results to the null.[51,52] Finally, while we did not measure physical activity in the sample as a mediator, previous work in our study area has found that walkability is directly associated with transportation-related physical activity.[19,20,43]

In sum, we found that individuals living in less walkable neighborhoods have a higher predicted risk of cardiovascular disease events. Future research is needed to confirm these findings using longitudinal designs, and to understand the underlying causes of the association between walkability and smoking. Our findings emphasize the importance of considering the health implications of urban design changes holistically. In particular, strategies to help curb smoking rates in highly walkable areas may help improve the public health impact of urban design improvements.

Acknowledgments

Parts of this material are based on data and information compiled and provided by the Canadian Institutes for Health Information (CIHI) and the Ontario Ministry of Health and Long-Term Care (MOHLTC). However, the analyses, conclusions, opinions and statements expressed in this manuscript are those of the authors and not necessarily those of CIHI or MOHLTC. Data on immigration history were obtained from Immigration, Refugees and Citizenship Canada Permanent Resident database. The opinions of the authors here do not necessarily reflect those of Immigration, Refugees and Citizenship Canada. We thank IMS Brogan Inc. for use of their Drug Information Database and Dynacare Medical Laboratories for the use of their laboratory data as part of the CANHEART initiative. Additional Information: Coauthor Jack V. Tu, MD, PhD, MSc, died during the preparation of this manuscript.

Sources of Funding

Dr Howell is supported by a Vanier Canada Graduate Scholarship from the Canadian Institutes for Health Research, a CIHR MD/PhD Studentship, a McLaughlin Centre MD/PhD Studentship, and a McLaughlin Centre Graduate Student Award. Dr Tu was supported by a Canada Research Chair in Health Services Research and an Eaton Scholar award from the Department of Medicine at the University of Toronto during the period of this research. Dr Booth is supported by a Clinician-Scientist Merit Award from the Department of Medicine at the University of Toronto. This study was funded by a Foundation Grant from CIHR (Dr Booth), and an Institute for Circulatory and Respiratory Health/CIHR Team Grant to the CArdiovascular HEalth in Ambulatory Care Research Team (CANHEART). This study was supported by ICES, which is funded by an annual grant from the Ontario MOHLTC. The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Data S1.

Description of Data Sources

1. Discharge abstract database (DAD): used to ascertain exclusion criteria (previous cardiovascular disease). The DAD contains records on all hospital admissions at acute, rehab, chronic, and day surgery hospitals in the province, including demographic, diagnostic, and information on procedures performed.
2. Electronic Medical Record Administrative Data Linked Database (EMRALD): used to determine outcomes (systolic blood pressures, HDL cholesterol, total cholesterol, smoking status), covariates (use of statin medication, use of anti-hypertensive medication), and auxiliary variables in multiple imputation (LDL cholesterol). Includes data from primary practice EMRs including laboratory test data, patient profiles, medications, consultation letters, and other clinical information.
3. Dynacare Medical Laboratories Database (GDML): used to ascertain individual lab values used to construct outcome variable (ACC/AHA Pooled Cohort Equation Risk Scores), secondary outcomes (HDL, total cholesterol), and auxiliary variables in multiple imputation (LDL cholesterol). Includes laboratory testing information for serum or urine samples conducted by Gamma-Dynacare Medical Laboratories, one of the largest commercial labs in the province.
4. Immigration, Refugees and Citizenship Canada Permanent Resident Database (IRCC): used for covariate ascertainment (immigration history). The extract we worked with includes all Canadian immigration applications for individuals landing first in Ontario after 1985. Data provided by Immigration, Refugees, and Citizenship Canada.

5. Ontario Canadian Census Profiles (CENSUS): used for covariate ascertainment (socioeconomic status proxy—dissemination area median household income). Contains census data aggregated to various geographic areas across Ontario.
6. Ontario Chronic Obstructive Pulmonary Disease Database (COPD): used to assess individual comorbidity (COPD). Database identifies individuals in Ontario with prevalent and incident cases of COPD among those 35 years and older based on diagnosis of COPD in physician billing claims or hospital discharge abstracts. Validation identified the algorithm had sensitivity and specificity of 85.0% and 78.5%, respectively.[1]
7. Ontario Diabetes Database (ODD): used to ascertain diabetes outcomes for patients. Database identifies individuals with diabetes mellitus using algorithm based on diabetes diagnoses from physician billings claims and hospital admissions.[2]
8. Ontario Drug Benefit Database (ODB): used to flag individuals residing in long-term care facilities for exclusion. Includes claims for medications insured by provincial insurance for eligible individuals.
9. Ontario Health Insurance Plan (OHIP) billings database: used to ascertain individual comorbidities using the Johns Hopkins Adjusted Clinical Groups and for exclusion criteria. Includes information on physician billings for services provided in Ontario that are insured by provincial health insurance.
10. Registered Persons Database (RPDB): used to define the study sample and for covariate ascertainment (sex, age, area-level socioeconomic status via linkage to Canadian Census data) and auxiliary variables used in multiple imputation (region of residence). Contains records for all individuals residing in Ontario who have been issued a provincial health insurance card.

11. Surname-based Ethnicity Group (ETHNIC): used for covariate ascertainment (ethnicity). The ETHNIC database includes classification of each individual into either South Asian, Chinese, or general population on the basis of surnames (surnames not included in database). Validation studies against self-identified ethnicity indicate specificities of 99.7% and 99.7% and sensitivities of 50.4% and 80.2% for South Asians and Chinese Canadians, respectively.[3]
12. Walkability database: used to assign exposure values (neighborhood walkability). Includes information on geographic locations and associated walkability values. Details on the index components are provided below.

V**ariable data collection and definitions**

Walkability: The present tool was developed using objective demographic and geographic features specific to the Ontario environment with a previously described protocol.[4] In brief, a literature review was first conducted to assess features of the built environment previously found to be related to transit activity, weight-measured (e.g. body mass index), or perceived walkability. Those factors for which data were available, scalable, and cost-permissible at the dissemination area (DA) level were then entered into a factor analysis to create a summary term explaining the common variance between built environment variables. The final index included four variables: (i) population density (population/km^2), (ii) residential density (number of dwellings/km^2), (iii) street connectivity ("count of 3-way or greater intersections within a 800 meter network buffer of the tract centroid"), and (iv) number of destinations within the neighbourhood ("count of locations of a given resource type within the 800 meter network buffer of each tract centroid").[1] Scores were Normalized with a mean of 0 and a variance of 1. Each of the items were correlated with the index with strengths ranging from 0.70 to 0.94 ($p < 0.001$), with a Chronbach's alpha = 0.85 indicating high internal reliability.[5] Since index values created using factor weights were highly correlated with a simpler index composed of the sum of the 4 normalized components, scores were generated using the latter approach. For analysis, walkability scores were divided into quintiles (Q1-least walkable, Q5-most walkable) based on the whole region that

[1] Resource types included grocery stores and fruit & vegetable stands, convenience/variety stores, bank branches, restaurants & cafes (including fast food), and other retail services. For areal geographic units, centroids are defined as the 'centre of mass' for that region, often representing the centre of the region (although this may not be the case if the region has an unusual shape, e.g. donut or crescent). Network buffers are those that calculate the distance from the area centroid along roads or paths that can be traveled by individuals instead of distance 'as the crow flies'.

walkability exposures were available for (Toronto & the Greater Toronto-Hamilton Area, Ottawa, and London).

Johns Hopkins Collapsed Aggregated Diagnostic Groups (CADGs): The Johns Hopkins Adjusted Clinical Groups (ACG) system (Johns Hopkins ACG® System Ver. 7.0) assigns individuals to a series of non-exclusive categories (ADGs, n = 32) based on hospital admissions and billing data.[6] These categories represent clinical and resource-intensity groups based on: duration of condition, severity of condition, diagnostic certainty, etiology, and need for specialty care. Designed to predict individuals' health resource needs, they have also been demonstrated to be predictive of 1-year mortality in the general population of Ontario and have been used to control for comorbidity in epidemiologic analyses.[7–9] To enhance the parsimony of the model, a set of 12 collapsed ADGs were generated on the basis of individuals' ADGs using a JHADG algorithm. A count of comorbidities (1 to 10) was created to describe the burden for each individual. CADG11 is unique in that it is not reflective of morbidity itself, rather the use of preventive or administrative health services. As such it is not counted as a 'comorbidity' for descriptive purposes, and was not included in the count.[7] We additionally have excluded CADG12 (pregnancy). For the secondary outcome smoking, since a variety of comorbidities could plausibly be consequences of smoking rather than confounders, we used two CADGs reflecting preventive care use and psychosocial comorbidities.

Table S1. Description of covariates used in multivariable models.

Variable	Level of measurement & units/levels	Data source
Age	Continuous (years)	RPDB
Sex	Dichotomous (male/female)	RPDB
Ethnicity	Nominal (Chinese, South Asian, General Population)	ETHNIC
Immigration history	Nominal (Immigration within 5 years of index, immigration 5-10 years prior to index date, other ('long-term resident'))	IRCC
Neighborhood income quintile	Nominal (quintiles)	CENSUS (2006)
COPD	Dichotomous (Case, non-case)	COPD
Comorbidities (JHACG)	Continuous (number, 0 to 10)	OHIP/DAD using John Hopkins ACG Algorithms
Smoking status	Dichotomous (family physician assessed smoker, not assessed as smoker)	EMRALD

Use of anti-hypertensive medication	Dichotomous (prescription, no prescription)	EMRALD
Use of statin medications	Dichotomous (prescription, no prescription)	EMRALD

Multiple imputation of missing data

Several variables had missing values in the present dataset: ACC/AHA Pooled Cohort Equation predicted risks (43.5%), systolic blood pressure (17.3%), total cholesterol (20.9%), HDL cholesterol (21.4%), current smoking status (17.7%), treated with statins within 1 year of HDL or TC measurement (21.4% and 20.9%, respectively), and neighborhood income quintile (0.4%). Missing estimated cardiovascular risk outcomes were primarily due to individuals missing one or more of the constituent components of the score (SBP, HDL, total cholesterol, smoking status) rather than individuals missing all components (1.9%). These variables are primarily outcome variables, although neighborhood income quintile and current smoking status are used as covariates in some models. Simulation studies have suggested that complete case analysis of data where only the outcome variable has missing values does not bias parameter estimates.[10] However, to address potential loss of statistical power due to missing data and to explore the effect of missing smoking data on secondary outcome models, we performed multiple imputation analyses using each of the above covariates and outcomes in the imputation model. A multiple imputation using chained equations (MICE) approach was used.[11] This technique has the advantage of being able to appropriately model non-continuous variables using logistic or discriminant analysis, rather than making an assumption of multivariate normality for all missing variables as is used in traditional multiple imputation.

Systolic blood pressure, HDL cholesterol, and total cholesterol were treated as continuous variables, while smoking status, treatment with statins within 1 year prior to HDL or TC measurement, and income quintile were modeled using logistic regression.

Smoking status and both statin variables were modeled with logit functions, while income quintile was modeled with a generalized logit function. Additional variables included in the imputation included diastolic blood pressure (continuous: mmHg; 17.3% missing), low density lipoprotein cholesterol (continuous: mmol/L; 22.3% missing), resource utilization band (RUB) score (0% missing), region of residence (categorical: Toronto, Ottawa, Hamilton, London, Other Greater Toronto Area; 0% missing), and treatment with statins within one year prior to LDL measurement (22.3% missing). Each individual CADG was treated separately rather than as a count, modeled as 12 individual binary variables (0% missing). RUB scores are generated with the JHACG software, and reflect differing levels of predicted resource utilization based on an individual's demographic and clinical characteristics.

To better approximate normal distributions, HDL, LDL, and total cholesterol were log transformed. Additionally, to better normalize data and preserve imputations in the allowable [0,1] range, 10-year cardiovascular disease risk was logit transformed prior to imputation. All data were converted back to their natural scale prior to analysis. Distributions of variables before and after imputation were checked to ensure imputed values were reasonable. For continuous variables, trace plots were also checked to ensure convergence before imputed values were drawn. Five imputations were generated and models were fit as usual for each of the datasets. Results for each dataset were pooled, with parameter estimates and their standard errors calculated using Rubin's rules (SAS proc mianalyse).

Two sensitivity analyses were performed to assess the robustness of our approach. First, we performed the imputation without DBP, LDL, and treatment on

statins within 1 year prior to LDL measurement, auxiliary variables that also had some missing data. We did not find our estimates changed materially, so results including these variables are reported. To further check our results to assess whether imputation dramatically changed our estimates, we compared the analyses using multiple imputation with complete case analyses. We found that the results were similar across models, with some contrasts changing status as statistically significant, but no overall change in conclusions (Table S3).

Table S2. Association between neighbourhood walkability and 10-year cardiovascular disease risk stratified by current smoking status.

Outcome	Smoking Status	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
ACC/AHA ≥ 7.5%	Non-Smoker			
	Walkability			
	Q1(Low)	1.15 (1.03, 1.28)	1.18 (1.06, 1.31)	1.18 (1.06, 1.32)
	Q2	1.37 (1.24, 1.52)	1.42 (1.28, 1.57)	1.42 (1.29, 1.58)
	Q3	1.34 (1.21, 1.48)	1.37 (1.24, 1.51)	1.39 (1.26, 1.54)
	Q4	1.24 (1.14, 1.36)	1.25 (1.15, 1.37)	1.28 (1.18, 1.40)
	Q5 (High)	Ref	Ref	Ref
	Smoker			
	Walkability			
	Q1(Low)	1.08 (0.83, 1.41)	1.06 (0.81, 1.39)	1.09 (0.84, 1.41)
	Q2	1.15 (0.94, 1.41)	1.15 (0.93, 1.42)	1.17 (0.94, 1.46)
	Q3	1.37 (1.16, 1.61)	1.39 (1.19, 1.64)	1.40 (1.19, 1.65)
	Q4	1.17 (1.02, 1.34)	1.17 (1.02, 1.34)	1.19 (1.03, 1.37)
	Q5 (High)	Ref	Ref	Ref
ACC/AHA ≥ 10.0%	Non-Smoker			
	Walkability			
	Q1(Low)	1.19 (1.06, 1.34)	1.22 (1.09, 1.37)	1.24 (1.10, 1.40)
	Q2	1.40 (1.24, 1.57)	1.44 (1.28, 1.62)	1.45 (1.28, 1.63)
	Q3	1.42 (1.27, 1.59)	1.44 (1.29, 1.61)	1.47 (1.32, 1.65)
	Q4	1.30 (1.17, 1.43)	1.30 (1.18, 1.45)	1.34 (1.21, 1.49)
	Q5 (High)	Ref	Ref	Ref
	Smoker			
	Walkability			
	Q1(Low)	1.14 (0.92, 1.42)	1.12 (0.90, 1.40)	1.15 (0.92, 1.44)
	Q2	1.16 (0.96, 1.41)	1.17 (0.96, 1.42)	1.19 (0.98, 1.45)
	Q3	1.27 (1.08, 1.50)	1.30 (1.11, 1.53)	1.31 (1.11, 1.55)
	Q4	1.09 (0.94, 1.27)	1.09 (0.94, 1.27)	1.11 (0.95, 1.30)
	Q5 (High)	Ref	Ref	Ref

All estimates presented are adjusted for the covariates described for the main models in the methods section. ACC/AHA: ACC/AHA pooled cohort equation risk score. CI: confidence interval. OR: odds ratio. Ref: reference category. Q: quintile.

Table S3. Model results from complete case analyses.

	ACC/AHA ≥ 7.5% OR (95% CI)	ACC/AHA ≥ 10.0% OR (95% CI)	SBP (mmHg) β (95% CI)	Total Cholesterol (mg/dL) β (95% CI)
Walkability				
Q1(Low)	1.05 (0.94, 1.18)	1.12 (0.99, 1.27)	2.61 (1.99, 3.23)	0.56 (-0.97, 2.09)
Q2	1.26 (1.13, 1.39)	1.24 (1.11, 1.39)	2.39 (1.76, 3.01)	-0.79 (-2.20, 0.63)
Q3	1.34 (1.20, 1.48)	1.38 (1.23, 1.54)	2.17 (1.57, 2.76)	0.30 (-1.21, 1.81)
Q4	1.20 (1.10, 1.32)	1.21 (1.09, 1.34)	1.44 (0.94, 1.95)	0.44 (-0.81, 1.71)
Q5 (High)	Ref	Ref	Ref	
	HDL Cholesterol (mg/dL) β (95% CI)	**Smoking Status OR (95% CI)**	**DM OR (95% CI)**	
Walkability				
Q1(Low)	-1.76 (-2.40, -1.13)	0.76 (0.67, 0.85)	1.27 (1.11, 1.44)	
Q2	-1.33 (-1.96, -0.71)	0.72 (0.65, 0.81)	1.17 (1.04, 1.33)	
Q3	-1.45 (-2.07, -0.82)	0.89 (0.80, 0.99)	1.14 (1.01, 1.29)	
Q4	-0.79 (-1.34, -0.23)	0.89 (0.81, 0.97)	1.12 (1.00, 1.25)	
Q5 (High)	Ref	Ref	Ref	

All estimates presented are adjusted for the covariates described for the main models in the methods section. ACC/AHA: ACC/AHA pooled cohort equation risk score. CI: confidence interval. DM: diabetes mellitus. HDL: high density lipoprotein. OR: odds ratio. Ref: reference category. SBP: systolic blood pressure. Q: quintile.

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