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Nonlinear Relationships Between The Environment And Health

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NONLINEAR RELATIONSHIPS BETWEEN THE ENVIRONMENT AND HEALTH

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ABSTRACT

Relationships between the environment and health outcomes are complex and likely nonlinear in nature. However, until recently, most studies used ordinary linear regression to model these relationships. The overall goal of this research was to investigate nonlinear relationships between the environment and health. To accomplish this goal, we used several large, national datasets across varying populations and local environments.

Destination accessibility is an important measure of the built environment that is associated with active transport and body mass index (BMI). In the first study, we sought to determine the relationship between the density of nonresidential destinations (a proxy for walkability) and BMI, allowing for the possibility of a nonlinear relationship. We merged information from 17.2 million driver's license records with the locations of 3.8 million nonresidential destinations and census tract socioeconomic data from six states. BMI peaked in the middle density, with significantly lower values in both the low and high-density extremes – a markedly nonlinear relationship.

Next, we confirmed our previous nonlinear findings in an independent sample of 2,405 primary care patients with multiple chronic conditions from 13 states, and extended our analysis to include mental and physical health outcomes, in addition to BMI. Several statistical methods were used to confirm the nonlinear relationship between nonresidential destinations and BMI. We also established novel nonlinear relationships between nonresidential destinations and mental health. All three health measures were significantly worse in middle density areas with better values on either extreme.

Then, we extended the previous analyses to the natural environment. We used data on 3,409 adults from 119 US counties and the natural amenities scale, a county-level measure of the natural environment, to assess the relationship between the natural environment and health at the intersection of various demographic and social factors, allowing for the possibility of a non-linear relationship. Health was generally worse in areas with poor natural environments; however, this relationship was not linear. In areas with low natural amenities, greater amenities were associated with better physical and mental health, but only for advantaged populations. Meanwhile greater amenities in high amenity areas was associated with a decrease in mental and physical health for disadvantaged populations.

Finally, in the review paper, we described the current state of the literature on the nonlinear relationships between walkability and health. We argue that using linear regression techniques to model nonlinear relationships could introduce bias and be partially responsible for the conflicting findings in the literature.

We conclude that there are nonlinear relationships between the environment and health. Complex relationships require complex modelling. Ignoring the possibility of a nonlinear relationship could obscure the true relationship and lead researchers and public health officials to draw incorrect conclusions. Future research should confirm these findings and investigate the mechanisms driving these relationships.

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CHAPTER 1: NONLINEAR RELATIONSHIP BETWEEN NONRESIDENTIAL DESTINATIONS AND BODY MASS INDEX ACROSS A WIDE RANGE OF DEVELOPMENT

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1.1. Abstract

Background: Destination accessibility is an important measure of the built environment that is associated with active transport and body mass index (BMI). In higher density settings, an inverse association has been consistently found, but in lower density settings, findings are limited. We previously found a positive relationship between the density of nonresidential destinations (NRD) and BMI in a low-density state. We sought to test the generalizability of this unexpected finding using data from six other states that include a broader range of settlement densities.

Methods: We obtained the address, height, and weight of 17.2 million residents with a driver's license or state identification cards, as well as the location of 3.8 million NRDs in Washington, Oregon, Texas, Illinois, Michigan, and Maine from Dun & Bradstreet. We tested the association between NRDs per hectare ($\cdot ha^{-1}$) within 1 km of the home address, and self-reported BMI ($kg \cdot m^{-2}$). Visualization by locally-weighted smoothing curves (LOWESS) revealed an inverted U-shape. A multivariable piecewise regression with a random intercept for state was used to assess the relationship.

Results: After accounting for age, sex, year of issue, and census tract social and economic variables, BMI correlated positively with NRDs in the low-to-mid density stratum (β=+0.005 $kg \cdot m^{-2}$/nonresidential building$\cdot ha^{-1}$; 95% CI: +0.004,+0.006) and negatively in the mid-to-high density stratum (β=-0.002; 95% CI: -0.004,-0.0003); a significant difference in slopes (P<0.001).

Conclusions: BMI peaked in the middle density, with lower values in both the low and high-density extremes. These results suggest that the mechanisms by which NRDs are associated with obesity may differ by density level.

1.2. Introduction

Obesity is a global public health crisis. In the United States, 42% of adults are obese, defined as a body mass index (BMI) ≥30 kg/m^2.[1] Obesity is a major risk factor for adverse health outcomes including heart disease, stroke, type 2 diabetes, kidney disease, and premature death.[2-4] These obesity-related conditions are largely preventable through lifestyle changes such as improving diet and increasing physical activity (PA).

The built environment influences PA, diet, and obesity in several ways, known as the 5Ds[5]: density (residential, populations *etc.*),[6] diversity (land use mix),[7,8] design (walkability),[9,10] distance (to transit),[11] and destination accessibility.[6,12] Each factor has been shown to be independently associated with obesity by facilitating or impeding healthful behaviors related to energy balance, such as active transport (including walking, cycling, and public transportation) or the food environment. Here, we focus on the density of nonresidential destinations (NRDs) as a measure of destination accessibility.

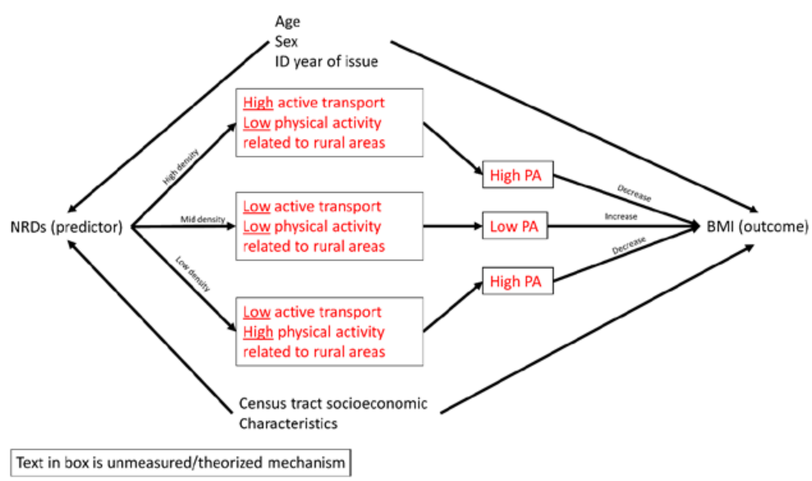
Proximity and access from residences to mixed NRDs can afford opportunities for active transport.[13-15] For instance, retail businesses, public offices, restaurants, schools, and places of worship serve as NRDs that may promote walking for transport if sufficiently close to homes and each other. In Western Australia, proximity to convenience stores, schools, and transit stops within 1.5 km of the home was significantly associated with increased walking for transport,[15] and similar results were confirmed by a systematic review.[13] Another review from China found that the strongest evidence for promoting active transport was proximity to nonresidential locations.[16] Little is known about proximity of NRDs and walking for transport in low-density settings.

In most of the published literature, as density of NRDs increase, proximity to NRDs increases and BMI tends to decrease on average. Increased accessibility to NRDs was associated with increased active transport and PA[17] and lower rates of obesity over time in Canada[18] and the US.[19] NRDs were inversely associated with BMI in urban Australia[12] and the United States[20] but positively associated with PA and obesity in older US women.[20]

Conversely, lower densities of NRDs implies longer average distances to destinations, increasing the likelihood of automobile reliance and higher BMI. A large study found car owners have higher BMIs than non-car owners.[21] Despite the research supporting a relationship among proximity to NRDs, PA, and reduced rates of obesity in dense urban areas,[6,12,18,19,22,23] there is little evidence from low-density contexts. A study from rural Arkansas, Missouri, and Tennessee, found that a lack of perceived NRDs was negatively related to obesity.[24] Rutt *et al.* found a positive relationship between NRDs and BMI in a small dataset from El Paso County, TX, a county with both low and high density areas.[25] A recent study in China found a positive relationship between density of grocery stores and restaurants (included in our definition of NRDs) and BMI; however, the effect was more pronounced in urban than rural areas.[26] Our prior work in a low-density area (Vermont)[27] demonstrated a positive correlation between NRD density and BMI using two independent datasets, raising the possibility that the association is not consistently negative across all levels of density. These results could be unique to Vermont, an artifact of measurement error in both datasets, or a generalizable phenomenon of predominantly rural areas with low density of NRDs.

It stands to reason that the mechanisms affecting the relationship between NRDs and BMI differ across densities. In high-density areas, we expect high levels of active transport and low reliability on automobiles resulting in high PA and low BMI, despite PA related to residing in rural areas (physically intensive employment, home property management, and greater access to outdoor recreation) being low. Likewise, in low-density areas, we expect low active transport and high automobile reliance but high levels of PA from residing in rural areas, resulting in low BMI. In contrast, we expect low levels of PA in mid-density areas due a lack of active transport and a lack of PA related to residing in rural areas, resulting low levels of PA and high BMI (Figure 1 - 1).

Figure 1 - 1: Directed acyclic graph (DAG)



We sought to test this model using data from six states with a broad range of NRD densities, considering the possibility of a nonlinear relationship. We hypothesized that BMI would increase as NRDs increased in the range from low the mid density but decrease in the range from mid to high densities, forming an inverted-U curve.

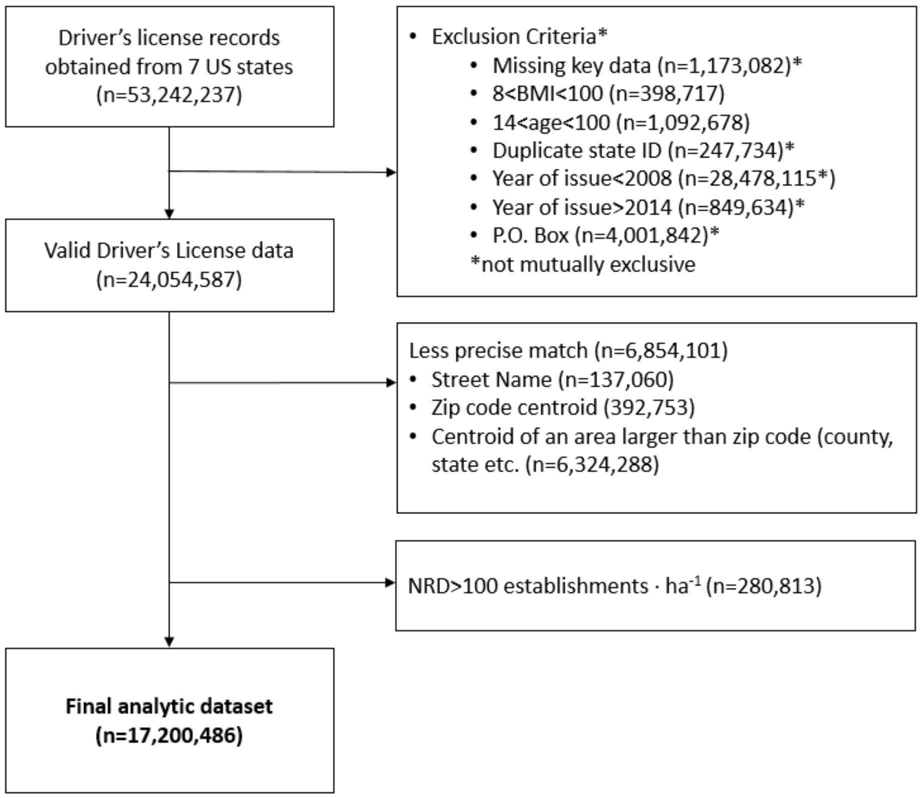
1.3. Methods

1.3.1 Data and Setting

We obtained three datasets. The first dataset contained 53.2 million records from the general population of residents with either a driver's license or state identification (ID) card from Washington, Oregon, Texas, Illinois, Michigan, and Maine. The completeness of the data varied by state, ranging from an estimated 31% in Oregon to roughly 100% in Washington. However, age and BMI distributions are similar to national averages.[28] The data included self-reported height and weight, date of birth, date of issue of license or ID card, and home address. We excluded records with BMI less than 8 kg/m^2 or greater than 100 kg/m^2 (likely erroneous entries), age greater than 100 or less than 14 years, duplicate state ID numbers, absence of street address data, if the date of issue was before 2008 or after 2014 (the year the data were collected), or if the NRD density was >100 $establishments \cdot ha^{-1}$. Records were de-duplicated by state ID code, which is unique to an individual and stable over time. Latitude and longitude were assigned to each record using the ArcGIS address geocoder (ESRI Inc., Redlands, CA) and the WGS 1984 coordinate system. Records lacking enough information to be identified with a single address were omitted. Importantly, there were no significant differences in BMI, age, sex, or driver's license year of issue between the 17.2 million records included in the study and the 6.8

million excluded due to geocoding inaccuracies. The final dataset contained 17.2 million records data (Figure 1 - 2). The primary outcome was self-reported BMI ($kg{\cdot}m^{-2}$).

Figure 1 - 2: Consort diagram



The second dataset contained 13,207,211 geocoded establishment records from 2018 Dun and Bradstreet data for the 6 states (Dun & Bradstreet Corp., Milburn, New Jersey). We classified establishments as likely destinations to increase active transport[15,16] based on their North American Industry Classification (NAICS) codes. We included retail establishments, personal service providers, restaurants, community centers, schools, places of worship, post offices and other government facilities, and commercial recreation and entertainment facilities (n=3,749,984; Table 1 - 1). We excluded establishments associated with agriculture, forestry, mining, quarrying, utilities, construction, manufacturing, and wholesale trade.

Table 1 - 1: North American Industry Classification System (NAICS) Codes Representing Nonresidential Destinations

NAICS Codes	Description	Example
445---	Food and Beverage Stores	Supermarkets, Convenience stores
446---	Health and Personal Care Stores	Pharmacy and drug stores *etc.*
447---	Gasoline Stations	Gas stations
448---	Clothing and Clothing Accessory Stores	Clothing stores
451---	Sporting Goods, Hobby, Musical Instrument, and Book Stores	Game stores, musical instrument stores
452---	General Merchandise Stores	Department stores
453---	Miscellaneous Store Retailers	Florists, pet stores
4851--	Urban Transit Systems	Commuter rail systems
4852--	Interurban and Rural Bus Transportation	Bus stations
491---	Postal Service	Post offices
51912	Libraries and Archives	Libraries
5221---	Depository Credit Intermediation	Banks
61----	Education services	Elementary schools, colleges
712---	Museums, Historical Sites, and Similar Institutions	Museums, zoos
7224--	Drinking Places (Alcoholic Beverages)	Bars
7225--	Restaurants and Other Eating Places	Full-services restaurants, cafes
8121--	Personal Care Services	Barber shops, Nail salons
81231-	Coin-Operated Laundries and Drycleaners	Laundromats
8129--	Pet Care (except Veterinary) Services	Grooming
8131--	Religious Organizations	Places of worship, churches, cathedrals, Mosques, *etc.*

- NAICS are structured hierarchically containing 6 total digits. Dashes are a wildcard that represent any number. Any NAICS code above with dashes includes all subcategories.

The third dataset contained census tract information on measures of income, education, employment, housing, household characteristics, transportation, rurality, population density, and demographics from the 2008-2012 American Community Survey 5-year estimates (Table 1 - 2). These variables were included in the model as potential confounders or mediators of the relationship between NRDs and BMI.

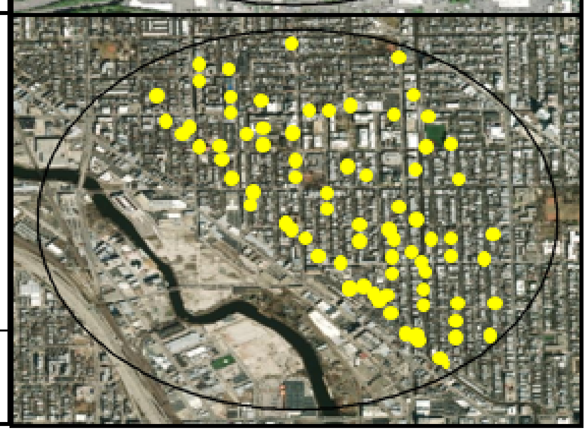
The primary predictor for this analysis was the absolute concentration of NRDs, which was assumed to proxy destination accessibility or ease of access by active transport mode (Figure 1 - 3). It was calculated by the ArcGIS Point Density function as the number of establishments$\cdot$ha^{-1} within 1 km of the address recorded on the driver's license or state ID. Each address was assigned to a 30 m pixel, which served as the center of a circle with an Euclidean or straight-line buffer radius of 1 km. The 1 km spatial scale was chosen based on prior literature that suggests the mean walking trip in the US is 0.61 miles.[29,30] We used locally-weighted smoothing (LOWESS) to visualize the relationship between BMI and NRDs across all subjects[31]. The LOWESS smoothing function is a nonparametric tool used to help explore the relationship between two variables without specifying an underlying form. LOWESS builds a function by fitting simple models to localized subsets of the data. The visual form of the LOWESS in this case suggested an inverted-U with a peak at 15 establishments$\cdot$ha^{-1}. This informed our piecewise linear function.

The socioeconomic variables used at the census tract level to control for potential confounding effects of the relationship between NRDs and BMI[32] included summary measures of income, education, employment, housing, household characteristics, transportation, rurality, population density, and demographics.

Table 1 - 2: Candidate covariates included in the final models (Model 1 & 2)

Level	Covariate	Units	Source
Individual	Age	Years	State Department of Motor Vehicles
	Sex	0: Female, 1: Male	
	Driver's license or State ID card date of Issue	Year	
	NRDs within 1 km of home address	ha^{-1}	
Census tract	Rural Urban Commuting Areas	1: Urban, 2: Large Town/Rural City, 3: Rural Town, 4: Isolated rural town	USDA Economic Research Service
	Population Density	persons·mi^{-2}	US Census and American Community Survey 2008-2012
	Population below 100% of the US federal poverty level	%	
	Population with less than 12 years of education (age >24)		
	Non-employment Rate		
	Population Foreign Born		
	Single-parent households with dependents < 18 years		
	Population black		
	Population Hispanic		
	Population without a car		
	% Living in crowded housing units		
	% Living in renter occupied units		
	% Age <5 years or >64 years		
State	State of driver's license or state ID card issue	1: Washington, 2: Oregon, 3: Texas, 4: Illinois, 5: Michigan, 6: Maine	State Department of Motor Vehicles

Figure 1 - 3: Examples of areas in the low-density stratum, at the inflection point, and in the high-density stratum.

a. Low density. Typical low density area with farming. Northern Michigan. NRDs = 0 establishments·ha^{-1}.	
b. Density range around the inflection point. Typical mid density area with mixed land use and residential housing. Western Washington outside Seattle. NRDs = 15 establishments·ha^{-1}.	
c. High density. Typical city center with multi-family buildings and ground floor destinations. Downtown Chicago, Illinois. NRDs = 100 establishments·ha^{-1}.	
Nonresidential destinations	

We performed sensitivity analyses at different radii (250m, 500m, and 2km) to test which conceptualization of density resulted in the strongest associations and enhanced reproducibility.

1.3.2 Statistical Analysis

We used Chi-squared tests, ANOVA, t-test, and Pearson's R to test the unadjusted associations between NRDs and BMI. Spatial autocorrelation of the error term was assessed using Lagrange Multiplier and Robust Lagrange Multiplier Tests. A mixed effects piecewise linear regression model was used to assess the main effect of NRDs on BMI. We accounted for individual-level and census tract-level covariates. Covariates included individual and census tract-level demographic information (See table 2). If the covariate changed the coefficient of NRDs on BMI by more than ±10% in a model containing only two predictors (NRDs and the covariate), it was included in the final model as a potential confounder. We modeled state as a random effect, clustering by state to account for the fact that individuals living closer together have BMIs that are more similar. All other variables were modeled as fixed effects. Covariates included individual and census tract-level demographic information based on prior literature and expertise of the authors (See Table 2). If the Lagrange tests for spatial autocorrelation were significant, a spatial error regression with a neighborhood matrix based on the three nearest neighbors was used.

All tests were two-tailed and the threshold for statistical significance for the main analysis was set at α=0.05. Stata 17 (StataCorp LP, College Station, Texas) was used for data management and statistical analysis.

We used the Spatial Lifecourse Epidemiology Reporting Standards guidelines.[33] The University of Vermont Institutional Review Board approved this study as the collection or study of existing data, waiving the requirement for individual consent. The authors have no conflicts of interest to report.

Results

Overall, the average BMI was 25.9 kg/m^2 with a standard deviation of 5.5, which is lower than the US average of 29.6 for women and 29.1 for men.[34] The mean age was 39 and 46% were men. Mean NRD density was 13.0 establishments·ha^{-1} (range 0 – 690) with median 5.4. 98% of the addresses had NRD density <100 establishments·ha^{-1}. Individuals living in lower densities were more likely to be older and female. Overall, average BMI was similar between low- and high-density areas (Table 1 - 3). The LOWESS revealed an inverted-U relationship with a peak at 15 establishments·ha^{-1}.

Table 1 - 3: Characteristics of Population Stratified by Non-Residential Destination (NRD) density (N=17,200,486)

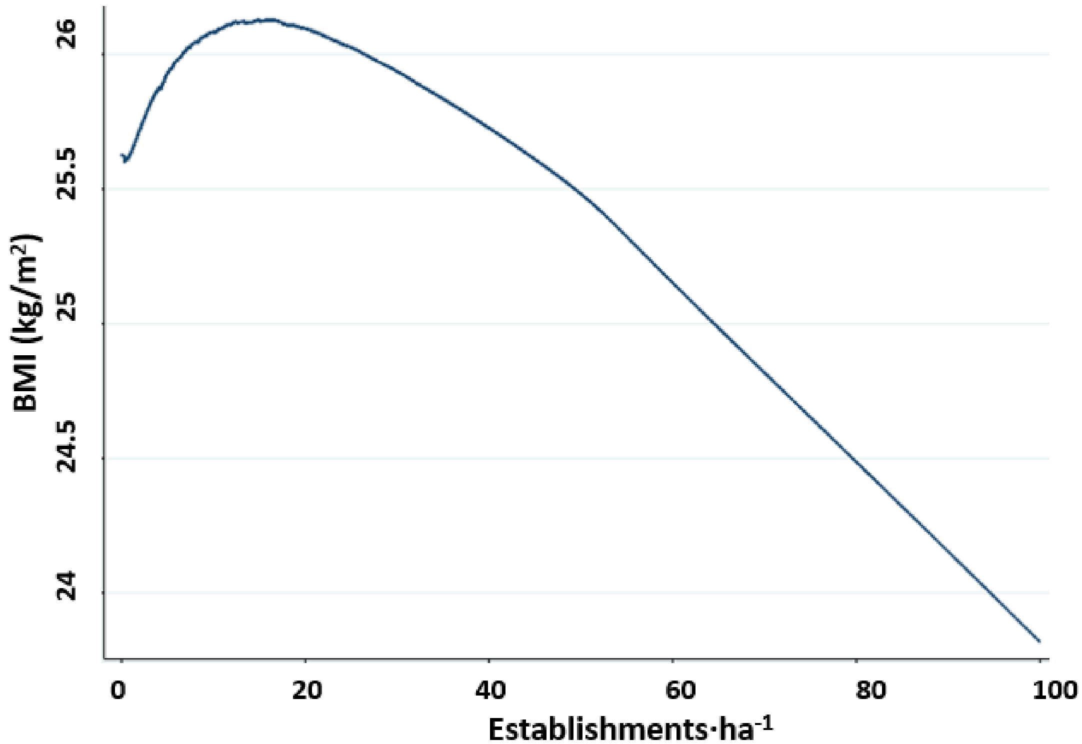
	Low-density Stratum NRDs < 15 establishments·ha^{-1} (n=12,903,827)	High-Density Stratum NRDs ≥ 15 establishments·ha^{-1} (n =4,296,659)
Individual Level		
*Age in years, mean ±SD	39.8 ±20.4	38.2 ±18.0
*Sex, % male	46%	51%
*Year of issue, mean ±SD	2008 ±4	2008 ±4
*BMI in kg·m^2, mean ±SD	25.9 ±5.5	25.8 ±5.4
Census tract social and economic determinants of health		
*Population Density per Square Mile, mean ±SD	2,592±2,812	11,137±14,634

*% Below 100% of the US federal poverty level, mean ±SD	13.5±10.6	19.3±13.2
*% Population with less than 12 years of education (age >24), mean ±SD	12.1±10.6	15.4±12.9
*% Non-employment, mean ±SD	8.4±5.1	9.7±6.7
*% Foreign Born, mean ±SD	12.0±11.2	19.6±14.8
*% Single-parent households with dependents < 18 years, mean ±SD	17.0±9.8	22.0±12.1
*% Population black, mean ±SD	9.8±18.3	16.7±26.4
*% Hispanic, mean ±SD	17.5±22.3	25.1±26.7
*% Without a car, mean ±SD	5.6±5.9	15.3±13.2
% Living in crowded housing units, mean ±SD	3.0±3.9	4.4±4.8
% Living in renter occupied units, mean ±SD	28.4±18.3	50.9±22.1
% Age <5 years or >64 years, mean ±SD	19.2±4.9	17.8±5.4

*Included as covariates in full multivariable model

In unadjusted analysis, we found an inverted-U. BMI was positively associated with NRD density below 15 establishments·ha^{-1} (β=+0.029 kg·m^{-2}/nonresidential buildings ha^{-1}; 95% CI: +0.028,+0.029), and was negatively associated with NRD in the mid-to-high density stratum (β=-0.012 ; -0.012,-0.011). The difference of the slopes was statistically significant (P<0.001). Results were slightly attenuated when adjusting for covariates. After accounting for age, sex, year of issue, and census tract characteristics as indicated in Table 2, BMI was positively associated with NRD density below 15 establishments·ha^{-1} (β=+0.004 kg·m^{-2}/nonresidential buildings ha^{-1}; 95% CI: +0.003,+0.006), and was negatively associated with NRD in the mid-to-high density stratum (β=-0.001 ; -0.002,-0.001). The difference of the slopes were statistically significant (P<0.001) (Figure 1 - 4 & Table 1 - 4).

Figure 1 - 4: LOWESS Curve used to visualize the relationship between nonresidential destinations and body mass index.



Both the Lagrange Multiplier and Robust Lagrange Multiplier tests were highly significant for both the unadjusted and adjusted piecewise linear regression models, indicating significant spatial autocorrelation of the error term and suggesting a spatial error regression might be appropriate. Due to computational constraints in processing such a large data set, several 1% random samples were drawn for use in running the spatial error regressions. In each model presented in table 4, the spatial error regression had the same coefficients and confidence intervals as the ordinary piecewise linear regression to the ten thousands place.

Because the choice of 1 km as the spatial scale size is somewhat arbitrary, we performed sensitivity analyses with other commonly used spatial scales[12,27,35]. We noticed that the optimum inflection point differed by search radius used in the density function. The inflection point was 25 ha^{-1} at a search radius of 250 m, 20 ha^{-1} at 500 m, 15 ha^{-1} at 1 km (Base case) and 10 ha^{-1} at 2 km (Table 1 - 4 & Figure 1 - 5). In the low-density stratum, all coefficients were positive except for at a spatial scale of 2 km. At all four spatial scales, the coefficient was negative in the high-density stratum (Table 1 - 4). 22% of residences between 10 ha^{-1} and 25 ha^{-1} would be reclassified depending on choice of inflection point. If the inflection point is switched to 10 ha^{-1} at a spatial scale of 2 km, then the coefficient becomes positive again in the low-density stratum.

Figure 1 - 5: LOWESS curves used to visualize the relationship and the corresponding piecewise linear regression to fit the model between nonresidential destinations and body mass index.

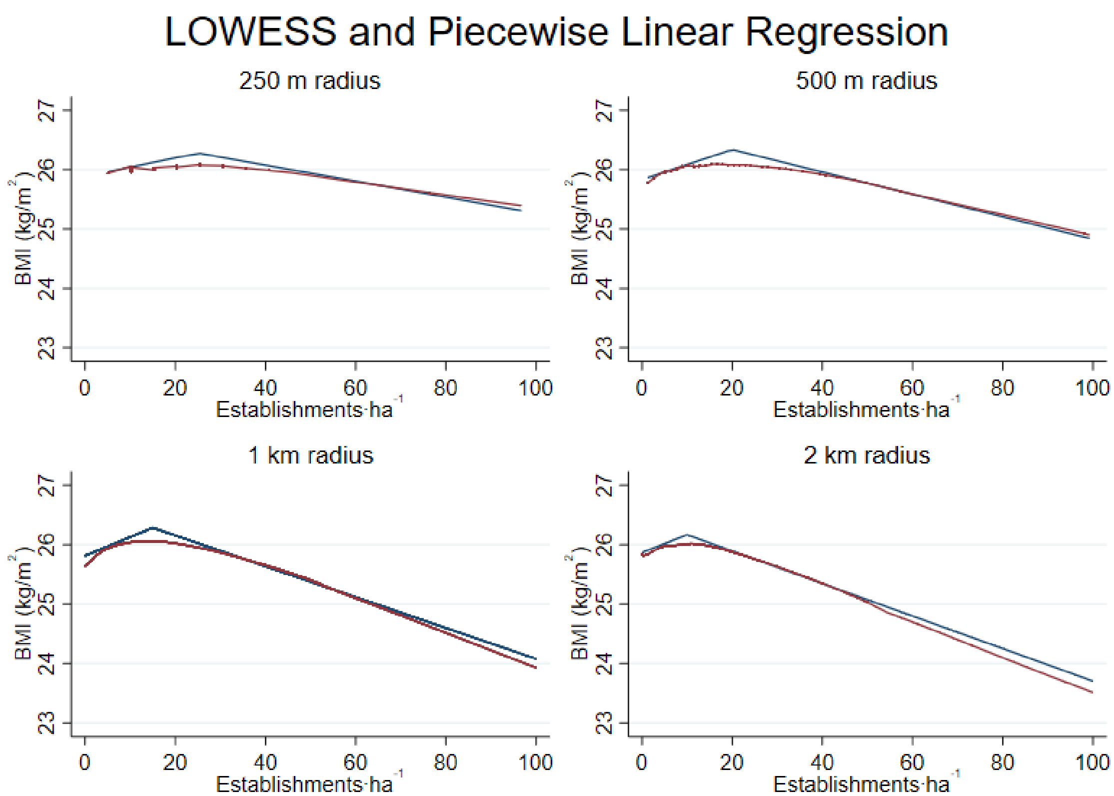


Table 1 - 4: Multivariable models of main analysis and other spatial scales (N=17,200,486)

Radius	Inflection Point (establishments·ha^{-1})	Low-density Stratum β Coefficient (CI)	High-density Stratum β Coefficient (CI)	*P*-value
		Unadjusted Model		
250 m	25	+0.014 (+0.014, +0.015)	-0.012 (-0.012, -0.011)	<0.001
500 m	20	+0.024 (+0.023, +0.024)	-0.020 (-0.020, -0.019)	<0.001
1 km (Base Case)	15	+0.029 (+0.028, +0.029)	-0.027 (-0.027, -0.026)	<0.001
2 km	10	+0.025 (+0.024, +0.026)	-0.028 (-0.028, -0.028)	<0.001
		Model adjusted for person-level covariates		
250 m	25	+0.009 (+0.009, +0.010)	-0.005 (-0.005, -0.009)	<0.001

500 m	20	+0.017 (+0.017, +0.018)	-0.009 (-0.009, -0.009)	<0.001
1 km (Base Case)	15	+0.023 (+0.023, +0.024)	-0.012 (-0.012, -0.011)	<0.001
2 km	10	+0.026 (+0.025, +0.026)	-0.016 (-0.016, -0.015)	<0.001
Full Multivariable Model				
250 m	25	+0.004 (+0.004, +0.006)	-0.001 (-0.002, -0.006)	<0.001
500 m	20	+0.007 (+0.005, +0.009)	-0.004 (-0.006, -0.001)	<0.001
1 km (Base Case)	15	+0.005 (+0.004, +0.006)	-0.009 (-0.012, -0.004)	<0.001
2 km	10	-0.008 (-0.019, +0.002)	-0.012 (-0.015, -0.009)	<0.001

All models include all individual and census-tract variables as fixed effects and state as a random intercept.

Discussion

In a previous study conducted in a predominantly rural state with a range of low to mid-densities of NRDs,[27] we found a positive relationship between NRDs and BMI. This contradicted much of the existing literature at the time, which was largely performed across a range of densities from mid to high. In the current study, we used over 17 million records from multiple states to investigate the relationship between the density of NRDs and BMI across a broader range of development. We found that BMI peaks in the middle density, with lower values at both extremes, supporting our previous findings that NRDs are positively correlated with BMI in lower density settings. Further, our results confirm the inverse relationship between BMI and NRDs found in other studies of high-density areas. To the best of our knowledge, this is the first study to explore the relationship between NRDs and BMI across such a broad range of development densities.

Using a search radius of 1 km around each household to calculate the density, we found a positive relationship between NRDs and BMI up until an inflection point of 15 destinations·ha^{-1}, at which point the relationship became negative, creating an inverse-U shaped curve. The inverted-U relationship holds at multiple spatial scales, except for the full multivariable model with a search radius of 2 km where the relationship between NRDs and BMI was negative in both high-density and low-density settings (although the mid- to high-density strata did have a significantly steeper negative slope). Another interesting finding was that the inflection point shifted depending on the radius. We hypothesize that larger search radii result in more NRD variability, where high-density portions cancel out low-density portions obscuring the inflection point.

The mechanisms by which NRDs are associated with obesity are uncertain but appear to differ with density. Based on our findings and the previous literature, the mechanism for low BMI in high-density areas includes opportunities for active transport (and therefore lack of car reliance) and PA afforded by destination proximity.[12] We expect fewer opportunities for active transport and more car reliance in high- and mid-density areas. In contrast, for those living in the lowest density range, lower average BMI may be attributable to more physically intensive employment (e.g. agricultural or resource extraction work) and home property management (wood chopping, snow removal, brush clearance, etc.), and greater access to outdoor recreation, in spite of relatively high car reliance. In other words, lifestyle factors in rural areas may play a similar role to active transport in high-density areas, even though car reliance is high and active transport is low. The mechanism may also involve the local food environment, geopolitical, socioeconomic, or social differences among others. We currently lack the data to firmly establish these mechanisms (Figure 1 - 1).

Although not conclusive, our proposed hypothesis for the mechanism behind lower BMI in low-density settings is consistent with previous literature. Two studies of rural Amish adults and children found very high levels of PA and very low rates of obesity.[36,37] Further, rural individuals are more likely to spend time outdoors, which may increase PA[38] and therefore reduce BMI. Higher levels of natural amenities common in rural areas have been linked with decreased BMI,[39] but this may be more a function of socioeconomic status than urban-rural status.[40]

Previous literature suggests a negative, monotonic relationship between the NRDs and BMI. There are two primary reasons why these studies could have missed the nonlinear relationship between NRDs and obesity demonstrated here. First, most studies were performed in mid- to high-density settings. Second, even if data from very rural areas were included, the investigators may not have considered a nonlinear relationship across development. Ignoring the possibility of a nonlinear relationship could obscure more nuanced relationships between NRDs and BMI and drastically attenuate the slope of the coefficient in high-density areas. Ultimately, researchers can draw incorrect conclusions from the data by failing to account for nonlinear relationships.

Our analysis of the full spectrum of development also leads to an important insight: areas with mid-densities have the highest BMI, nearly 1 BMI point higher than in low-density areas and over 3 points higher than high-density areas. Both high-density and low-density environments encourage PA, although for different reasons. That leaves the middle range of density as the most susceptible for obesity related to inactivity. The suburbs are also the dominant settlement pattern in the US today, which raises important public health and planning questions.

The results of this study could have important implications for built environment research methods as well as practical applications, but first, the mechanisms of action need to be explicated. We need to explore causative relationships between NRDs and health across a wider range of development than has been usual in the past. More importantly, these findings suggest that solutions extracted from one density may not apply to areas with different densities. Once confirmed, these findings could help customize allocation of building permits and zoning laws of NRDs based on how dense an area is, which could ultimately have positive impacts on BMI. Urban planners and public officials could have the potential to combat obesity in mid-density settings by adding a few units of NRD density, potentially making the area more walkable, while adding NRDs to low-density setting may be counterproductive. Future studies should investigate if the type of NRD has different effects on BMI and obesity across densities.

There are several important limitations to this study. Although we had information on individuals with a driver's license or state ID card, we likely missed undocumented immigrants and others without a formal state ID card. Self-reported height and weight are subject to both differential and non-differential misclassification bias. Weight is consistently underreported while height is over reported, and the magnitude varies by US region.[41,42] However, we do not expect self-reported BMI to vary by proximity to NRDs, mitigating the effect of these errors on the reported associations. Like most studies in this arena, these data are cross-sectional, and individuals are prone to self-assignment of neighborhoods. However, others have shown that neighborhood self-selection bias in studies of the built environment and health attenuates the estimates toward the null.[43] Therefore, associations may be even stronger in actuality. We assume residential proximity to walkable destinations correlates with active transport, but people move around in their daily life in many ways and may engage in active transport away from home. We do not know how much time individuals spend outside of the 1 km buffer from their residence. Euclidean buffers, such as those used here, may not optimally represent active transport burden. This factor may vary depending on density, potentially introducing bias.

While primary data collection is considered the gold standard for identifying business locations, it is time consuming, not available for historical periods, and often infeasible in large studies.[44,45] An advantage of commercially sourced data is that they use consistent methods across multiple areas. Although accuracy can be increased by combining multiple sources, they were not available for this analysis. However, we did de-duplicate records and remove PO Boxes.[44] There was a temporal mismatch between the NRD and driver's license data. NRDs were collected later (2016) than height and weight (2008-2014), but we do not expect NRDs to drastically change over this short time. Using a static measure of NRDs could introduce bias through the uncertain geographic context problem.[46]

We did not measure all the potential mechanisms of the association between NRD and BMI. While the preponderance of literature strongly suggests that walking to destinations is important in high-density contexts, our knowledge of PA in lower-density areas is far less complete. We did not include all potential effect modifiers that could support or impede walking such as the availability of sidewalks, street connectivity,[47] residential density,[48] access to public transit,[11] and traffic speed, although we did control for car ownership at the census tract level. We treated all nonresidential destinations as equally important, but it is likely that some types of establishments (fast food restaurants, for example) have a different relationship with BMI than others (such as recreational facilities). Finally, we had a lack of data on many potential individual level confounders, but the broad distribution of subjects allowed adjustment for many measures of social and economic deprivation at the neighborhood (census tract) level.

This study is unique in the size of the datasets used. Prior studies on the built environment and obesity at the individual level had relatively small sample sizes[49], while larger studies relied on BMI aggregated across relatively large areas such as zip codes, census tracts, or counties[50] and may suffer from the ecologic fallacy.[51] In contrast, this study used large data sets with individual-level street address, BMI, and NRDs measures. There has also been a lack of consistency on the spatial scale used to measure the built environment making comparing between studies difficult[52]. Our study used four common spatial scales to enhance comparability.

In this analysis of over 17 million US residents, BMI peaked in the mid-density range of NRDs with lower values in both the lower and higher ranges. We pose a question for future studies to consider: Do other relationships between the built environment and health vary across levels of density?

References

1. Hales CM, Carroll MD, Fryar CD, CL. O. Prevalence of obesity and severe obesity among adults: United States, 2017–2018. NCHS Data Brief, no 360. *Hyattsville, MD: National Center for Health Statistics* 2020.
2. Baker JL, Olsen LW, Sorensen TI. Childhood body-mass index and the risk of coronary heart disease in adulthood. *The New England journal of medicine.* 2007;357(23):2329-2337.
3. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk for end-stage renal disease. *Ann Intern Med.* 2006;144(1):21-28.
4. Murakami Y, Huxley RR, Lam TH, et al. Diabetes, body mass index and the excess risk of coronary heart disease, ischemic and hemorrhagic stroke in the Asia Pacific Cohort Studies Collaboration. *Prev Med.* 2012;54(1):38-41.
5. Cervero R, Kockelman K. Travel demand and the 3Ds: density, diversity, and design. *Transp Res Part D.* 1997;78:48-58.
6. Glazier RH, Creatore MI, Weyman JT, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. *PLoS One.* 2014;9(1):e85295.
7. Brown BB, Yamada I, Smith KR, Zick CD, Kowaleski-Jones L, Fan JX. Mixed land use and walkability: Variations in land use measures and relationships with BMI, overweight, and obesity. *Health Place.* 2009;15(4):1130-1141.
8. Jia P, Pan X, Liu F, et al. Land use mix in the neighbourhood and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13098.
9. Rundle AG, Heymsfield SB. Can Walkable Urban Design Play a Role in Reducing the Incidence of Obesity-Related Conditions? *JAMA.* 2016;315(20):2175-2177.
10. Wei J, Wu Y, Zheng J, Nie P, Jia P, Wang Y. Neighborhood sidewalk access and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13057.
11. Xu F, Jin L, Qin Z, et al. Access to public transport and childhood obesity: A systematic review. *Obes Rev*. 2021;22 Suppl 1:e12987.
12. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. *BMJ Open.* 2016;6(2):e008878.
13. Sugiyama T, Neuhaus M, Cole R, Giles-Corti B, Owen N. Destination and route attributes associated with adults' walking: a review. *Med Sci Sports Exerc.* 2012;44(7):1275-1286.
14. Gunn LD, Mavoa S, Boulange C, Hooper P, Kavanagh A, Giles-Corti B. Designing healthy communities: creating evidence on metrics for built environment features associated with walkable neighbourhood activity centres. *Int J Behav Nutr Phys Act*. 2017;14(1):164.
15. McCormack GR, Giles-Corti B, Bulsara M. The relationship between destination proximity, destination mix and physical activity behaviors. *Prev Med.* 2008;46(1):33-40.

16. Day K. Built environmental correlates of physical activity in China: A review. *Prev Med Rep.* 2016;3:303-316.
17. Grasser G, Van Dyck D, Titze S, Stronegger W. Objectively measured walkability and active transport and weight-related outcomes in adults: a systematic review. *Int J Public Health.* 2013;58(4):615-625.
18. Creatore MI, Glazier RH, Moineddin R, et al. Association of Neighborhood Walkability With Change in Overweight, Obesity, and Diabetes. *JAMA.* 2016;315(20):2211-2220.
19. Smith KR, Brown BB, Yamada I, Kowaleski-Jones L, Zick CD, Fan JX. Walkability and body mass index density, design, and new diversity measures. *Am J Prev Med.* 2008;35(3):237-244.
20. Troped PJ, Starnes HA, Puett RC, et al. Relationships between the built environment and walking and weight status among older women in three U.S. States. *J Aging Phys Act.* 2014;22(1):114-125.
21. Inagami S, Cohen DA, Brown AF, Asch SM. Body mass index, neighborhood fast food and restaurant concentration, and car ownership. *J Urban Health.* 2009;86(5):683-695.
22. Thielman J, Copes R, Rosella LC, Chiu M, Manson H. Is neighbourhood walkability related to body mass index among different age groups? A cross-sectional study of Canadian urban areas. *BMJ Open.* 2019;9(11):e032475.
23. Frank LD, Andresen MA, Schmid TL. Obesity relationships with community design, physical activity, and time spent in cars. *Am J Prev Med.* 2004;27(2):87-96.
24. Boehmer TK, Lovegreen SL, Haire-Joshu D, Brownson RC. What constitutes an obesogenic environment in rural communities? *Am J Health Promot.* 2006;20(6):411-421.
25. Rutt CD, Coleman KJ. Examining the relationships among built environment, physical activity, and body mass index in El Paso, TX. *Prev Med.* 2005;40(6):831-841.
26. Zhang X, Zhang M, Zhao Z, et al. Obesogenic environmental factors of adult obesity in China: a nationally representative cross-sectional study. *Environmental Research Letters.* 2020;15(4):044009.
27. Troy AR, Bonnell LN, Littenberg B. Relationship Between the Built Environment and Body Mass Index in a Rural Context: A Cross-Sectional Study from Vermont. *Cureus.* 2018;10(7):e3040.
28. Littenberg B, Lubetkin D. Availability, Strengths and Limitations of US State Driver's License Data for Obesity Research. *Cureus.* 2016;8(3):e518.
29. Buehler R, Pucher J, Merom D, Bauman A. Active travel in Germany and the U.S. Contributions of daily walking and cycling to physical activity. *Am J Prev Med.* 2011;41(3):241-250.
30. Pucher J, Buehler R, Merom D, Bauman A. Walking and cycling in the United States, 2001-2009: evidence from the National Household Travel Surveys. *Am J Public Health.* 2011;101 Suppl 1:S310-317.

31. Royston P. Lowess Smoothing. *Stata Tech Bull Reprints.* 1991;1:41-44.
32. Butler DC, Petterson S, Phillips RL, Bazemore AW. Measures of social deprivation that predict health care access and need within a rational area of primary care service delivery. *Health Serv Res.* 2013;48(2 Pt 1):539-559.
33. Jia P, Yu C, Remais JV, et al. Spatial Lifecourse Epidemiology Reporting Standards (ISLE-ReSt) statement. *Health Place.* 2020;61:102243.
34. Fryar CD, Kruszon-Moran D, Gu Q, Ogden CL. Mean Body Weight, Height, Waist Circumference, and Body Mass Index Among Adults: United States, 1999-2000 Through 2015-2016. *Natl Health Stat Report.* 2018(122):1-16.
35. Nelson MC, Gordon-Larsen P, Song Y, Popkin BM. Built and social environments associations with adolescent overweight and activity. *Am J Prev Med.* 2006;31(2):109-117.
36. Bassett DR, Schneider PL, Huntington GE. Physical activity in an Old Order Amish community. *Med Sci Sports Exerc.* 2004;36(1):79-85.
37. Bassett DR, Jr., Tremblay MS, Esliger DW, Copeland JL, Barnes JD, Huntington GE. Physical activity and body mass index of children in an old order Amish community. *Med Sci Sports Exerc.* 2007;39(3):410-415.
38. Matz CJ, Stieb DM, Davis K, et al. Effects of age, season, gender and urban-rural status on time-activity: CanadianHuman Activity Pattern Survey 2 (CHAPS 2). *Int J Environ Res Public Health.* 2014;11(2):2108-2124.
39. Littenberg B, Bonnell LN, LeBruin AS, Lubetkin DA, Troy AR, Zia A. The Relationship Between Access to Natural Environmental Amenities and Obesity. *Cureus.* 2015;7(11):e377.
40. Witten K, Hiscock R, Pearce J, Blakely T. Neighbourhood access to open spaces and the physical activity of residents: a national study. *Prev Med.* 2008;47(3):299-303.
41. Stewart AW, Jackson RT, Ford MA, Beaglehole R. Underestimation of relative weight by use of self-reported height and weight. *Am J Epidemiol.* 1987;125(1):122-126.
42. Le A, Judd SE, Allison DB, et al. The geographic distribution of obesity in the US and the potential regional differences in misreporting of obesity. *Obesity (Silver Spring).* 2014;22(1):300-306.
43. Boone-Heinonen J, Guilkey DK, Evenson KR, Gordon-Larsen P. Residential self-selection bias in the estimation of built environment effects on physical activity between adolescence and young adulthood. *Int J Behav Nutr Phys Act.* 2010;7:70.
44. Jones KK, Zenk SN, Tarlov E, Powell LM, Matthews SA, Horoi I. A step-by-step approach to improve data quality when using commercial business lists to characterize retail food environments. *BMC Res Notes.* 2017;10(1):35.
45. Fleischhacker SE, Evenson KR, Sharkey J, Pitts SB, Rodriguez DA. Validity of secondary retail food outlet data: a systematic review. *Am J Prev Med.* 2013;45(4):462-473.

46. Kwan M-P. The Uncertain Geographic Context Problem. *Annals of the Association of American Geographers*. 2012;102(5):958-968.
47. Jia P, Zou Y, Wu Z, et al. Street connectivity, physical activity, and childhood obesity: A systematic review and meta-analysis. *Obes Rev*. 2021;22 Suppl 1:e12943.
48. Zou Y, Ma Y, Wu Z, et al. Neighbourhood residential density and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13037.
49. Boehmer TK, Hoehner CM, Deshpande AD, Brennan Ramirez LK, Brownson RC. Perceived and observed neighborhood indicators of obesity among urban adults. *Int J Obes (Lond)*. 2007;31(6):968-977.
50. Xu Y, Wang F. Built environment and obesity by urbanicity in the U.S. *Health Place*. 2015;34:19-29.
51. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. *Progress in Physical Geography: Earth and Environment*. 2007;31(5):471-479.
52. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. *Health Place*. 2010;16(2):175-190.

CHAPTER 2: EXPLORING NONLINEAR RELATIONSHIPS BETWEEN NEIGHBORHOOD WALKABILITY AND HEALTH: A CROSS SECTIONAL STUDY AMONG US PRIMARY CARE PATIENTS WITH CHRONIC CONDITIONS

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2.1. Abstract

Background

A recent study of licensed drivers found a nonlinear relationship between density of nonresidential destinations (NRDs), a proxy for walkability, and Body Mass Index (BMI) across a wide range of development patterns. It is unclear if this relationship can be replicated in a population with multiple chronic conditions, or translated to health outcomes other than BMI.

Methods

We obtained health data and home addresses for 2,405 adults with multiple chronic conditions from 44 primary care clinics across 13 states using the Integrating Behavioral health and Primary Care Trial. In this cross-sectional study, the relationships between density of NRDs (from a commercial database) within 1 km of the home address and self-reported BMI, and mental and physical health indices were assessed using several nonlinear methods, including restricted cubic splines, LOWESS smoothing curves, nonparametric regression with a spline basis, and piecewise linear regression.

Results

All methods demonstrated similar nonlinear relationships. Piecewise linear regression was selected for ease of interpretation. BMI was positively related to NRDs below the inflection point of 15 establishments·ha^{-1} (β=+0.09 kg·m^{-2}/nonresidential buildings ha^{-1}; 95% CI: +0.01, +0.14), and negatively associated above the inflection point (β=-0.02;-0.06, +0.02). Mental health decreased with NRD density below the inflection point (β=-0.24;-0.31,-

0.17), and increased above it (β=+0.03; -0.00, +0.07). Results were similar for physical health (β=-0.28;-0.35,-0.20) and (β=+0.06; +0.01, +0.10).

Conclusion

Health indicators were the lowest in middle density (typically suburban) areas and got progressively better moving in either direction from the peak. NRDs may affect health differently depending on home-address NRD density.

2.2 Introduction

Chronic medical conditions such as heart and lung disease, diabetes, musculoskeletal conditions, and obesity are among the most common causes of morbidity, mortality, and healthcare costs in the United States (US). These medical conditions often coincide with mental and behavioral health conditions such as anxiety, depression, chronic pain and substance abuse, increasing the likelihood of poor health outcomes.[1] The US Centers for Disease Control and Prevention (CDC) recommend regular aerobic exercise such as walking for individuals with chronic conditions and disabilities to increase daily living activities, promote independence, prevent the worsening of disease, decrease anxiety, depression, and pain, and increase longevity.[2] Given that only 1 in 4 older adults meet the minimum aerobic activity levels and even fewer meet the full physical activity guidelines,[3] it is essential to find population-level approaches to increase physical activity. One solution backed by the US surgeon general's Step It Up initiative[4] is the promotion of neighborhood walkability to increase physical activity.

A walkable environment is characterized by diverse land uses in proximity, connected and pedestrian-friendly street network design, short distances to transit, and destination accessibility.[5-10] These characteristics reduce obesity[11] and enhance mental[12-14] and physical health[15] by promoting walking and other forms of active transport.[16,17] For this study we focused on destination accessibility, measured as the density of nonresidential destinations (NRDs) surrounding the participant's home residence. Living within a walkable distance to retail businesses, employers, public offices, restaurants, schools, commuter rail and bus stops, and places of worship can promote active transport and reduce automobile use.

Four systematic reviews examining nearly 200 studies of older adults found that access to NRDs was positively associated with total physical activity participation, overall walking[16,18,19], and walking for transportation[17]. Residing in areas with a high density of NRDs can also improve health. Two longitudinal studies found that accessibility to NRDs was associated with lower rates of obesity in the US[20] and Canada.[6] A fifth review of 23 articles about the built environment and physical function found some evidence that NRDs can improve physical function but concluded that more research was necessary.[15] Less is known about this relationship between NRDs and mental health. Living in walkable areas may have benefits for individuals with chronic conditions, but the literature is sparse. Adults living in high-walkability areas had lower 10-year incidences of diabetes[21] and cardiovascular disease[22] than those in low-walkability areas, although not glycemic control.[23]

While the literature suggests an inverse relationship between NRDs and body mass index (BMI) and a positive relationship between NRDs and physical function in high-density settings, there are few studies that include lower density settings. Data from the rural US found that a perceived lack of NRDs was associated with obesity.[24] Studies from China[25] and Texas[26] that spanned a wide range of development found positive relationships between NRDs and BMI. In Vermont – a low-density area – a positive correlation between

NRD density and BMI was found using two independent datasets, suggesting that this relationship may vary nonlinearly across the density spectrum.[27]

More recent literature has confirmed a nonlinear relationship between NRDs and obesity. Using nearly 17 million driver's license records from six US states, Bonnell *et al.* found a positive relationship between NRDs and self-reported BMI below 15 destinations·ha^{-1}, at which point the relationship became negative, creating an inverted-U shaped curve.[28] Lower density areas were characterized by farmlands and farming communities typical of the rural Midwest, while higher density areas were often cities with multi-family buildings and ground floor destinations, such as downtown Chicago or The Bronx, New York. The middle density areas where the inflection point occurred largely corresponded to suburban areas characterized by automobile-oriented development, or near town centers of small rural towns.

There are two goals of the current study: 1) to confirm the nonlinear relationship between NRD densities and self-reported BMI across a wide range of development in a national sample of primary care patients with chronic conditions and 2) to assess if the nonlinear relationship applies to other health outcomes, including indices of mental and physical health. We hypothesized that BMI would increase as NRDs increased in the range from low to mid densities (typical of suburban areas), but decrease in the range from mid to high densities, forming an inverted-U curve. Conversely, we expected mental and physical health would decrease as NRDs increased in the range from low to mid densities but increase in the range from mid to high densities, forming a U-shaped curve.

2.3 Methods

2.3.1 Data and Setting

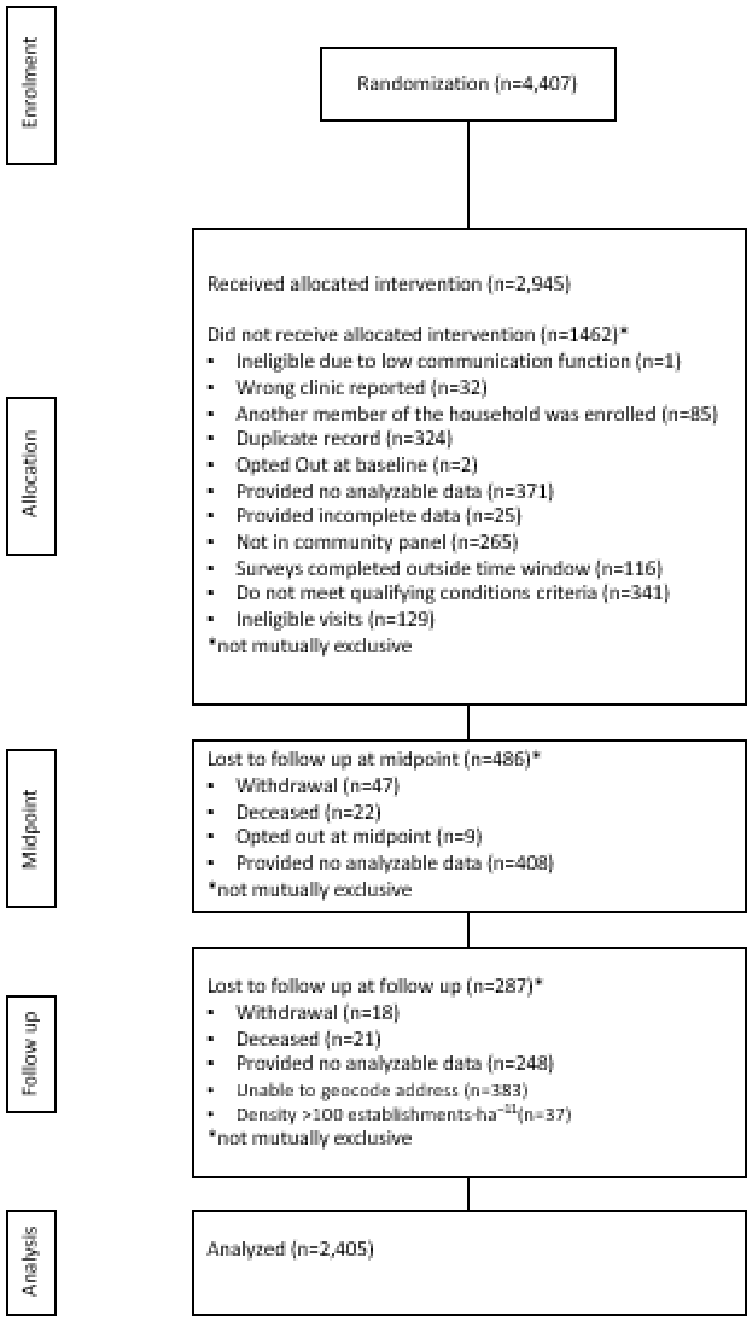
The characterization of NRDs as a proxy for walkability is described elsewhere.[28] Briefly, 13 million potential destinations were geocoded using a 2018 database of commercial establishments (Dun & Bradstreet Corp., Milburn, New Jersey). We filtered the dataset for facility types likely to serve as destinations for active transport based on their North American Industry Classification (NAICS) codes. Retail establishments, personal service providers, restaurants, community centers, schools, places of worship, post offices and other government facilities, and commercial recreation and entertainment facilities were included (n=3,749,984). We excluded establishments likely to discourage or at least not initiate walking such as agriculture, forestry, mining, quarrying, utilities, construction, manufacturing, and wholesale trade.

A second data set contained survey results from the *Integrating Behavioral Health and Primary Care*, a multi-center, prospective randomized study of a practice-level intervention among chronically ill primary care patients from 2016-2021, described in detail elsewhere.[29] Briefly, we obtained health data and home addresses on 3,797 adults with multiple chronic conditions from 44 primary care clinics across 13 US states including Alaska, Hawaii, California, Oregon, Washington, Idaho, Texas, Georgia, Kentucky, Ohio, New York, Massachusetts, and Vermont (see Figure 2 - 1).

Figure 2 - 1: Map of practice locations from the Integrating Behavioral Health and Primary Care trial

All patients had multiple chronic conditions (arthritis, obstructive lung disease, chronic bronchitis or asthma, non-gestational diabetes, heart failure or hypertension, anxiety or depression, chronic pain (including headache, migraine, neuralgia, fibromyalgia, or chronic musculoskeletal pain), insomnia, irritable bowel syndrome, substance use disorder, tobacco use, or problem drinking) as determined by review of electronic health record visit data, problem lists, medication lists and laboratory results. Data were collected at three timepoints, baseline, midpoint, and follow-up, but for this study, we only used the cross-section of data from the follow-up timepoint. Follow-up was used because BMI was not available at baseline data collection. Patients were excluded if they had fewer than 2 chronic conditions, missing PROMIS-29 data at follow up timepoint, missing address information, or density of nonresidential destinations >100 establishments $\cdot ha^{-1}$ (see Figure 2 - 2). Our final analytic dataset contained complete information on 2,405 adult primary care patients with multiple chronic conditions. After exclusions, there were no missing data. Those with complete data and no address information available tended to be more rural than those with addresses that were geocoded. However, the distribution of demographic variables were statistically similar (age, sex, race, education, marital status, and employment status).

Figure 2 - 2: Consort diagram



The predictor for this analysis was the absolute concentration of NRDs, which was taken as a proxy for destination accessibility or opportunities for active transport and walkability. It was calculated by the ArcGIS Point Density function as the number of establishments·ha^{-1} within 1 km of the home address of participants. Each address was assigned the density value of its coinciding 30 m pixel from the point density raster output surface. Each pixel in this surface can be interpreted as giving the density value for an area around it with a Euclidean buffer radius of 1 km. The 1 km spatial scale was chosen based on prior literature that suggests the mean walking trip in the US is 0.98 km, about a 15-minute walk.[30,31] NRDs were spatially joined to the survey results based on the home address of the respondent. Density of NRDs ranged from 0-400 establishments ·ha^{-1} however, we excluded records with NRD density >100 establishments ·ha^{-1} because they were statistical outliers and not representative of the majority of places people reside. The statistical techniques used in this study become unstable and tend to over-fit the data with very small sample sizes. Only 1% of data (n=37 records) had densities between 100 and 400 establishments ·ha^{-1} and the resulting findings were unreliable. These participants were statistically similar to the main study participants in terms of age, sex, race, education, marital status, and employment status. In the current study, 0 to 100 establishments·ha^{-1} represents a wide and representative spectrum of development, ranging from rural south-central Idaho (low density), to the suburbs of Worcester, MA (middle density), to Bronx, NY (high density).

The outcome variables were BMI, calculated from self-reported height and weight, physical health as measured by the Patient-Reported Outcomes Measurement Information System® (PROMIS-29) physical health summary score, and mental health as measured by the PROMIS-29 mental health summary score. The PROMIS-29 is a self-reported questionnaire that assesses eight domains of health including pain interference, pain intensity, physical function, depression, anxiety, fatigue, sleep disturbance, and social participation. Physical and mental health summary scores are calculated from these eight domains. Scores range from zero to 100 and are standardized to the US population, where 50 is the mean with a standard deviation of 10. Higher scores indicate better functional health.

Potential covariates were considered for inclusion in the multivariable analysis based on prior knowledge. This process was strictly exploratory and used for the purposes of hypothesis generation. Participant-level demographic covariates included age, sex, race, ethnicity, marital status, annual household income, education, and number of chronic conditions. Neighborhood rurality and social deprivation were measured at the census-tract level by The Social Deprivation Index[32] (SDI) and rural urban commuting area (RUCA) codes.[33] The SDI is a composite measure of deprivation based on income, education, employment, housing, single-parent household, and access to transportation.

2.3.2 Geocoding

Point locations (latitude and longitude) were assigned for each participant's home address using the ArcGIS address geocoder (ESRI Inc., Redlands, CA) with the WGS 1984 coordinate system. Addresses that had less than 100% match to a point location were checked for errors and manually geocoded. 2,405 (86%) were matched to a street address.

The others addresses consisted of P.O. Boxes and rural routes that could only be matched to a zip code centroid. These were excluded because NRDs are a granular measure at the street address level. Demographics (age, sex, race, ethnicity, marital status, income, education) and outcomes (BMI, mental and physical health) did not vary systematically by geocoding status. Records that were correctly geocoded were more likely to be urban and have higher NRDs, consistent with previous literature.[34]

2.3.3 Statistical Analysis

To allow for the possibility of a nonlinear relationship, we used piecewise linear regression to assess BMI and mental and physical health as a function of NRDs. Next, we used restricted cubic splines, LOWESS smoothing curves,[35] and nonparametric regression with a spline basis to confirm a similar data fit and make sure the results were not spurious due to the statistical method chosen. After confirmation of similar results with the more complex models using visual assessment and Bayesian Information Criteria (when possible), we proceeded with the piecewise linear regression only, due to the ease of interpretation of the coefficients. We included covariates in the multivariable model that changed the association between the predictor and outcome by >10%. The main analysis consisted of three separate adjusted models estimating BMI, mental health, and physical health as a function of NRDs with 95% confidence intervals (CI). Spatial autocorrelation of the error term was assessed using Lagrange Multiplier Tests.[36] The Lagrange multiplier test for spatial autocorrelation was significant in the models, suggesting spatial autocorrelation was present and spatial error regression may be warranted. All tests were two-tailed and the threshold for statistical significance was $P<0.05$. Stata 16.1 (StataCorp LP, College Station, Texas) was used for data management and statistical analysis. GeoDa was used to assess spatial error regression.[37] We used the Spatial Lifecourse Epidemiology Reporting Standards guidelines.[38]

2.4 Results

This study included 2,405 participants. The majority were older and female, non-Hispanic, white, married, retired, and had low incomes (See table 1). The mean BMI was 31.9 kg/m^2, which is much higher than the US national average (26.5 kg/m^2 men, 26.6 kg/m^2 women)[39], likely because we selected for individuals with multiple chronic conditions that are often related to obesity. Likewise, the average physical health summary score was worse (45.5) than the national average (50). However, the average mental health summary score was slightly higher (51.1) than the national average (50).

Table 2 - 1: Participant characteristics

	n (%) or mean ±SD
N	2,405
Age, years	63.8 ±12.9
Sex	
Female	1,544 (64%)
Male	855 (36%)
Other/Prefer not to say	6 (0%)
Race	
White	1,843 (77%)
Black or African American	298 (12%)
Asian	75 (3%)
Native Hawaiian/Other Pacific Islander	25 (1%)
American Indian or Alaskan Native	19 (1%)
Other/Prefer not to say	141 (6%)
Ethnicity	
Hispanic	167 (7%)

Non-Hispanic	2,197 (92%)
Prefer not to say	23 (1%)
Marital Status	
Never married	387 (16 %)
Married	1,069 (45%)
Living as married	62 (3%)
Separated	52 (2%)
Divorced	514 (21%)
Widowed	306 (13%)
Employment	
Full-time	409 (17%)
Part-time	172 (7%)
Retired	1,043 (44%)
Disabled	593 (25%)
Homemaker	87 (4%)
Student	10 (0%)
Unemployed/Looking	80 (3 %)
Other/Prefer not to say	3 (0%)
Annual household income	
<$15,000	652 (27%)
$15,000-$29,999	492 (21%)
$30,000-$44,999	302 (13%)
$45,0000-$59,999	229 (10%)
$60,000-$74,999	189 (8%)
$75,000-$99,999	189 (8%)
>$100,000	305 (13%)
Mean number of chronic conditions	4.1 ±1.8
Arthritis	1,115 (40%)
Asthma	587 (21%)
Chronic Obstructive Pulmonary Disease	359 (13%)
Chronic pain	2,204 (79%)
Non-Gestational Diabetes	1,248 (44%)
Heart failure	222 (8%)
Hypertension	2,265 (81%)
Irritable bowel syndrome	117 (4%)
Anxiety	880 (31%)
Depression	1,224 (44%)
Insomnia	610 (22%)
Substance use disorder	592 (21%)
Neighborhood characteristics (home census tract)	
Social Deprivation Index (higher indicates more deprivation)	52.6 ±28.4

Rural	378 (16%)
Population density, persons per square mile	3,917 ±5998
Primary Predictor	
Nonresidential destinations	10.8 ±14.4
Primary Outcomes – PROMIS-29 t-scores	
PROMIS-29 Physical Health Summary t-score*	45.5 ±9.7
PROMIS-29 Mental Health Summary t-score*	51.1 ±8.8
BMI kg/m^2	31.9 ±8.7

*Higher score is better

Because similar functional forms were found for all nonlinear methods, the piecewise linear method was used for ease of interpretation. Ordinary piecewise linear models and piecewise linear models using spatial error regression were performed. Because the results were statistically similar, we opted to report only the ordinary linear regression results.

We defined the low-to-mid density range from zero to 15 establishments$\cdot$ha^{-1} and the mid-to-high density range from 15-100 establishments$\cdot$ha^{-1}. We found an inverted U-shaped relationship between NRDs and BMI (see Figure 2 - 3). On average, BMI increased as NRD density increased from low-density (BMI=~31kg/m^2 at 1 establishments$\cdot$ha^{-1}) to mid-density (BMI=~33 at 15 establishments$\cdot$ha^{-1}) and then decreased from mid-density to high-densities (BMI=~30 at 80 establishments$\cdot$ha^{-1}). Using piecewise linear regression, BMI was positively associated with NRD density below 15 establishments$\cdot$ha^{-1} (β=+0.09 kg$\cdot$m^{-2}/nonresidential buildings ha^{-1}; 95% CI: +0.01, +0.14), and was negatively associated with NRD above 15 establishments$\cdot$ha^{-1} (β=-0.02; -0.06, +0.02). Conversely, we found *U-shaped* relationships between NRDs and physical and mental health. Mental and physical health was negatively associated with NRD density below 15 establishments$\cdot$ha^{-1} (β=-0.24;

-0.31, -0.17) (β=-0.28; -0.35, -0.20), and was positively associated with NRDs above 15 establishments·ha^{-1} (β=+0.03; -0.00, +0.07) (β=+0.06; +0.01, +0.10), respectively. The slopes before and after the inflection point were statistically different (P<0.001) in each model (see Figure 2 - 3 & Table 2 - 2).

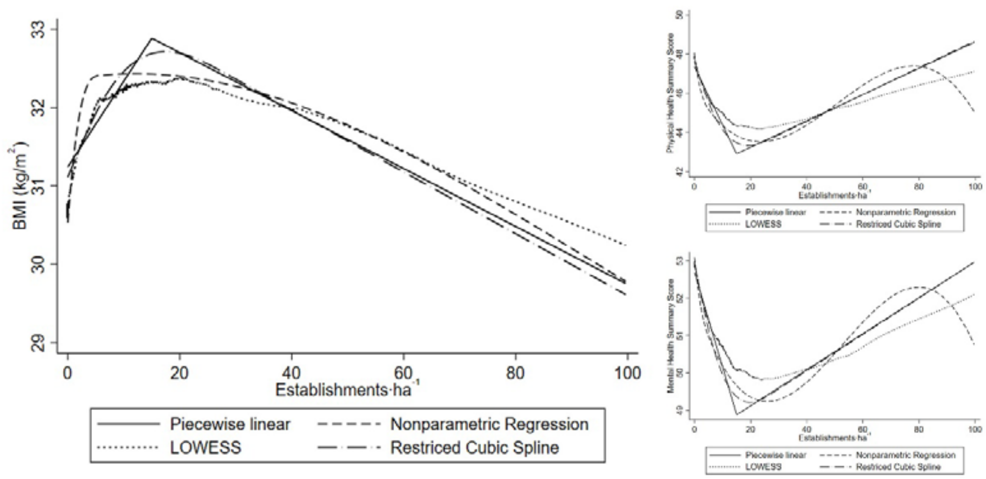
Several variables attenuated the nonlinear relationship between NRDs and health outcomes. For the BMI model, age, income, and neighborhood SDI changed the low-to-mid density or the mid-to-high density coefficient more than 10%. Likewise, mental health was attenuated by age, income, marital status, and neighborhood SDI. Finally, the physical health model was attenuated by income, marital status, and neighborhood SDI (Table 2 - 2).

Table 2 - 2: Mental and physical health and BMI as a function of NRDs (N=2405)

Radius	Low-density Stratum (0-15 establishments·ha^{-1}) β Coefficient (CI)	High-density Stratum (15-100 establishments·ha^{-1}) β Coefficient (CI)	Difference in Slopes P
	Unadjusted		
BMI	+0.09 (+0.01,+0.14)	-0.02 (-0.06,+0.02)	<0.001
Mental Health	-0.24 (-0.31,-0.17)	+0.03 (-0.00,+0.07)	<0.001
Physical Health	-0.28 (-0.35,-0.20)	+0.06 (+0.01,+0.10)	<0.001
	Adjusted		
*BMI	-0.05 (-0.12,+0.02)	0.00 (-0.04,+0.04)	0.55
†Mental Health	-0.09 (-0.16,-0.02)	+0.01 (-0.03,+0.05)	<0.001
§Physical Health	-0.10 (-0.18,-0.02)	+0.04 (-0.00,+0.08)	<0.001

*Adjusted for age, income, and neighborhood SDI
†Adjusted for age, income, marital status, and neighborhood SDI
§Adjusted for income, marital status, and neighborhood SDI

Figure 2 - 3: **Non-parametric regression with a spline basis, LOWESS smoothing curve, restricted cubic splines and piecewise linear regression used to visualise BMI as a function of NRDs. Non-parametric regression with a spline basis, LOWESS (locally weighted scatterplot smoothing) curve, restricted cubic splines and piecewise linear regression used to visualise mental health summary score as a function of NRDs. Non-parametric regression with a spline basis, LOWESS smoothing curve, restricted cubic splines and piecewise linear regression used to visualise physical health summary score as a function of NRDs. BMI, body mass index; NRDs, non-residential destinations.**



2.5 Discussion

We sought to test the nonlinear relationship between NRDs and health outcomes in a highly vulnerable, older population with chronic conditions. Our results are consistent with those from a prior study[28] where BMI peaked in the mid-density range with lower values on either extreme. Mental and physical health were also worse in mid-density areas with better values found in both lower and higher density areas. The largest associations were seen between NRDs and physical and mental health in low-density areas. An increase of 10 establishments·ha^{-1} was associated with a decrease of about ¼ of a standard deviation of physical health. Although the associations are partially attenuated in multivariable models, especially in high-density areas, there is still a significant negative association between NRDs and mental and physical health in low-density areas after covariates variables are added. Further, the differences between the slopes between low and high-density areas remains significant for mental and physical health, suggesting that the association between NRDs and health varies based on the underlying level of development.

The mechanisms by which NRDs are associated with health are unclear, but are likely similar for obesity, mental health, and physical health. In higher density areas, previous literature suggests that an increase in accessible destinations promotes walking in the form of active transport, which leads to a reduction in obesity, better physical function, and improved mental health. In mid-density areas, corresponding with many suburbs, we expect fewer opportunities for active transport and more reliance on cars, resulting in higher levels of obesity, and worse mental and physical health, as seen in our results. The mechanism behind lower BMI in lower densities areas is less clear. The lowest density levels of NRDs may be a proxy for more physically intensive rural lifestyles through greater access to outdoor recreation, physical employment, or home property management as evidenced in the low prevalence among rural Amish community.[40,41]

There is an expansive yet conflicting literature on the benefits of neighborhood walkability and health benefits for older adults, some of whom may have chronic conditions. However, there is very little information on this relationship among this highly vulnerable population of adults with coexisting medical and behavioral problems. Similar to our results in higher density areas, adults living in more walkable neighborhoods had lower 10-year cardiovascular risk.[22] In contrast, a recent study found no relationship between neighborhood walkability and glycemic markers in people with type 2 diabetes.[23] Another study found no relationship between walkability and mental and physical health among older adults after acute myocardial infarction.[42] However, the two contrasting studies did not consider nonlinear relationships. Therefore, it is possible that the conflicting results in the literature are due to linear models missing a nonlinear effect, something that future research should consider.

Although our population had similar mental health summary scores to the US population as a whole, their physical health summary scores were much lower. Even after accounting for personal and neighborhood characteristics, NRDs were significantly associated with lower physical health scores in low-density areas. Perhaps other improvements in the built environment, such as crime safety[24], are more important in low-density areas than increasing NRDs.

Density is used in this study over alternatives such as the Walk Score® (Walk Score, Seattle, WA) and the National Walkability Index (US EPA, Washington D.C.). This is because, although these alternatives take into account several aspects of the built environment including NRDS and intersections, they suffer from the modifiable areal unit problem because their spatial scales are aggregated from points to census tracts or zip codes.[43] NRD density, as measured here, is precise within 30 meters of the home address, allowing for granular variability in walkability within zip code or census tracts. This spatial scale may be especially helpful to distinguish the nuances of small rural towns that have town centers.

There are several limitations to consider. First, the health outcomes data are self-reported. Individuals tend to underreport weight and over-report height (used to calculate BMI) and this has been shown to vary by geographic location.[44] However, we have no evidence that the misreporting of height and weight varies systematically with respect to density of NRDs. Second, these findings may only generalize to primary care patients in the US with multiple chronic conditions. However, this highly vulnerable population is understudied in the health geography literature. Third, the COVID-19 pandemic occurred during data collection and may have affected participants differently at different times based on their home location and density of NRDs. Fourth, LOWESS smoothing and nonparametric regression are subject to overfitting when sample sizes are small, but we found an acceptable level of concordance between four different methods.[35] Fifth, participants with multiple chronic conditions may have experienced the pandemic differently (more worried about health), and thus may have answered the questionnaire differently than healthier subjects may have.[45]

We confirmed a nonlinear relationship between a measure of neighborhood walkability and BMI in a highly vulnerable population with multiple chronic conditions. Further, this may be the first study to investigate nonlinear relationships between neighborhood walkability and mental and physical health. Other studies should consider nonlinear relationships when studying the built environment and health.

2.6 References

1. Druss B, Walker E. Mental Disorders and medical comorbidity THE SYNTHESIS PROJECT. Access June 18. In:2011.
2. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans. 2nd ed. Washington, DC: U.S. Department of Health and Human Services; 2018.
3. Wingood M, Bonnell L, LaCroix AZ, et al. Community-Dwelling Older Adults and Physical Activity Recommendations: Patterns of Aerobic, Strengthening, and Balance Activities. *J Aging Phys Act*. 2021:1-13.
4. U.S. Department of Health and Human Services. Step It Up! The Surgeon General's Call to Action to Promote Walking and Walkable Communities. Washington, DC: U.S. Dept of Health and Human Services, Office of the Surgeon General. 2015.
5. Ewing R, Cervero R. Travel and the Built Environment: A Synthesis. *Transportation Research Record.* 2001;1780(1):87-114.
6. Creatore MI, Glazier RH, Moineddin R, et al. Association of Neighborhood Walkability With Change in Overweight, Obesity, and Diabetes. *JAMA*. 2016;315(20):2211-2220.
7. Glazier RH, Creatore MI, Weyman JT, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. *PLoS One.* 2014;9(1):e85295.
8. Jia P, Pan X, Liu F, et al. Land use mix in the neighbourhood and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13098.
9. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. *BMJ Open.* 2016;6(2):e008878.
10. Rundle AG, Heymsfield SB. Can Walkable Urban Design Play a Role in Reducing the Incidence of Obesity-Related Conditions? *JAMA*. 2016;315(20):2175-2177.
11. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. *Health Place.* 2010;16(2):175-190.
12. Roe J, Mondschein A, Neale C, Barnes L, Boukhechba M, Lopez S. The Urban Built Environment, Walking and Mental Health Outcomes Among Older Adults: A Pilot Study. *Front Public Health.* 2020;8:575946.
13. Evans GW. The built environment and mental health. *J Urban Health.* 2003;80(4):536-555.
14. Berke EM, Gottlieb LM, Moudon AV, Larson EB. Protective association between neighborhood walkability and depression in older men. *J Am Geriatr Soc.* 2007;55(4):526-533.
15. Rachele JN, Sugiyama T, Davies S, et al. Neighbourhood built environment and physical function among mid-to-older aged adults: A systematic review. *Health Place.* 2019;58:102137.

16. Barnett DW, Barnett A, Nathan A, et al. Built environmental correlates of older adults' total physical activity and walking: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act*. 2017;14(1):103.
17. Cerin E, Nathan A, van Cauwenberg J, et al. The neighbourhood physical environment and active travel in older adults: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act*. 2017;14(1):15.
18. Sugiyama T, Neuhaus M, Cole R, Giles-Corti B, Owen N. Destination and route attributes associated with adults' walking: a review. *Med Sci Sports Exerc*. 2012;44(7):1275-1286.
19. Day K. Built environmental correlates of physical activity in China: A review. *Prev Med Rep*. 2016;3:303-316.
20. Troped PJ, Starnes HA, Puett RC, et al. Relationships between the built environment and walking and weight status among older women in three U.S. States. *J Aging Phys Act*. 2014;22(1):114-125.
21. Booth GL, Creatore MI, Luo J, et al. Neighbourhood walkability and the incidence of diabetes: an inverse probability of treatment weighting analysis. *J Epidemiol Community Health*. 2019;73(4):287-294.
22. Howell NA, Tu JV, Moineddin R, Chu A, Booth GL. Association Between Neighborhood Walkability and Predicted 10-Year Cardiovascular Disease Risk: The CANHEART (Cardiovascular Health in Ambulatory Care Research Team) Cohort. *J Am Heart Assoc*. 2019;8(21):e013146.
23. Braver NRd, Rutters F, Wagtendonk AJ, et al. Neighborhood walkability, physical activity and changes in glycemic markers in people with type 2 diabetes: The Hoorn Diabetes Care System cohort. *Health Place*. 2021;69:102560.
24. Boehmer TK, Lovegreen SL, Haire-Joshu D, Brownson RC. What constitutes an obesogenic environment in rural communities? *Am J Health Promot*. 2006;20(6):411-421.
25. Zhang X, Zhang M, Zhao Z, et al. Obesogenic environmental factors of adult obesity in China: a nationally representative cross-sectional study. *Environmental Research Letters*. 2020;15(4):044009.
26. Rutt CD, Coleman KJ. Examining the relationships among built environment, physical activity, and body mass index in El Paso, TX. *Prev Med*. 2005;40(6):831-841.
27. Troy AR, Bonnell LN, Littenberg B. Relationship Between the Built Environment and Body Mass Index in a Rural Context: A Cross-Sectional Study from Vermont. *Cureus*. 2018;10(7):e3040.
28. Bonnell LN, Troy AR, Littenberg B. Nonlinear relationship between nonresidential destinations and body mass index across a wide range of development. *Prev Med*. 2021;153:106775.
29. Crocker AM, Kessler R, van Eeghen C, et al. Integrating Behavioral Health and Primary Care (IBH-PC) to improve patient-centered outcomes in adults with

multiple chronic medical and behavioral health conditions: study protocol for a pragmatic cluster-randomized control trial. *Trials*. 2021;22(1):200.
30. Buehler R, Pucher J, Merom D, Bauman A. Active travel in Germany and the U.S. Contributions of daily walking and cycling to physical activity. *Am J Prev Med*. 2011;41(3):241-250.
31. Pucher J, Buehler R, Merom D, Bauman A. Walking and cycling in the United States, 2001-2009: evidence from the National Household Travel Surveys. *Am J Public Health*. 2011;101 Suppl 1:S310-317.
32. Butler DC, Petterson S, Phillips RL, Bazemore AW. Measures of social deprivation that predict health care access and need within a rational area of primary care service delivery. *Health Serv Res*. 2013;48(2 Pt 1):539-559.
33. Rural Health Research Center (RHRC). Rural-urban commuting area codes (RUCAs), 2008. Available at: http://depts.washington.edu/uwruca/.
34. Khan S, Pinault L, Tjepkema M, Wilkins R. Positional accuracy of geocoding from residential postal codes versus full street addresses. *Health Rep*. 2018;29(2):3-9.
35. Royston P. Lowess Smoothing. *Stata Tech Bull Reprints*. 1991;1:41-44.
36. Moran P. Notes on continuous stochastic phenomena. *Biometrika*. 1950;37(1-2):17-23.
37. Anselin L, Syabri I, Kho Y. GeoDa: An Introduction to Spatial Data Analysis. In: Fischer MM, Getis A, eds. *Handbook of Applied Spatial Analysis: Software Tools, Methods and Applications*. Berlin, Heidelberg: Springer Berlin Heidelberg; 2010:73-89.
38. Jia P, Yu C, Remais JV, et al. Spatial Lifecourse Epidemiology Reporting Standards (ISLE-ReSt) statement. *Health Place*. 2020;61:102243.
39. Stierman B AJ, Carroll MD, Chen TC, Davy O, Fink S. National Health and Nutrition Examination Survey 2017–March 2020 prepandemic data files—Development of files and prevalence estimates for selected health outcomes. National Health Statistics Reports; no 158. Hyattsville, MD: National Center for Health Statistics. 2021.
40. Bassett DR, Jr., Tremblay MS, Esliger DW, Copeland JL, Barnes JD, Huntington GE. Physical activity and body mass index of children in an old order Amish community. *Med Sci Sports Exerc*. 2007;39(3):410-415.
41. Bassett DR, Schneider PL, Huntington GE. Physical activity in an Old Order Amish community. *Med Sci Sports Exerc*. 2004;36(1):79-85.
42. Roy B, Hajduk AM, Tsang S, et al. The association of neighborhood walkability with health outcomes in older adults after acute myocardial infarction: The SILVER-AMI study. *Prev Med Rep*. 2021;23:101391.
43. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. *Progress in Physical Geography: Earth and Environment*. 2007;31(5):471-479.

44. Le A, Judd SE, Allison DB, et al. The geographic distribution of obesity in the US and the potential regional differences in misreporting of obesity. *Obesity (Silver Spring)*. 2014;22(1):300-306.
45. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430-436.

CHAPTER 3: NONLINEAR RELATIONSHIPS AMONG THE NATURAL ENVIRONMENT, HEALTH, AND SOCIODEMOGRAPHIC CHARACTERISTICS ACROSS US COUNTIES

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3.1. Abstract

Background: To explore the nonlinear relationships between natural amenities and health at the intersection of sociodemographic characteristics among primary care patients with chronic conditions.

Methods: We used survey data from 3,409 adults across 119 US counties. PROMIS-29 mental and physical health summary scores were the primary outcomes. The natural environment (measured by the County USDA Natural Amenities Scale (NAS)) was the primary predictor. Piecewise spline regression models were used to explore the relationships between NAS and health at the intersection of sociodemographic factors.

Results: We identified a nonlinear relationship between NAS and health. Low-income individuals had a negative association to health with each increase in NAS in high amenities areas only. However, white individuals had a stronger association to health with each increase in NAS in low amenities areas.

Conclusions: In areas with low natural amenities, more amenities are associated with better physical and mental health, but only for advantaged populations. Meanwhile, for disadvantaged populations, increasing amenities in high amenity areas are associated with decreases in mental and physical health. Understanding how traditionally advantaged populations utilize the natural environment could provide insight into the mechanisms driving these disparities.

3.2 Introduction

There is a vast literature on the built environment and health.[1] Constructs such as population and housing density,[2] access to healthy food,[3-5] proximity to walkable destinations and transit,[6] and varied land use[7] can bolster active travel and a healthful diet,[8] improving mental and physical health and obesity. The literature on the *natural* environment and health is less developed.

Much like the built environment, the natural environment is a multifaceted construct. Traditionally the natural environment has been interpreted in terms of toxicity, focusing on how air pollution,[9] climate change,[9] natural disasters,[10] and agricultural chemicals[11] negatively impact health, and beneficence, focusing on healthful benefits of exposure to nature, and more recently urban greenspace,[12] and the 'biophilia hypothesis', where humans possess an innate tendency to connect with nature.[13, 14] Fewer studies focus on nonmodifiable domains of the natural environment in which individuals reside, such as topography and climate. One study used weather station data and found that populations that reside in places with better climate had lower Body Mass Index (BMI), seemingly through increased physical activity.[15] Another study found an inverse association between county natural amenities and BMI using several large datasets.[16] Although these factors influencing health are nonmodifiable, if we can identify differences between populations, there may be ways to reduce the inequalities and improve health.

The relationships between the environment and health are complex and therefore may require complex modelling. Only recently have studies started to include models that allow for the possibility of nonlinear relationships. Three recent studies found convincing evidence that aspects of the built environment and walkability are not monotonically related to BMI. Each study found that increasing walkability was associated with increased BMI in areas with lower walkability, but hit an inflection point, where increasing walkability was associated with decreased BMI in areas with higher walkability.[17-19] To our knowledge, no studies have assessed whether the relationship between the natural environment and health is nonlinear.

Many studies in this realm focus on children or the elderly because they are assumed to be more dependent on their local environment, but very few focus on adults with chronic conditions. It is unclear if the natural environment influences health differently for different populations.

We sought to explore the relationship between the natural environment and health at the intersection of various demographic factors and social determinants of health among primary care patients with multiple chronic conditions, allowing for the possibility of a nonlinear relationship. Similar to previous built environment work, we hypothesized that there may be a nonlinear relationship between the natural environment and health and that these relationships may differ by certain patient characteristics. This was an exploratory analysis; we did not have an *a priori* hypothesis of the shape of the nonlinear relationship.

3.3 Methods

3.3.1 Data and Setting

We used pre-COVID, baseline survey results from a multi-center randomized trial of primary care patients, described elsewhere.[20] Data were collected from 3,929 adults with chronic conditions (heart disease, diabetes, lung disease, arthritis, mood disorder, insomnia, substance abuse, chronic pain, or irritable bowel syndrome) from 44 primary care practices across 13 states. Records were included in this sub-study if they provided a home address and had complete data for the primary predictor and outcomes. After exclusions, the final analytic sample had 3,409 records from 119 US counties.

Our primary outcomes were mental and physical health summary scores measured by the PROMIS-29,[21, 22] a validated survey that assesses emotional, physical, and social function, and well-being. The PROMIS-29 produces mental and physical health summary t-scores from 0 (poor health) to 100 (excellent health) that are standardized to the US population with a mean of 50, and a standard deviation of 10.

The primary predictor was the natural environment measured by the USDA Economic Research Service's Natural Amenities Scale (NAS), a county-level composite score derived from winter and summer temperatures, winter sunlight hours, summer humidity, topographical variation, and total water area.[23, 24] This scale ranges from -6.4 (Red Lake, MN) to 11.2 (Ventura, CA) overall, and from -2.4 (Lexington, KY) to 9.8 (San Diego, CA) in this sample. Higher values represent more attractive natural amenities. The top ten scoring counties are in California, while the ten lowest are from Indiana, North

Dakota, and Minnesota. Alaska and Hawaii are not included in the NAS. The NAS is an empirical construction that describes the revealed preferences of US adults and estimates retiree population change. Traditionally in the US, retirees tend to migrate towards places with warmer winters, mild summers, varied topography, and access to water features.

Clinical knowledge and prior literature informed the selection of subgroups, including older age (<65 *vs.* $\geq$65 years), sex (male *vs.* female), race (white *vs.* other), ethnicity (Hispanic *vs.* Non-Hispanic), marital status (currently married *vs.* not), low annual household income (<$30,000 *vs.* ≥$30,000), education (college graduate or more *vs.* associates degree or less), employment status (employed or retired *vs.* not), population density, county size (square miles), and rural-urban status (rural *vs.* urban defined by Rural Urban Commuting Areas (RUCA) codes).[25] Race and ethnicity are considered different constructs in the US to allow for the classification of individuals within any race and simultaneously as Hispanic or non-Hispanic cultural groups.

3.3.2 Geocoding

Each participant's household was geocoded and assigned the corresponding NAS score. Latitude and longitude points were assigned for each participant's home address using the ArcGIS address geocoder (ESRI Inc., Redlands, CA) and the WGS 1984 coordinate system. Addresses that had less than 100% match were manually checked for errors. After removing records without an address and manually geocoding, 100% were matched to a county. Rural routes and P.O. Boxes that could only be matched to a zip code centroid were included as zip code centroids are nested within counties.

3.3.3 Statistical Analysis

Based on previous work,[16,17] we hypothesized that the relationship between the natural environment and health may be nonlinear However, we did not have an *a priori* shape in mind. We used locally-weighted scatterplot smoothing (LOWESS) curves to make first order estimations of best fit.[26] The LOWESS function explores the relationship between two variables by fitting many simple models to various subsets of the data, resulting in a unique, nonlinear visual description of the relationship. The resulting graph identified a clear inflection point near NAS=0 for both mental and physical health, indicating that a piecewise linear regression may be appropriate (see Figure 3 - 1 & Figure 3 - 2). We confirmed nonlinearity by comparing linear regressions and piecewise linear spline regressions with a knot at zero using the Akaike Information Criterion (AIC).[27] Multilevel models with a random intercept at the county-level were assessed. However, the likelihood ratio test suggested the results were similar and therefore the single-level multivariable technique was used. Once confirming the best-fit model, we investigated different subgroups using the same modelling technique. The regression models have added advantages over LOWESS in interpretability and statistical testing. We forced the model to have continuity at the inflection point. After unadjusted models, we performed multivariable analyses controlling for age, sex, race, ethnicity, marital status, income, education, employment status, and rural-urban status. Sub-groups were investigated if the interactions term had a $P<0.20$. For the subgroup models, the moderating term was omitted as a covariate in the model. There were 119 counties represented in this study but the majority (90%) of participants reside in 24 counties. Therefore, we performed a sensitivity analysis using only participants residing in the 24 counties.

All tests were two-tailed and the threshold for statistical significance was set at $\alpha=0.05$. Stata 16.1 (StataCorp LP, College Station, Texas) was used for data management and statistical analysis.

All study procedures were approved by The University of Vermont Committees on Human Research (CHRMS#16-554). Informed consent was provided by all study participants.

Figure 3 - 1: LOWESS curves and piecewise linear splines visualizing the unadjusted relationships among NAS and mental and physical health.

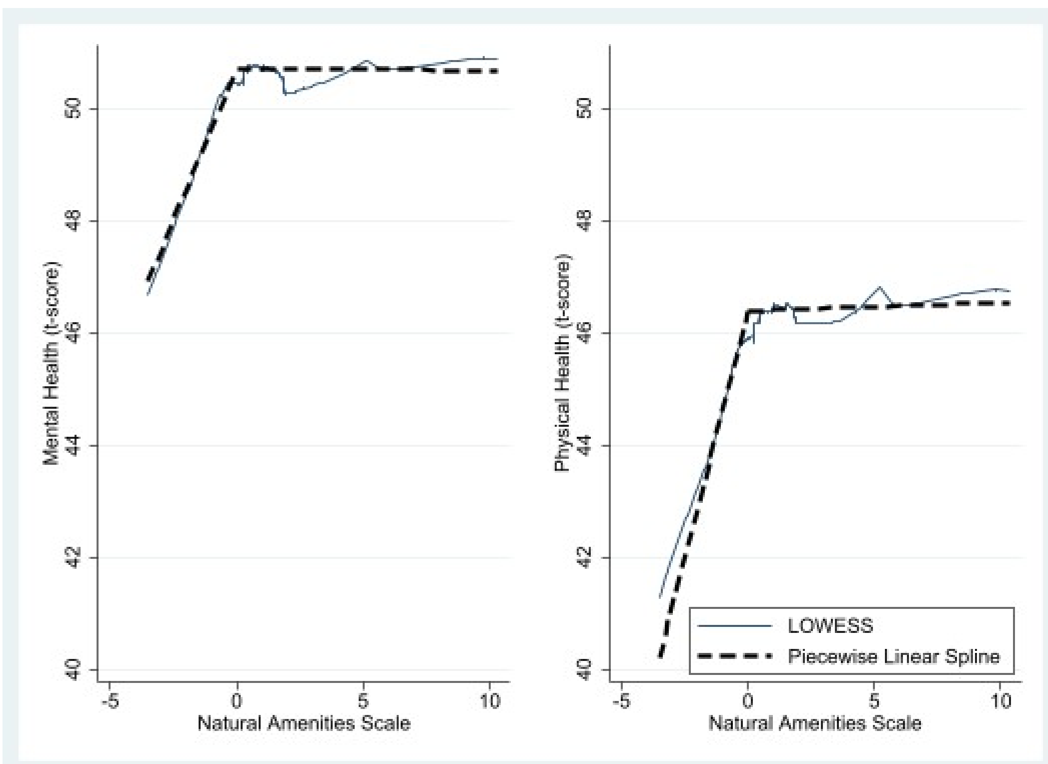
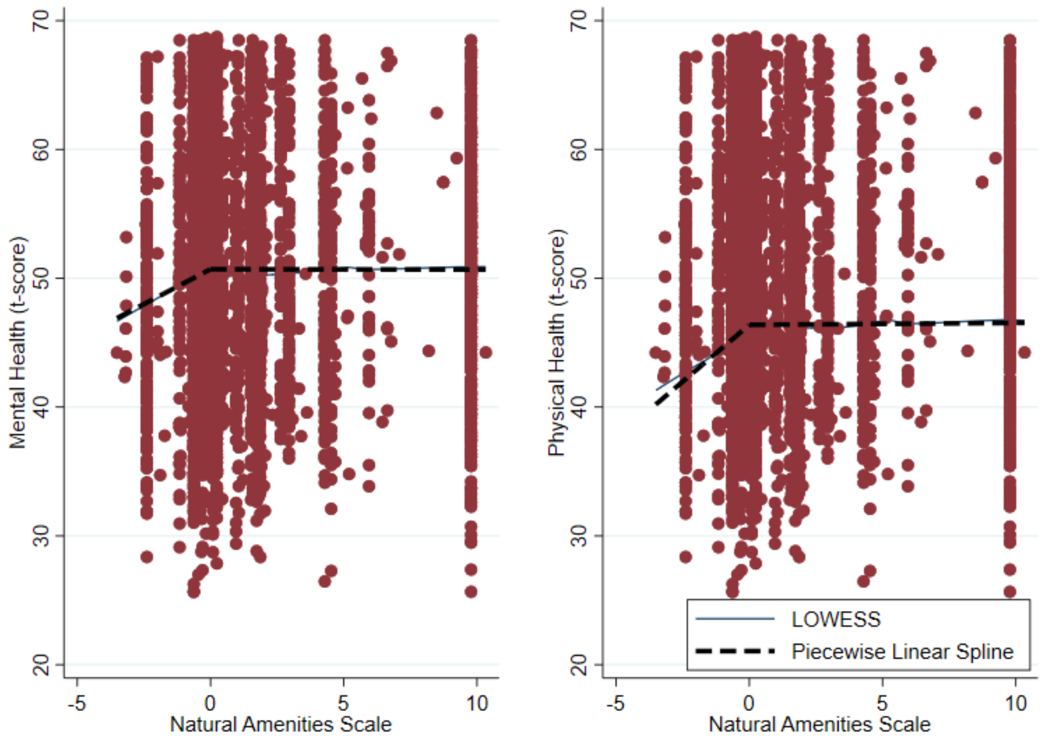


Figure 3 - 2: LOWESS curves, piecewise linear splines, and data points visualizing the unadjusted relationships among NAS and mental and physical health.



3.4 Results

Participants' mean age was 64 years old and 46% were aged <65. The sample was primarily female (63%), non-Hispanic (92%), white (79%), and unemployed or retired (67%). About half were unmarried (51%), low income (50%), and did not graduate college (53%). The mean physical and mental health summary scores were 46 and 50, respectively, where the average US population average is 50. The mean NAS score was 1.8, while 33% lived in low amenity areas (NAS<0). Many participant characteristics differed between low and high amenities. See Table 3 - 1.

Table 3 - 1: Participant characteristics stratified by the natural amenities scale

	Low amenities NAS<0	High amenities NAS ≥0	*P*
N	1,140	2,269	
Mean age ±SD	64 ±12	63 ±14	0.12
Sex, female	734 (65%)	1,398 (62%)	0.11
Race, white	769 (69%)	1,873 (84%)	<0.001
Ethnicity, Hispanic	57 (5%)	204 (9%)	<0.001
Marital status, married	515 (45%)	1,148 (51%)	0.003
Employment, working	372 (33%)	767 (34%)	0.47
Income, <$30k/year	666 (58%)	1,055 (47%)	<0.001
Education, college graduate or more	429 (38%)	1,183 (52%)	<0.001
Mean physical health summary score ±SD	45 ±10	46 ±10	<0.001
Mean mental health summary score ±SD	50 ±9	50 ±9	0.96

AIC values were smaller for the piecewise linear spline models for physical (AIC=25083) and mental (AIC=24558) health than the linear models (AIC=25,110, AIC=24,569, respectively), suggesting the nonlinear models had less prediction error and better fit. Upon visual inspection, the piecewise linear spline model closely approximated the LOWESS curve (see Figure 3 - 1 & Figure 3 - 2). For both mental and physical health, we found a "hockey stick" shaped curve. In areas with lower natural amenities, increasing amenities were associated with better health, but in higher amenities areas, health did not change with additional amenities. Specifically, in low amenities areas (NAS<0), more amenities was associated with better physical (ß=1.76, 95% confidence interval (CI) 1.17, 2.36) and mental (ß=1.08, 95% CI 0.53, 1.63) health. However, in high amenity areas

(NAS≥0), more amenities was not associated with physical (ß= -0.01, 95% CI -0.09, 0.12) or mental (ß= -0.00, 95% CI -0.09, 0.09) health. See Table 3 - 2.

Unadjusted analyses were also performed for sub-groups. Based on the significance of interactions terms, income, race, ethnicity, and rural-urban status sub-groups were investigated for both mental and physical health, marital status was assessed for physical health, and education was assessed for mental health. In high amenity areas only, low-income individuals had a negative association of amenities to mental health with each additional NAS. Further, living in rural high amenities areas was associated with lower mental health while living in urban high amenities areas was associated with lower physical health. In low amenities areas only, non-Hispanic white individuals had a stronger association of amenities to mental and physical health compared to non-white and Hispanic individuals (see **Figure 3 - 3** & Figure 3 - 4). Those living in urban low amenities areas had an improvement in mental health, while those living in rural low amenities areas had an improvement in physical health for each increase in NAS. Further, in low amenities areas only, married individuals had an improvement in physical health and those with higher education had an improvement in mental health, compared to their counterparts (see Table 3 - 2).

Table 3 - 2: Unadjusted piecewise spline regression overall and sub-group models

	Mental Health ß (95% CI)		**Physical health ß (95% CI)**	
	Low amenities (NAS <0) ß (95% CI)	**High amenities (NAS ≥0) ß (95% CI)**	**Low amenities (NAS <0) ß (95% CI)**	**High amenities (NAS ≥0) ß (95% CI)**
	Unadjusted models			
Simple model	***1.08 (0.53, 1.63)**	*-0.00 (-0.09, 0.09)	***1.76 (1.17, 2.36)**	*-0.01 (-0.09, 0.01)
Subgroups				

Low income, y	*0.13 (-0.50, 0.76)	***-0.17 (-0.33, -0.02)**	0.50 (-0.14, 1.12)	-0.14 (-0.29, 0.01)
Low income, n	0.40 (-0.70, 1.51)	-0.00 (-0.11, 0.11)	1.15 (-0.07, 2.41)	-0.02 (-0.15, 0.11)
White race, y	***1.21 (0.51, 1.91)**	*0.02 (-0.08, 0.13)	***2.00 (1.23, 2.77)**	*0.01 (-0.11, 0.14)
White race, n	0.36 (-0.67, 1.39)	-0.02 (-0.23, 0.20)	0.51 (-0.54, 1.56)	0.13 (-0.09, 0.35)
Hispanic, y	1.13 (-1.27, 3.52)	-0.03 (-0.36, 0.30)	1.40 (-1.07, 3.87)	-0.03 (-0.37, 0.31)
Hispanic, n	***1.06 (0.48, 1.68)**	*0.01 (-0.36, 0.30)	***1.75 (1.13, 2.37)**	*0.02 (-0.09, 0.13)
Married, y	--	--	*1.51 (0.40, 2.63)	*0.00 (-0.15, 0.16)
Married, n	--	--	**1.07 (0.26, 1.88)**	0.06 (-0.10, 0.21)
Graduated college, y	***1.63 (0.61, 2.65)**	*-0.05 (-0.17, 0.06)	**--**	--
Graduated college, n	0.56 (-0.11, 1.23)	-0.16 (-0.33, 0.01)	**--**	--
Rural residence, y	1.59 (-0.22, 3.40)	**-0.83 (-1.51, -0.16)**	**1.97 (1.34, 2.61)**	0.06 (-0.04, 0.17)
Rural residence, n	**1.09 (0.51, 1.67)**	0.03 (-0.07, 0.13)	1.53 (-0.39, 3.45)	**-1.73 (-2.45, -1.02)**

Each coefficient present is the linear slope of health as a function of NAS across a range of amenities. For instance, mental health was positively associated with NAS in low amenities areas with a slope of 1.08 but in not in high amenities areas where the slope was 0.00. Slopes that significantly differ from zero are shown in **bold** type. *Significant difference (*P*<0.05) in slopes between low and high-amenity areas.

Figure 3 - 3: Unadjusted piecewise linear spline models visualizing the relationships between NAS and mental and physical health for white (gray lines) and non-white (black lines) individuals.

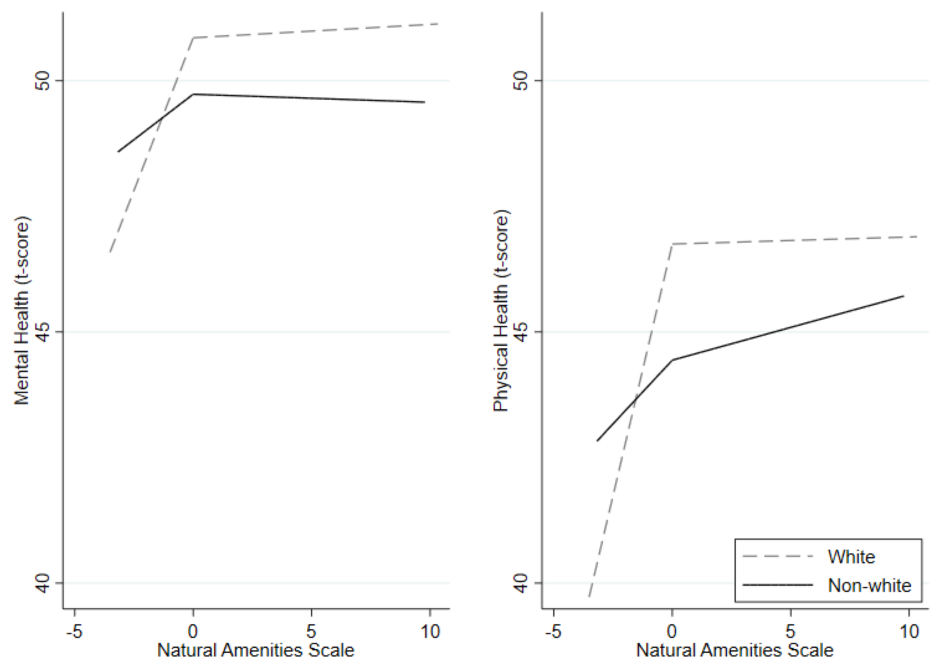
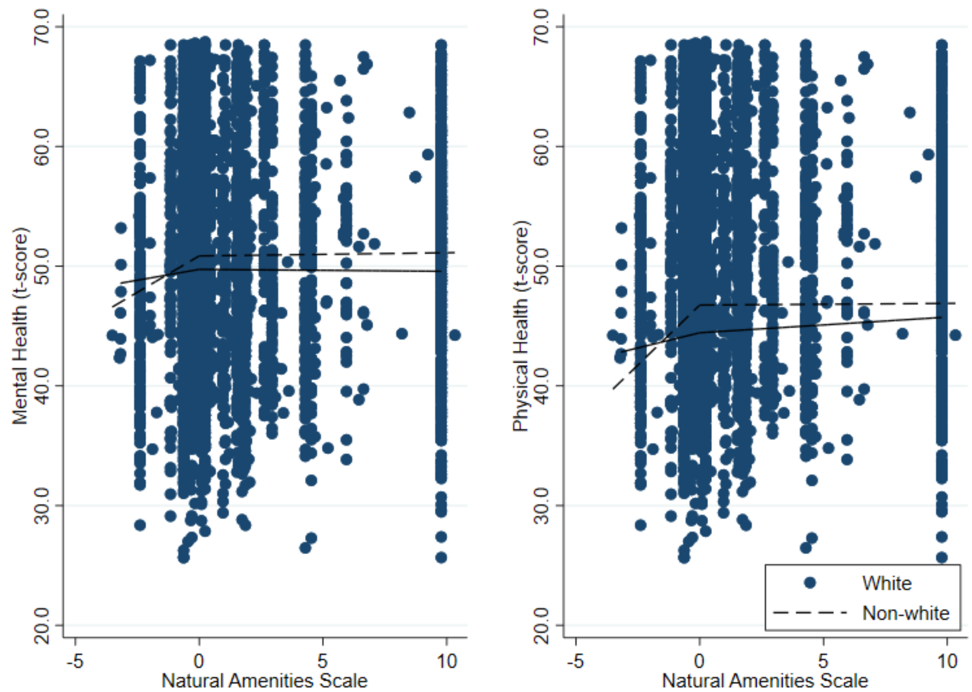


Figure 3 - 4: Unadjusted piecewise linear spline models visualizing the relationships between NAS and mental and physical health for white (gray lines) and non-white (black lines) individuals.



After adjusting for relevant confounding variables, the overall relationship of the NAS and health was attenuated and no longer significant. However, there were still important and consistent associations within the subgroups. Similar to the unadjusted analysis, in low amenities areas only, white individuals had a stronger association of amenities to mental and physical health compared to non-white individuals. However, in high amenity areas, mental health had a negative association of amenities to mental and physical health for each additional increase in natural amenities, and this was especially prominent among low-income individuals. Further, living in a rural high amenities area was associated with worse physical health for each additional increase in NAS. The slopes differed significantly between low and high-amenity areas for many of the models (see Table 3 - 3).

Table 3 - 3: Multivariable piecewise spline regression overall and sub-group models

	Mental Health ß (95% CI)		**Physical health ß (95% CI)**	
	Low amenities (NAS <0) ß (95% CI) Adjusted models†	**High amenities (NAS ≥0) ß (95% CI)**	**Low amenities (NAS <0) ß (95% CI)**	**High amenities (NAS ≥0) ß (95% CI)**
Full model	0.30 (-0.28, 0.88)	**-0.09 (-0.20, 0.00)**	0.50 (-0.12, 1.13)	-0.05 (-0.15, 0.06)
Subgroups				
Low income, y	*****0.64 (-0.08, 1.36)	***-0.27 (-0.44, -0.10)**	*****0.64 (-0.09, 1.37)	***-0.21 (-0.39, -0.04)**
Low income, n	-0.07 (-1.18, 1.04)	-0.01 (-0.11, 0.13)	0.43 (-0.83, 1.69)	0.04 (-0.10, 0.17)
White race, y	***0.75 (0.04, 1.46)**	*-0.08 (-0.19, 0.02)	***1.03 (0.25, 1.81)**	*-0.07 (-0.19, 0.05)
White race, n	0.00 (-1.14, 1.15)	-0.11 (-0.35, 0.13)	-0.13 (-1.26, 1.01)	0.00 (-0.23, 0.24)
Hispanic, y	0.01 (-2.81, 2.83)	0.00 (-0.35, 0.36)	0.31 (-2.52, 3.13)	-0.07 (-0.42, 0.29)
Hispanic, n	0.45 (-0.16, 1.05)	**-0.10 (-0.21, -0.00)**	0.57 (-0.09, 1.22)	-0.06 (-0.17, 0.06)
Married, y	--	--	0.62 (-0.50, 1.73)	-0.05 (-0.20, 0.10)
Married, n	--	--	0.45 (-0.32, 1.22)	-0.05 (-0.21, 0.10)
Graduated college, y	0.40 (-0.64, 1.45)	-0.09 (-0.21, 0.02)	**--**	--
Graduated college, n	0.36 (-0.37, 1.10)	-0.08 (-0.26, 0.10)	**--**	--
Rural residence, y	0.62 (-1.15, 2.39)	0.13 (-0.67, 0.70)	0.51 (-1.38, 2.40)	**-0.84 (-1.57, -0.10)**
Rural residence, n	0.30 (-0.34, 0.94)	-0.07 (-0.18, 0.03)	0.64 (-0.04, 1.33)	-0.02 (-0.13, 0.09)

Models were adjusted for age, sex, race, ethnicity, marital status, education, and employment. In subgroup analysis, moderating variables were omitted.
Slopes that significantly differ from zero are shown in **bold** type.
*Significant difference (P<0.05) in slopes between low and high-amenity areas.

We performed a sensitivity analysis using 90% of the participants that reside in 24 counties. No results significantly changed. For instance, in unadjusted analysis in low amenities areas, the coefficient shaped from 1.76 to 1.80 for physical health and from 1.08

to 1.09 for mental health. Similar small differences were observed in high amenities areas. In adjusted analysis in high amenities areas, the coefficient for mental health became slightly more negative but lost significance, likely due to the decrease in sample size. No other notable changes were noticed in the sensitivity analysis.

3.5 Discussion

Previous research found nonlinear relationships between the *built* environment and health. Here, we extend these findings to the *natural* environment and to various subgroups. In this exploratory analysis, we found that the effect of the natural environment on physical and mental health was important in areas with lower natural amenities, but not in areas with higher natural amenities. After adjustment, these relationships appeared to be significant especially among more advantaged populations. In low amenity areas, White individuals seemed to benefit from an improving natural environment, while in higher amenity areas, the health of lower income individuals *decreased* with improving amenities.

The relationship of the natural environment to health is complex and there are likely several mechanisms at work. In general, as seen here, health improves as the natural environment improves. Better climate and more varied topography can lead to more physical activity and better health.[15, 16] Residing near green space can increase physical activity and subsequently improve health.[28] Simply being "in nature" can reduce stress and lead to lower blood pressure, anxiety, depression, and risk of poor health outcomes.[29-31] In turn, residing in places with high air pollution or near large agricultural farms can lead to health issues.[32, 33] There is also a budding literature on geographical psychology focusing on how individual psychological characteristics interact with the local environment and ultimately affect health.[34-36] A possible explanation for the nonlinear association in our study is that once some criteria are met for a favorable natural environment (milder, sunnier winters, less humid summers, some variation in topography or access to some blue and green space), other county-level competing factors (urban-rural continuum, built environment, cost of living) come into play. But then, why do advantaged populations have health benefits in low amenity areas while disadvantaged populations do not? Perhaps, advantaged populations in low amenities areas can focus on health and physical activity through means outside the natural environment (gyms, yoga, *etc*.). Meanwhile, in high amenity areas, low-income individuals have a decline in mental and physical health with additional amenities while there is no impact on higher income individuals. This could be due to increases in cost of living associated with high amenity areas. Low-income individuals may need to work multiple jobs to make ends meet and therefore have less time or money to take advantage of the natural environment.

As expected in a population with chronic conditions, the average physical health was lower than the average US population. The mental health scores were similar to the US population even though we included individuals with known behavioral conditions. In the worst natural environments, however, physical and mental health were much worse than the national level. Improving the natural environment in which one resides from -4 to 0 on the NAS is associated with an increase in mental health and physical health, although after adjustment, only for white individuals.

There are important policy implications if this work can be confirmed. Although most natural amenities are nonmodifiable, there are strategies to improve health by reducing the health benefit inequities between certain groups that are associated with improvements in the natural environment. One could improve some aspects of the natural environment by adding green space, recreation areas, and hiking trails that have been shown to increase physical activity and improve health.[18] It will be important to identify potential mechanisms that are driving improved health in low amenity areas for advantaged populations. Because we only see improvements in health for traditionally advantaged populations, perhaps identifying how these populations are benefiting could inform outreach campaigns geared towards disadvantaged populations.

There are several limitations. The spatial granularity of the NAS is low and may not accurately measure the natural environment at the sub-county level. However, many of the characteristics that make up the NAS probably do not likely differ drastically within county. The theory behind the creation of the NAS may not generalize outside the US as other countries may find colder winters appealing. Further, there is a discordance in dates between the survey data (2018) and NAS (2000). Although survey data are self-reported, the PROMIS-29 is validated and reliable. We collected data from 44 primary care practices of various sizes, structures, and settings across the United States. However, not all states or regions are represented and therefore the results of this study may not be generalizable to areas outside the study area. Most of the range of the natural amenity scale is represented. Although 119 counties are represented in this study, the majority (90%) of participants reside in 24 counties, further hampering generalizability and questioning whether the findings of this study are an artifact of the data. However, a similar inflection point has been shown using a nationwide dataset.[16] Future research should investigate why the inflection point is at zero and explore more complex modelling techniques such as general additive models (GAMs). Further, all study participants have multiple chronic conditions, which limits generalizability to otherwise healthy adults. As with most studies of the environment, these data cannot distinguish if the environment affects health or if health and sociodemographic characteristics influence where people live.

There are many strengths to this study. While most studies in this realm focus on children or the elderly, we examined a large sample of adult primary care patients with chronic conditions. While other studies have relied on aggregated health information that may suffer from the ecologic fallacy,[37] we used individual-level data. This may be the first study to investigate nonlinear relationships between the natural environment and health. Future studies should include information on cost of living and explore how the built, natural, and social environment affect health.

In this nationwide analysis of adults with chronic conditions, we found that the natural environment affects health differently depending on the number of natural amenities available. Further, the benefits of the natural environment are not homogenous across different populations. Understanding why these differences exist could lead to strategies to improve health through improving equitable access to the natural environment and ultimately to improved mental and physical health.

3.6 References

1. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. Health Place. 2010;16(2):175-90.
2. Glazier RH, Creatore MI, Weyman JT, Fazli G, Matheson FI, Gozdyra P, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. PLoS One. 2014;9(1):e85295.
3. Muldoon KA, Duff PK, Fielden S, Anema A. Food insufficiency is associated with psychiatric morbidity in a nationally representative study of mental illness among food insecure Canadians. Social Psychiatry and Psychiatric Epidemiology. 2013;48(5):795-803.
4. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. BMJ Open. 2016;6(2):e008878.
5. Pan L, Sherry B, Njai R, Blanck HM. Food insecurity is associated with obesity among US adults in 12 states. J Acad Nutr Diet. 2012;112(9):1403-9.
6. Xu F, Jin L, Qin Z, Chen X, Xu Z, He J, et al. Access to public transport and childhood obesity: A systematic review. Obes Rev. 2021;22 Suppl 1:e12987.
7. Brown BB, Yamada I, Smith KR, Zick CD, Kowaleski-Jones L, Fan JX. Mixed land use and walkability: Variations in land use measures and relationships with BMI, overweight, and obesity. Health Place. 2009;15(4):1130-41.
8. Gunn LD, Mavoa S, Boulange C, Hooper P, Kavanagh A, Giles-Corti B. Designing healthy communities: creating evidence on metrics for built environment features associated with walkable neighbourhood activity centres. Int J Behav Nutr Phys Act. 2017;14(1):164.
9. Manisalidis I, Stavropoulou E, Stavropoulos A, Bezirtzoglou E. Environmental and Health Impacts of Air Pollution: A Review. Front Public Health. 2020;8:14.
10. Leaning J, Guha-Sapir D. Natural disasters, armed conflict, and public health. The New England journal of medicine. 2013;369(19):1836-42.
11. Alavanja MC, Sandler DP, McMaster SB, Zahm SH, McDonnell CJ, Lynch CF, et al. The Agricultural Health Study. Environ Health Perspect. 1996;104(4):362-9.
12. Gianfredi V, Buffoli M, Rebecchi A, Croci R, Oradini-Alacreu A, Stirparo G, et al. Association between Urban Greenspace and Health: A Systematic Review of Literature. Int J Environ Res Public Health. 2021;18(10).
13. Kellert SR, Wilson EO. The biophilia hypothesis: Island press; 1993.
14. Jimenez MP, DeVille NV, Elliott EG, Schiff JE, Wilt GE, Hart JE, et al. Associations between Nature Exposure and Health: A Review of the Evidence. Int J Environ Res Public Health. 2021;18(9).
15. Lin G, Spann S, Hyman D, Pavlik V. Climate amenity and BMI. Obesity (Silver Spring). 2007;15(8):2120-7.

16. Littenberg B, Bonnell LN, LeBruin AS, Lubetkin DA, Troy AR, Zia A. The Relationship Between Access to Natural Environmental Amenities and Obesity. Cureus. 2015;7(11):e377.
17. Bonnell LN, Troy AR, Littenberg B. Nonlinear relationship between nonresidential destinations and body mass index across a wide range of development. Prev Med. 2021;153:106775.
18. James P, Kioumourtzoglou MA, Hart JE, Banay RF, Kloog I, Laden F. Interrelationships Between Walkability, Air Pollution, Greenness, and Body Mass Index. Epidemiology. 2017;28(6):780-8.
19. Yin C, Yao X, Sun B. Population density and obesity in rural China: Mediation effects of car ownership. Transportation Research Part D: Transport and Environment. 2022;105:103228.
20. Crocker AM, Kessler R, van Eeghen C, Bonnell LN, Breshears RE, Callas P, et al. Integrating Behavioral Health and Primary Care (IBH-PC) to improve patient-centered outcomes in adults with multiple chronic medical and behavioral health conditions: study protocol for a pragmatic cluster-randomized control trial. Trials. 2021;22(1):200.
21. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. J Clin Epidemiol. 2010;63(11):1179-94.
22. Hays RD, Spritzer KL, Schalet BD, Cella D. PROMIS((R))-29 v2.0 profile physical and mental health summary scores. Qual Life Res. 2018;27(7):1885-91.
23. Natural Amenities Scale. Internet. U.S. Department of Agriculture. Economic Research Service. 1999. Available from: http://www.ers.usda.gov/data-products/natural-amenities-scale.aspx.
24. McGranahan DA. Natural Amenities Drive Rural Population Change. Agricultural Economic Report No. (AER-781). United States Department of Agriculture Economic Research Service. 1999, AER-781:.
25. Ratcliffe M, Burd C, Holder K, Fields A. Defining Rural at the U.S. Census Bureau, ACSGEO-1, U.S. Census Bureau, Washington, DC. 2016.
26. Royston P. Lowess Smoothing. Stata Tech Bull Reprints. 1991;1:41-4.
27. Bozdogan H. Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. Psychometrika. 1987;52(3):345-70.
28. Nieuwenhuijsen MJ, Khreis H, Triguero-Mas M, Gascon M, Dadvand P. Fifty Shades of Green: Pathway to Healthy Urban Living. Epidemiology. 2017;28(1):63-71.
29. Beyer KM, Kaltenbach A, Szabo A, Bogar S, Nieto FJ, Malecki KM. Exposure to neighborhood green space and mental health: evidence from the survey of the health of Wisconsin. Int J Environ Res Public Health. 2014;11(3):3453-72.
30. Grahn P, Stigsdotter UK. The relation between perceived sensory dimensions of urban green space and stress restoration. Landscape and Urban Planning. 2010;94(3):264-75.

31. Yang BY, Markevych I, Bloom MS, Heinrich J, Guo Y, Morawska L, et al. Community greenness, blood pressure, and hypertension in urban dwellers: The 33 Communities Chinese Health Study. Environ Int. 2019;126:727-34.
32. Dominski FH, Lorenzetti Branco JH, Buonanno G, Stabile L, Gameiro da Silva M, Andrade A. Effects of air pollution on health: A mapping review of systematic reviews and meta-analyses. Environ Res. 2021;201:111487.
33. Khan KM, Karnati J, Hamid I, Koceja D, Zahirul Islam M, Khan MA. Residential Proximity to Agricultural Fields and Neurological and Mental Health Outcomes in Rural Adults in Matlab, Bangladesh. Int J Environ Res Public Health. 2019;16(18).
34. Rentfrow PJ. Statewide differences in personality: toward a psychological geography of the United States. Am Psychol. 2010;65(6):548-58.
35. Rentfrow PJ. Geographical psychology. Curr Opin Psychol. 2020;32:165-70.
36. Rentfrow PJ, Gosling SD, Jokela M, Stillwell DJ, Kosinski M, Potter J. Divided we stand: three psychological regions of the United States and their political, economic, social, and health correlates. J Pers Soc Psychol. 2013;105(6):996-1012.
37. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. Progress in Physical Geography: Earth and Environment. 2007;31(5):471-9.

CHAPTER 4: NONLINEAR RELATIONSHIPS BETWEEN WALKABILITY AND HEALTH: A REVIEW OF THE LITERATURE

4.1. Abstract

Background

Most studies of the association between walkability and adiposity assume a linear relationship. In reality, however, these relationships are more complex and possibly nonlinear in nature. Using linear regression techniques to model nonlinear relationships could introduce bias and be partially responsible for conflicting findings in the literature. We aimed to review studies that used nonlinear methods to model the relationship between walkability and health.

Methods

We searched PubMed and Web of Science through August 2022. Original research that assessed a nonlinear relationship between walkability and health were included. We recorded the definition of walkability, the outcome, the location, the statistical methods, and the findings from each study. These were synthesized to identify patterns.

Results

The search identified 50 articles, 8 of which met the inclusion criteria. Six of 8 studies explicitly tested and found that nonlinear models had better fit than linear models. Further, despite heterogeneity in the definition of walkability and statistical methods used, most studies found an inverse-U shaped relationship between walkability and BMI.

Conclusions

We reviewed the recent literature on the nonlinear relationship between walkability and health. In some instances, nonlinear models may be superior to linear models in modelling this relationship. Ignoring the possibility of nonlinearity could miss important insights into these relationships and ultimately lead to incorrect conclusions. Future studies should attempt to fit nonlinear models when assessing walkability and health.

4.2 Introduction

Chronic medical conditions such as heart disease and obesity are prevalent in the United States (US) and often occur in conjunction with mental and behavioral health conditions such as anxiety and depression, increasing the likelihood of poor health outcomes.[1] These conditions are largely preventable through lifestyle changes such as improving diet or increasing physical activity.[2] The built environment can facilitate or impede healthful behaviors and lifestyle choices and ultimately help prevent or reduce morbidity and mortality from chronic medical and behavioral health conditions.[3,4]

The built environment, defined as the space in which people live, work, and recreate on a day-to-day basis, promotes or impedes healthful lifestyles though access to healthy foods and walkable infrastructure.[5] One aspect of the built environment is walkability, or how favorable an area is to pedestrian walking.[6,7] There are several ways to measure walkability including residential density, population density, street intersection density, land use mix, design of walkable streets with little traffic and large sidewalks, distance to transit, and destination accessibility.[8-11] These attributes of walkability can independently promote active travel, a healthful diet, and result in better mental and physical health.

However, systematic reviews have highlighted significant heterogeneity in the relationship of walkability and health.[12-14] These conflicting results may be partially attributed to disagreements in how walkability is defined, differences in spatial scales used (country *vs.* census tract *vs.* household), differences in the underlying population sampled, or differences in the underlying level of development (large metro areas, suburban areas, rural areas *etc*.).

Previous studies have assumed a pre-specified, *positive*, monotonic relationship between walkability and health or a *negative*, monotonic relationship between walkability and adiposity.[12] Most studies have focused on urban areas where automobile reliance is low and active travel is high. Fewer studies have investigated this relationship in rural or suburban areas.[15] In rural and suburban areas where automobile reliance is high, it is unclear if a walkability has the same impact on active transport or health. Regardless, it is plausible that walkability may affect health differently depending on the level of development, suggesting that a nonlinear relationship may exist.

Modelling true nonlinear relationships using linear models could result in bias and conflicting findings. For example, if the true relationship is U-shaped and linear model is fit, there is potential for a null finding. Ignoring the possibility of nonlinearity could result in incorrect or misleading results and ultimately impact local built environment policy.

There has been a recent uptick in articles published using nonlinear methods. The goal of this review is to summarize the walkability and health literature that used nonlinear methods. We highlight definitions of walkability, the outcome, the location, the statistical methods, and the findings from each study.

4.3 Methods

We identified original research articles through August 2022 using PubMed and Web of Science databases. A medical librarian assisted in the development of the search strategy. The PubMed search was conducted using Medical Subject Headings (MeSH) related to the 5Ds of walkability including density (residential, populations *etc.*), diversity (land use mix), design (walkability), distance (to transit), and destination accessibility, as well as mental and physical health, and nonlinear methods. An iterative approach was used to refine the searches. All searches were performed on August 26, 2022. A similar approach was used for the Web of Science database. The complete list of MeSH terms can be found in Table 4 - 1.

Table 4 - 1: Complete searches

TOPIC: ("built environment" or "walk*" or "density" or "destinations" or "transit" or "development" or "residential" or "land use mix" or "nonresidential destinations" or "food outlet" or "rural" or "urban" or "suburban") AND TOPIC: ("non-linear" or "nonlinear: or "statistical interaction" or "gradient" or "nonmonotonic" or "non-monotonic" or "modify" or "stratify") AND TOPIC: ("health" or "bmi" or "body mass index" or "obesity" or "function" or "health related quality of life")

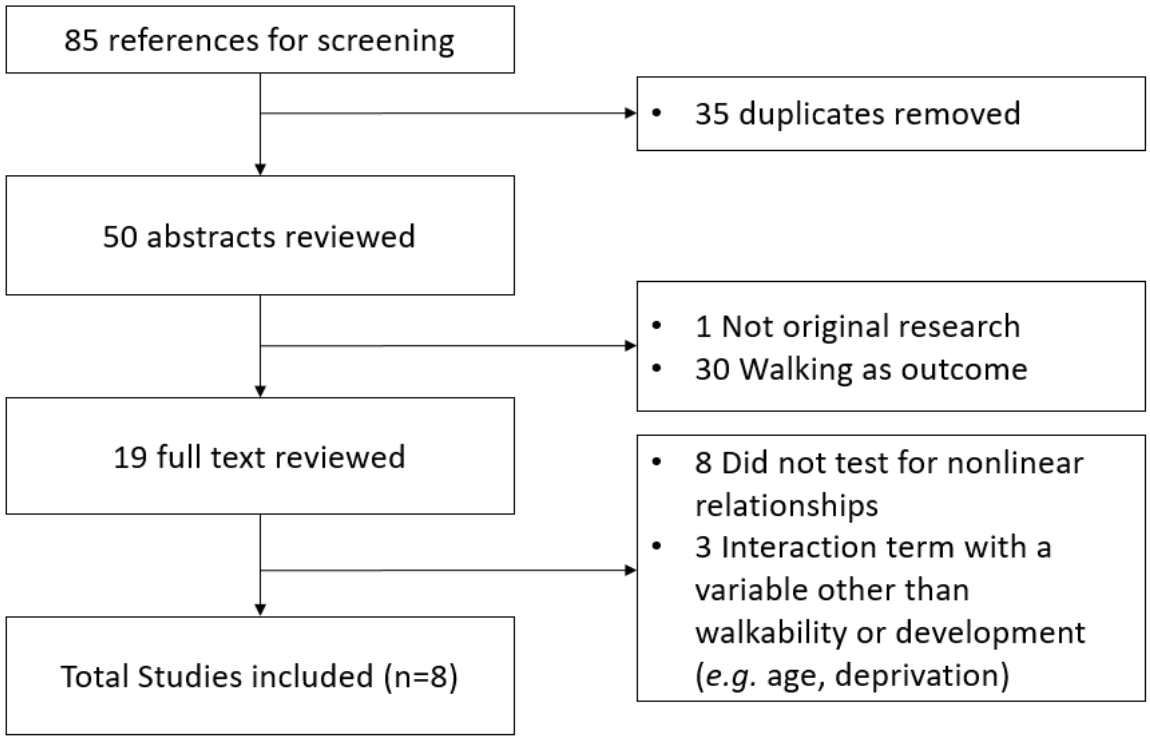
Studies were manually screened within each database and selected if there was mention of any aspect of walkability, health, and nonlinear methods in the title or abstract. Articles were excluded if they were not original research, if the outcome assessed was walking or physical activity rather than an indicator of health such as obesity, if nonlinear relationships were not assessed, or if an interaction term other than walkability or development was included (*e.g.* age, neighborhood deprivation). The results were limited to the English language (see Table 4 - 2).

Table 4 - 2: Inclusion and exclusion criteria

Inclusion criteria	Original research articles published in English in peer-reviewed journals
	Predictor is one of the 5Ds of walkability (density, diversity, design, distance to transit, and destination accessibility).
	Outcome is some measure of health (obesity, mental health, physical health, etc.)
	Nonlinear methods used
Exclusion criteria	Review articles, study protocols, letters to editors, and conference papers
	Walking or other forms of active travel as the outcome measure
	Did not test for a nonlinear relationship
	Interaction term with a variable other than walkability or development

The systematic searches of PubMed and Web of Science databases identified a total of 85 references, which were pooled in a table in Microsoft Excel. After de-duplicated, 50 articles underwent review of their titles and abstracts by the lead author (LNB). Thirty-one articles were excluded because they were not original research or used walking as an outcome. The remaining 19 articles were read in full, where an additional 8 references were found to not test for a nonlinear relationship (including mediation models), and another 3 references included an interaction term with variables other than walkability such as age or deprivation, leaving a total of 8 articles (see Figure 4 - 1). Relevant information was extracted including authors, location of study, definition of walkability, and health indicators used as outcomes. Statistical methods were evaluated, including if the authors considered both linear and nonlinear models and which had the better fit.

Figure 4 - 1: Flow diagram



4.4 Results

The majority of studies (88%) included in this review used a measure of adiposity (waist circumference, whole body fat, waist-to-hip ratio, or body mass index (BMI)) as an outcome measure. Other outcomes assessed were mental and physical health and sarcopenia. Over half (63%) were published after 2019. Most articles defined walkability using a measure of density, including population density (n=2)[16,17], nonresidential destination density (n=2)[18,19], residential density (n=1)[20], and fast food density.[21] Two studies used composite measures of walkability (n=2)[22,23], that includes the aforementioned attributes of walkability and more. A variety of methods were used to model the nonlinear relationships including restricted cubic splines (n=2), general additive models (n=3), piecewise linear regression (n=2), general estimating equations (n=1), and gradient boosted decision trees (n=1) (note these are not mutually exclusive as some studies implemented multiple statistical methods). The studies were conducted in the US (n=3), China (n=2), England (n=1), and Taiwan (n=1). Sample sizes ranged from 1,056 (Park 2017) to 17.2 million (Bonnell 2021). See Table 4 - 3.

Table 4 - 3: Characteristics of selected studies

Authors	Year	Predictors: Definition of walkability	Outcomes: Health indicators	Population	Statistical methods	Findings
Bonnell, LN	2021	Access and proximity to destinations (nonresidential destinations)	BMI	17.2 million residents from 6 US states	Piecewise linear regression; LOWESS curves	Inverse U-shaped relationship between commercial building density and BMI
Bonnell, LN	2022	Access and proximity to destinations (nonresidential destinations)	BMI, mental health, physical health	2,405 US adult primary care patients with multiple chronic conditions	Restricted cubic splines, LOWESS smoothing curves, non-parametric regression with a spline basis and piecewise linear regression	Inverse U-shaped relationship between commercial building density and BMI. U-shaped relationship between commercial building density and mental and physical health
James, P	2017	Walkability (a composite of population density, street connectivity, and business access)	BMI	23,435 older US women from the Nurses Health Study	Generalized additive models with penalized splines	U-shaped relationship between walkability and BMI
Murphy, M	2018	Access and proximity to destinations (fast food outlet density)	BMI	3,141 Australian adults	General estimating equations stratified by level of development	Inverse U-shaped relationship between fast food outlet density and BMI

Park, JH*	2021	Walkability (walk score)	Sarcopenia	1,056 older Taiwanese adults	General additive models	Inverse U-shaped relationship between WalkScore and sarcopenia
Sarkar, C	2017	Residential density	Adiposity, waist circumference, whole body fat	502,649 English older adults	Restricted cubic splines	Inverse U-shaped relationship between residential density and Adiposity, waist circumference, whole body fat
Sun, B	2022	Population density	Abdominal obesity	36,422 Chinese adults	General additive models	N-shaped relationship between population density and abdominal obesity
Yin, C*	2021	Population density	waist-to-hip ratio	3,581 Chinese adults	Gradient boosted decision trees	Inverse U-shaped relationship between population density and waist-to-hip ratio
*Studies that found inconsistent results						

4.4.1 Review of each article

Bonnell *et al.* found an inverse-U shaped curve between the density of nonresidential destinations and BMI among 17.2 million US residents across six states.[18] Although the authors did not explicitly test if a linear model was a better fit, they did use a LOWESS curve, which allows the data to specify the functional form, rather than shaping the data to a pre-specified shape. After identifying a nonlinear relationship, they fit the inverse-U shaped curve suggested by the LOWESS, using a piecewise linear model with an inflection point at 15 establishments·ha^{-1}. This study had an unprecedented sample size with a granular measure of walkability and used a 1km buffer, which is a common buffer size and comparable to other studies. However, it lacked information on many key individual level covariates and did not explicitly test whether linear regression had a better fit than the nonlinear model. Despite the granularity of the predictor, this measure of walkability may not be comparable to other studies.

Bonnell *et al.* then sought to generalize their nonlinear results to a different population and to additional health outcomes.[19] Their second study found a nonlinear relationship between density of nonresidential destinations and BMI, mental health, and physical health among 2,405 adult primary care patients with chronic conditions. A LOWESS function was used to model these relationships and identified an inflection point at 15 establishments·ha^{-1}. Then, after confirming a nonlinear relationship, nonparametric regression, restricted cubic splines (RCS), and piecewise linear regression were used to model the relationships. This study extended previous findings to a new population and new health indicators including mental and physical health. The sample size is smaller in the study but there were a plethora of individual-level characteristics considered in each model. Again, the measure of walkability may not be comparable to other studies, besides the previous study performed by the same authors.

James *et al.* found a nonlinear relationship between a composite score of walkability and BMI among 23,435 US women from the Nurses Health Study.[23] Generalized additive models (GAMs) with penalized splines were used to model the relationship, which utilize a generalized cross-validation technique that includes a linear or nonlinear model, depending on which is a better fit of the data. They found a positive relationship between walkability and BMI up until a walkability score of 1.8, at which point the relationship became negative. This study had a large sample size and used methods that explicitly tested if linear or nonlinear models were a better fit of the data. They created a residence-level walkability index that incorporates many aspects of walkability. This measure of walkability is quite strong but may not be reproducible unless the authors publish it. The population was limited to healthcare professionals and may not be generalizable.

Murphy *et al.* found a nonlinear relationship between fast food density and BMI among 3,141 Australian adults.[21] General estimating equations with an interaction term between fast food density and area of residence (established residential areas *versus* urban-growth area) was used to model the relationship with BMI. Fast food density was negatively associated with BMI in urban-growth areas but positively associated in established residential areas. No relationship was found with grocery stores. It is unclear if this finding generalizes to areas densities outside suburban areas. The authors used both qualitative (outside scope of this review) and quantitative methods to assess this relationship and included several covariates in the model including a measure of physical activity. The authors did not test to see if this relationship was better fit by linear or nonlinear methods.

Park *et al.* found a nonlinear relationship between neighborhood Walk Score and sarcopenia among 3.2 million Taiwanese adults aged 65 years and older.[22] GAMs were used to model the relationship and indicated that nonlinear models had a lower Akaike Information Criterion (AIC)[24] than linear models, suggesting the nonlinear model were a better fit. The risk of sarcopenia was highest in areas with low (Walk Score=0), mid (Walk Score=60 somewhat walkable), and high (Walk Score=100), and lowest in areas with a Walk Score of 40 (car dependent) and 80 (very walkable), creating a sinusoidal wave. This study had a very large sample and found a novel relationship. The predictor is less granular than some of the other studies and may be subject to the modifiable areal unit problem.[25] With that said, the Walk Score is intuitive and may be the most easily interpretable measure in terms of dissemination. This relationship may only be generalizable to older adults or Taiwanese adults.

Sarkar *et al.* found an inverse-U shaped relationship between residential density and BMI, waist circumference, and whole-body fat among 502,649 English older adults.[20] The authors performed both linear regressions in addition to RCS and used AIC to determine which had a better fit. Once the relationship was confirmed to be nonlinear, RCS were used to fit the data and then piecewise linear regression was used to model the relationship for ease of interpretation. Measures of adiposity increased until an inflection point of 1800 units/km^2 at which point the relationship started to decrease. The authors used a very large dataset and had several measures of adiposity, all showing similar results. It is unclear if residential density can be compared to population density or the density of nonresidential destinations.

Sun *et al.* found an N-shaped relationship between population density and waist circumference and waist-to-hip ratio among 36,422 Chinese adults.[16] The study employed GAMs which allows the comparison of traditional linear approaches as well as nonlinear approaches. Abdominal obesity increases as population increased until 12,000 people/km^2, at which point abdominal obesity started to decrease. Then, at 50,000 people/km^2 the abdominal obesity started to increase again, creating an N-shaped relationship. This study utilized a large sample size and checked for both linear and nonlinear relationships. Over the range of population densities similar to other studies (*i.e.*, excluding ultra-dense areas that may be unique to China and other Eastern countries), the observed relationship was consistent with an inverted-U shape.

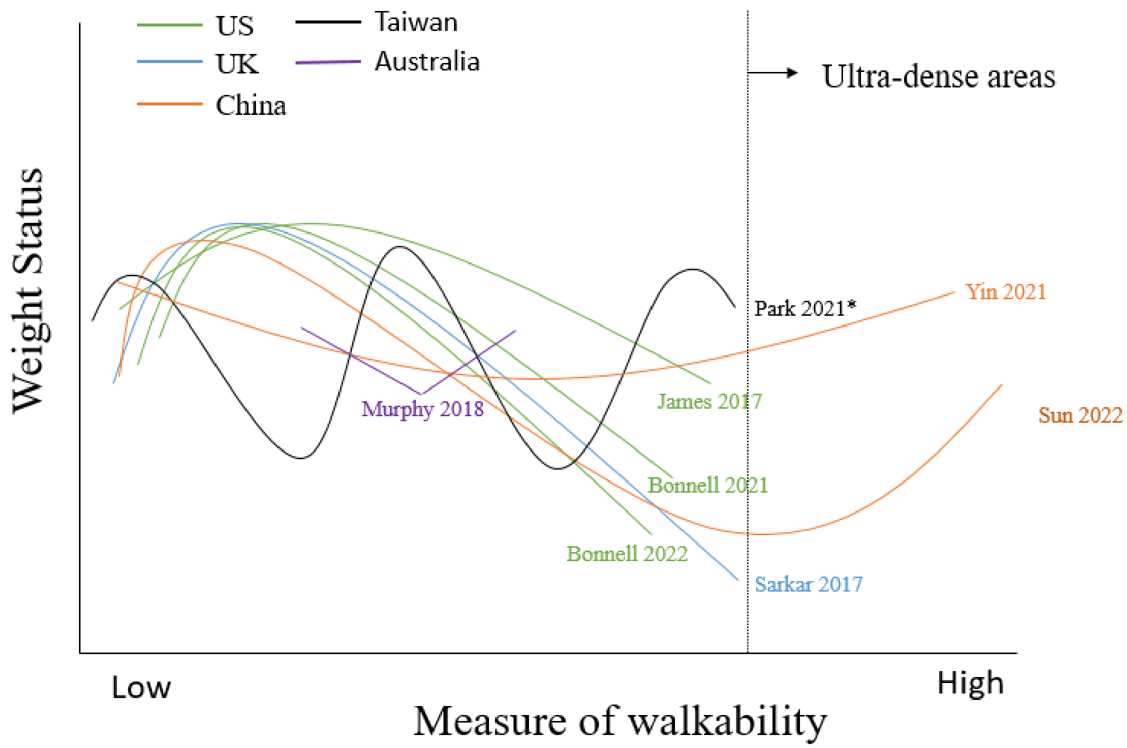
Yin *et al.* found nonlinear relationships between local and regional population density, distance to city center, and predicted waist-to-hip ratio and among 3,581 Chinese respondents.[17] Gradient boosted decision trees were used to identify nonlinear relationships. However, the relationship was not tested to see if a linear relationship fit the data better. Predicted waist-to-hip ratio decreased as local population density increased until an inflection point of 10,000 persons/km^2 at which point waist-to-hip increased with local population density. In contrast, predicted waist-to-hip ratio decreased as regional population density increased. Predicted waist-to-hip ratio increased as distance to city center increased, hitting an inflection point at 7 km, and then started to gradually flatten and decrease. Unlike the other studies, all measures of the built environment were included in the model simultaneously. This study included a large sample size and included ultra-dense areas in China. The predictors were not granular and it's unclear if a traditional linear model is a better fit or the boosted trees model due to the small change in adiposity reported.

Interestingly, the measures of walkability were more important in predicting adiposity than individual characteristics.

4.4.2 Synthesizing results

A trend emerged among the majority of studies included in this review. Five of 8 studies found an inverse U-shaped relationship between walkability and adiposity, where the extremes had better outcomes than the middle range. This trend is especially remarkable because others have shown that findings between the built environment and obesity can be affected by data-processing, model-specification, as well as what covariates are included in the models (age, income, education), and how missing data is handled in the measure of walkability.[27] Although comparison of the different measures of walkability is challenging, we attempted to summarize these results in a graphic. One found contradictive results, where adiposity was lowest in mid-ranges and highest on the extremes. Another found that sarcopenia was worse at the extremes and in the middle, with low points in between. The third paper assessed areas within a suburban context but found that fast food density was positively associated with BMI in established residential areas but negatively associated in urban-growth areas (Figure 4 - 2).

Figure 4 - 2: Nonlinear relationships between walkability and adiposity



*Outcome measured is Sarcopenia not weight status.

4.5 Discussion

4.5.1 Overview of evidence

Although a vast literature exists on the built environment and health, only recently have nonlinear methods been incorporated. This review sought to summarize the budding literature evaluating nonlinear relationships between walkability and health. Despite heterogeneity in the measures of walkability and the health indicators, location, and the statistical methods used, the majority of studies found an inverse U-shaped relationship between walkability and adiposity. In general, adiposity increased as walkability increased until an inflection point, at which point adiposity started to decrease as walkability increased.

4.5.2 Predictors: measures of walkability

Eight studies met the inclusion criteria for this review and they used a wide variety of different measures for walkability. Although previous literature has shown that population density[9], residential density[8,9], Walk Score,[12] proximity to nonresidential destinations,[11] and composite walkability indices[12] are individually associated with health and adiposity, comparisons between these measures are challenging. Each measure cannot be directly translated to the other. For instance, the inflection points from the eight papers are at 15 establishments per hectare (n=2 papers), 1.8 walkability units, 40 and 80 Walk Score units, 1800 residential units/km^2, 12,000 and 50,000 people/km^2, 10,000 people/km^2, and the point between urban-growth areas and established residential areas. It is unclear if these findings are similar by coincidence or if a true nonlinear relationship exists. However, the mechanisms driving these relationships are thought to be the same. In general, a walkable environment can promote active travel and thus improve mental and physical health. Therefore, although heterogeneity in predictors exist, it makes theoretical sense that the same relationship was found across studies.

4.5.3 Outcomes: health indicators

Seven of eight studies included a measure of adiposity as an outcome measure, while the other study used sarcopenia. Among the 7 studies that included a measure of adiposity, 4 reported BMI and 3 reported waist circumference, waist-to-hip ratio, abdominal obesity, or whole-body fat. BMI has its limitations and other measures of adiposity may be more relevant in China[17], future studies should consider including BMI as an additional outcome measure, if available, for between-study comparability purposes. One study extended these nonlinear findings to measures of mental health, opening a new door of potential research.

4.5.4 Differences in methodology

The majority of studies tested whether a linear or nonlinear model was a better fit. Although Bonnell *et al.* did not test this analytically, they did use a LOWESS curve that allows the data to specify a form, and then fit a piecewise linear model to this functional form.[18,19] Sarkar et al. used a similar method of fitting a nonlinear relationship with a piecewise linear model for ease of interpretability.[20] Most papers implemented GAMs, which do test if linear *vs.* nonlinear are better fit. Only Yin *et al.* and Murphy *et al.* did not test whether a linear model fit their data better.[17,21] Future research should consider both linear and nonlinear models and explicitly test which is a better fit.

4.5.5 Differences in location

The studies were conducted in different locations where the relationship between walkability and health may fundamentally differ due to differences in culture, policy, and infrastructure. In the US, where 3 studies took place and the UK where 1 study took place, high walkability is typically indicative of city centers with a variety of destinations to walk to, lots of intersections for safe travel, and safe and clean environments.[5] However, these same conditions may not hold in eastern countries such as China, where 2 studies were performed, and Taiwan, where 1 study was performed. Other authors have suggest that in city centers in some eastern countries, air, light, and noise pollution can be high, there are food swamps, where only low nutrient food are available, and traffic is unpredictable and heavy.[17,22,28,29] This could result in less active travel and explain why these two studies found worse health at the extreme-high end.

4.5.6 Contradictive results

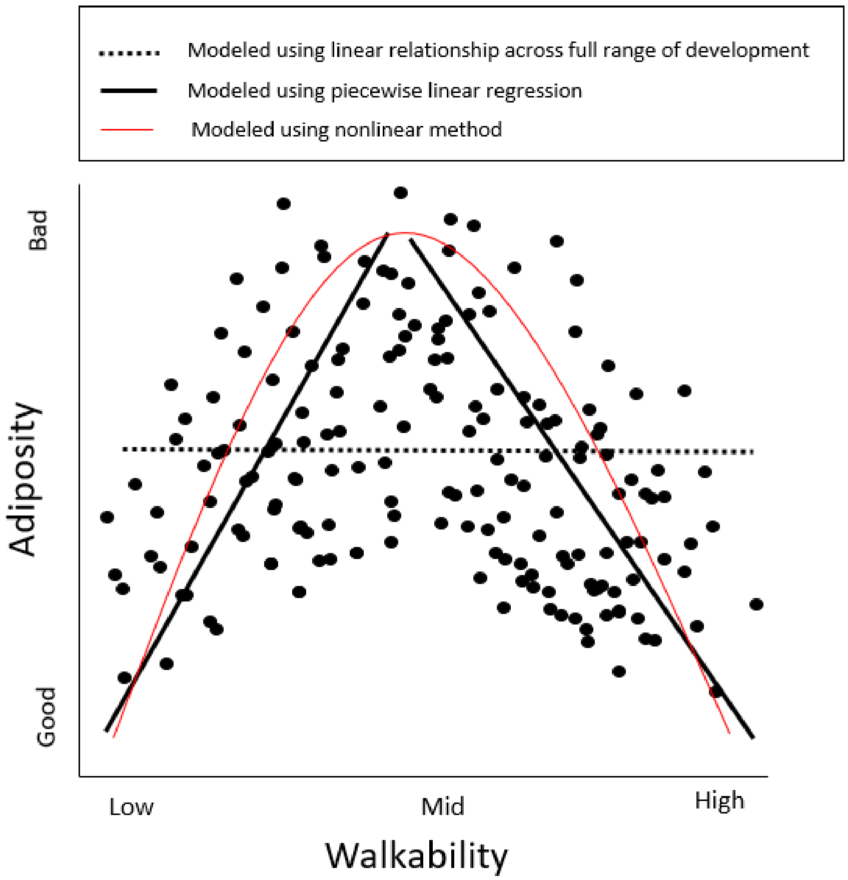
Despite the differences in walkability, outcomes, methodology, and location addressed above, 5 of 8 studies found an inverse U-shaped relationship between walkability and adiposity. There are several potential reasons why three studies could have found contradictive findings.[17,21,22] First, they were performed in Australia, China, and Taiwan, and built environments may affect people differently in these areas compared to the US and UK. However, the other study included from China found an inverse U-shaped relationship.[16] Yin *et al.* used gradient boosted decision trees and included several measures of the built environment in a single model, which could attenuate or potentially flip the relationship. Further, this method incorporates higher level interactions that the other methods do not, and produces a final predicted measure of adiposity, whereas the other papers use an observed measure of adiposity. Murphy *et al.* used an interaction term between fast food density and area of residence (established residential *versus* urban-growth area), which only included suburban residences. Perhaps if the authors included a larger range of development (urban and rural) a more complete picture of the nonlinear relationship would have been discovered. Both Park and Yin used a less granular measure of walkability, which could introduce several biases.[26] Park *et al.* was the only study to include sarcopenia as an outcome measure. However, Bonnell *et al.* also included a measure of physical health, but found differing results.[19] More research is needed on nonlinear relationships between walkability and measures of physical health outside adiposity.

4.5.7 Other considerations

Most of the nonlinear studies identified in the initial literature search used walking or some other form of physical activity as the outcome, as opposed to a measure of health. Active transport via walking or some other form of transportation is the posited mechanism between the built environment and health (at least in urban areas). Many of these papers identified nonlinear, U-shaped relationships between walkability and health. Although outside the scope of this review, these articles should be explored further as they may help explain the nonlinear relationships found between walkability and health.

Modelling nonlinear relationships using linear models could result in bias and conflicting findings. For example (Figure 4 - 3), if a true nonlinear relationship exists (fit by the red line using nonlinear methods) and linear model is used, then the relationship could be null (dotted line). The dotted line fit by the linear regression is clearly incorrect. This hypothetical relationship should be fit with a nonlinear model or, at the very least, a piecewise linear model (solid black lines). Ignoring the possibility of nonlinearity could result in incorrect or misleading results with serious implications.

Figure 4 - 3: Theory of nonlinear relationship between walkability and health



There are several limitations to report. First, the studies could not be compared using meta-analyses or other formal techniques due to heterogeneity in study designs, predictors, and outcomes. Second, these studies were not formally evaluated for quality, generalizability, or other important characteristics. However, every article was subjected to the peer-review process. The searches and review of the data were performed by one author, and although a systematic approach was taken, the article selection process could be incomplete. Further, although the search terms were seemingly comprehensive, this review may not have identified articles that tested for nonlinear relationships but only found linear relationships or no relationship at all.

The built environment and health literature has been around for nearly 30 years, yet only recently have nonlinear methods been incorporated into the studies. Why did it take over 20 years to start using these methods? The increase in computing power and development of new nonlinear methods has increased dramatically in the last 10 years. Further, the availability and access of large datasets necessary to perform these analyses are becoming more available at cheaper costs. The literature will likely see an influx of nonlinear analyses in the future.

With the increase in nonlinear analysis in the walkability and health literature, new relationships are starting to appear. These findings could provide important insights into complex forces that could have impact on public policy regarding the implementation of local built environment initiatives. Future research on walkability and health should test whether linear or nonlinear methods are a better fit.

4.7 References

1. Druss B, Walker E. Mental Disorders and medical comorbidity THE SYNTHESIS PROJECT. Access June 18. 2011.
2. Wingood M, Bonnell L, LaCroix AZ, et al. Community-Dwelling Older Adults and Physical Activity Recommendations: Patterns of Aerobic, Strengthening, and Balance Activities. J Aging Phys Act 2021:1-13.
3. Ding D, Gebel K. Built environment, physical activity, and obesity: what have we learned from reviewing the literature? Health Place 2012;18:100-5.
4. Ewing R, Cervero R. Travel and the Built Environment: A Synthesis. Transportation Research Record 2001;1780:87-114.
5. Handy SL, Boarnet MG, Ewing R, Killingsworth RE. How the built environment affects physical activity: views from urban planning. Am J Prev Med 2002;23:64-73.
6. Barnett DW, Barnett A, Nathan A, et al. Built environmental correlates of older adults' total physical activity and walking: a systematic review and meta-analysis. Int J Behav Nutr Phys Act 2017;14:103.
7. Cerin E, Nathan A, van Cauwenberg J, et al. The neighbourhood physical environment and active travel in older adults: a systematic review and meta-analysis. Int J Behav Nutr Phys Act 2017;14:15.
8. Creatore MI, Glazier RH, Moineddin R, et al. Association of Neighborhood Walkability With Change in Overweight, Obesity, and Diabetes. JAMA 2016;315:2211-20.
9. Glazier RH, Creatore MI, Weyman JT, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. PLoS One 2014;9:e85295.
10. Jia P, Pan X, Liu F, et al. Land use mix in the neighbourhood and childhood obesity. Obes Rev 2021;22 Suppl 1:e13098.
11. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. BMJ Open 2016;6:e008878.
12. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. Health Place 2010;16:175-90.
13. Center for Substance Abuse Treatment. Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders. Substance Abuse and Mental Health Services Administration (US). Treatment Improvement Protocol (TIP) Series, No. 54. Rockville (MD). 2012.
14. Schulz M, Romppel M, Grande G. Built environment and health: a systematic review of studies in Germany. J Public Health (Oxf) 2018;40:8-15.

15. Troy AR, Bonnell LN, Littenberg B. Relationship Between the Built Environment and Body Mass Index in a Rural Context: A Cross-Sectional Study from Vermont. Cureus 2018;10:e3040.
16. Sun B, Yao X, Yin C. An N-Shaped Association between Population Density and Abdominal Obesity. Int J Environ Res Public Health 2022;19.
17. Yin C, Cao J, Sun B. Examining non-linear associations between population density and waist-hip ratio: An application of gradient boosting decision trees. Cities 2020;107:102899.
18. Bonnell LN, Troy AR, Littenberg B. Nonlinear relationship between nonresidential destinations and body mass index across a wide range of development. Prev Med 2021;153:106775.
19. Bonnell LN, Troy AR, Littenberg B. Exploring non-linear relationships between neighbourhood walkability and health: a cross-sectional study among US primary care patients with chronic conditions. BMJ Open 2022;12:e061086.
20. Sarkar C, Webster C, Gallacher J. Association between adiposity outcomes and residential density: a full-data, cross-sectional analysis of 419 562 UK Biobank adult participants. Lancet Planet Health 2017;1:e277-e88.
21. Murphy M, Badland H, Jordan H, Koohsari MJ, Giles-Corti B. Local Food Environments, Suburban Development, and BMI: A Mixed Methods Study. Int J Environ Res Public Health 2018;15.
22. Park JH, Lai TF, Chang CS, Huang WC, Cho JS, Liao Y. A Nonlinear Association between Neighborhood Walkability and Risks of Sarcopenia in Older Adults. J Nutr Health Aging 2021;25:618-23.
23. James P, Kioumourtzoglou MA, Hart JE, Banay RF, Kloog I, Laden F. Interrelationships Between Walkability, Air Pollution, Greenness, and Body Mass Index. Epidemiology 2017;28:780-8.
24. Bonnell LN, Littenberg B. Nonlinear Relationships among the Natural Environment, Health, and Sociodemographic Characteristics across US Counties. Int J Environ Res Public Health 2022;19.
25. Bozdogan H. Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. Psychometrika 1987;52:345-70.
26. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. Progress in Physical Geography: Earth and Environment 2007;31:471-9.
27. Bodea TD, Garrow LA, Meyer MD, Ross CL. Explaining obesity with urban form: a cautionary tale. Transportation 2008;35:179-99.
28. Yin C, Yao X, Sun B. Population density and obesity in rural China: Mediation effects of car ownership. Transportation Research Part D: Transport and Environment 2022;105:103228.
29. Day K. Built environmental correlates of physical activity in China: A review. Prev Med Rep 2016;3:303-16.

5.1 References

1. Hales CM, Carroll MD, Fryar CD, CL. O. Prevalence of obesity and severe obesity among adults: United States, 2017–2018. NCHS Data Brief, no 360. *Hyattsville, MD: National Center for Health Statistics* 2020.
2. Baker JL, Olsen LW, Sorensen TI. Childhood body-mass index and the risk of coronary heart disease in adulthood. *The New England journal of medicine*. 2007;357(23):2329-2337.
3. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk for end-stage renal disease. *Ann Intern Med*. 2006;144(1):21-28.
4. Murakami Y, Huxley RR, Lam TH, et al. Diabetes, body mass index and the excess risk of coronary heart disease, ischemic and hemorrhagic stroke in the Asia Pacific Cohort Studies Collaboration. *Prev Med*. 2012;54(1):38-41.
5. Cervero R, Kockelman K. Travel demand and the 3Ds: density, diversity, and design. *Transp Res Part D*. 1997;78:48-58.
6. Glazier RH, Creatore MI, Weyman JT, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. *PLoS One*. 2014;9(1):e85295.
7. Brown BB, Yamada I, Smith KR, Zick CD, Kowaleski-Jones L, Fan JX. Mixed land use and walkability: Variations in land use measures and relationships with BMI, overweight, and obesity. *Health Place*. 2009;15(4):1130-1141.
8. Jia P, Pan X, Liu F, et al. Land use mix in the neighbourhood and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13098.
9. Rundle AG, Heymsfield SB. Can Walkable Urban Design Play a Role in Reducing the Incidence of Obesity-Related Conditions? *JAMA*. 2016;315(20):2175-2177.
10. Wei J, Wu Y, Zheng J, Nie P, Jia P, Wang Y. Neighborhood sidewalk access and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13057.
11. Xu F, Jin L, Qin Z, et al. Access to public transport and childhood obesity: A systematic review. *Obes Rev*. 2021;22 Suppl 1:e12987.
12. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. *BMJ Open*. 2016;6(2):e008878.
13. Sugiyama T, Neuhaus M, Cole R, Giles-Corti B, Owen N. Destination and route attributes associated with adults' walking: a review. *Med Sci Sports Exerc*. 2012;44(7):1275-1286.
14. Gunn LD, Mavoa S, Boulange C, Hooper P, Kavanagh A, Giles-Corti B. Designing healthy communities: creating evidence on metrics for built environment features associated with walkable neighbourhood activity centres. *Int J Behav Nutr Phys Act*. 2017;14(1):164.
15. McCormack GR, Giles-Corti B, Bulsara M. The relationship between destination proximity, destination mix and physical activity behaviors. *Prev Med*. 2008;46(1):33-40.
16. Day K. Built environmental correlates of physical activity in China: A review. *Prev Med Rep*. 2016;3:303-316.
17. Grasser G, Van Dyck D, Titze S, Stronegger W. Objectively measured walkability and active transport and weight-related outcomes in adults: a systematic review. *Int J Public Health*. 2013;58(4):615-625.
18. Creatore MI, Glazier RH, Moineddin R, et al. Association of Neighborhood Walkability With Change in Overweight, Obesity, and Diabetes. *JAMA*. 2016;315(20):2211-2220.

19. Smith KR, Brown BB, Yamada I, Kowaleski-Jones L, Zick CD, Fan JX. Walkability and body mass index density, design, and new diversity measures. *Am J Prev Med*. 2008;35(3):237-244.
20. Troped PJ, Starnes HA, Puett RC, et al. Relationships between the built environment and walking and weight status among older women in three U.S. States. *J Aging Phys Act*. 2014;22(1):114-125.
21. Inagami S, Cohen DA, Brown AF, Asch SM. Body mass index, neighborhood fast food and restaurant concentration, and car ownership. *J Urban Health*. 2009;86(5):683-695.
22. Thielman J, Copes R, Rosella LC, Chiu M, Manson H. Is neighbourhood walkability related to body mass index among different age groups? A cross-sectional study of Canadian urban areas. *BMJ Open*. 2019;9(11):e032475.
23. Frank LD, Andresen MA, Schmid TL. Obesity relationships with community design, physical activity, and time spent in cars. *Am J Prev Med*. 2004;27(2):87-96.
24. Boehmer TK, Lovegreen SL, Haire-Joshu D, Brownson RC. What constitutes an obesogenic environment in rural communities? *Am J Health Promot*. 2006;20(6):411-421.
25. Rutt CD, Coleman KJ. Examining the relationships among built environment, physical activity, and body mass index in El Paso, TX. *Prev Med*. 2005;40(6):831-841.
26. Zhang X, Zhang M, Zhao Z, et al. Obesogenic environmental factors of adult obesity in China: a nationally representative cross-sectional study. *Environmental Research Letters*. 2020;15(4):044009.
27. Troy AR, Bonnell LN, Littenberg B. Relationship Between the Built Environment and Body Mass Index in a Rural Context: A Cross-Sectional Study from Vermont. *Cureus*. 2018;10(7):e3040.
28. Littenberg B, Lubetkin D. Availability, Strengths and Limitations of US State Driver's License Data for Obesity Research. *Cureus*. 2016;8(3):e518.
29. Buehler R, Pucher J, Merom D, Bauman A. Active travel in Germany and the U.S. Contributions of daily walking and cycling to physical activity. *Am J Prev Med*. 2011;41(3):241-250.
30. Pucher J, Buehler R, Merom D, Bauman A. Walking and cycling in the United States, 2001-2009: evidence from the National Household Travel Surveys. *Am J Public Health*. 2011;101 Suppl 1:S310-317.
31. Royston P. Lowess Smoothing. *Stata Tech Bull Reprints*. 1991;1:41-44.
32. Butler DC, Petterson S, Phillips RL, Bazemore AW. Measures of social deprivation that predict health care access and need within a rational area of primary care service delivery. *Health Serv Res*. 2013;48(2 Pt 1):539-559.
33. Jia P, Yu C, Remais JV, et al. Spatial Lifecourse Epidemiology Reporting Standards (ISLE-ReSt) statement. *Health Place*. 2020;61:102243.
34. Fryar CD, Kruszon-Moran D, Gu Q, Ogden CL. Mean Body Weight, Height, Waist Circumference, and Body Mass Index Among Adults: United States, 1999-2000 Through 2015-2016. *Natl Health Stat Report*. 2018(122):1-16.
35. Nelson MC, Gordon-Larsen P, Song Y, Popkin BM. Built and social environments associations with adolescent overweight and activity. *Am J Prev Med*. 2006;31(2):109-117.
36. Bassett DR, Schneider PL, Huntington GE. Physical activity in an Old Order Amish community. *Med Sci Sports Exerc*. 2004;36(1):79-85.

37. Bassett DR, Jr., Tremblay MS, Esliger DW, Copeland JL, Barnes JD, Huntington GE. Physical activity and body mass index of children in an old order Amish community. *Med Sci Sports Exerc*. 2007;39(3):410-415.
38. Matz CJ, Stieb DM, Davis K, et al. Effects of age, season, gender and urban-rural status on time-activity: CanadianHuman Activity Pattern Survey 2 (CHAPS 2). *Int J Environ Res Public Health*. 2014;11(2):2108-2124.
39. Littenberg B, Bonnell LN, LeBruin AS, Lubetkin DA, Troy AR, Zia A. The Relationship Between Access to Natural Environmental Amenities and Obesity. *Cureus*. 2015;7(11):e377.
40. Witten K, Hiscock R, Pearce J, Blakely T. Neighbourhood access to open spaces and the physical activity of residents: a national study. *Prev Med*. 2008;47(3):299-303.
41. Stewart AW, Jackson RT, Ford MA, Beaglehole R. Underestimation of relative weight by use of self-reported height and weight. *Am J Epidemiol*. 1987;125(1):122-126.
42. Le A, Judd SE, Allison DB, et al. The geographic distribution of obesity in the US and the potential regional differences in misreporting of obesity. *Obesity (Silver Spring)*. 2014;22(1):300-306.
43. Boone-Heinonen J, Guilkey DK, Evenson KR, Gordon-Larsen P. Residential self-selection bias in the estimation of built environment effects on physical activity between adolescence and young adulthood. *Int J Behav Nutr Phys Act*. 2010;7:70.
44. Jones KK, Zenk SN, Tarlov E, Powell LM, Matthews SA, Horoi I. A step-by-step approach to improve data quality when using commercial business lists to characterize retail food environments. *BMC Res Notes*. 2017;10(1):35.
45. Fleischhacker SE, Evenson KR, Sharkey J, Pitts SB, Rodriguez DA. Validity of secondary retail food outlet data: a systematic review. *Am J Prev Med*. 2013;45(4):462-473.
46. Kwan M-P. The Uncertain Geographic Context Problem. *Annals of the Association of American Geographers*. 2012;102(5):958-968.
47. Jia P, Zou Y, Wu Z, et al. Street connectivity, physical activity, and childhood obesity: A systematic review and meta-analysis. *Obes Rev*. 2021;22 Suppl 1:e12943.
48. Zou Y, Ma Y, Wu Z, et al. Neighbourhood residential density and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13037.
49. Boehmer TK, Hoehner CM, Deshpande AD, Brennan Ramirez LK, Brownson RC. Perceived and observed neighborhood indicators of obesity among urban adults. *Int J Obes (Lond)*. 2007;31(6):968-977.
50. Xu Y, Wang F. Built environment and obesity by urbanicity in the U.S. *Health Place*. 2015;34:19-29.
51. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. *Progress in Physical Geography: Earth and Environment*. 2007;31(5):471-479.
52. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. *Health Place*. 2010;16(2):175-190.
53. Druss B, Walker E. Mental Disorders and medical comorbidity THE SYNTHESIS PROJECT. Access June 18. In:2011.
54. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans. 2nd ed. Washington, DC: U.S. Department of Health and Human Services; 2018.

55. Wingood M, Bonnell L, LaCroix AZ, et al. Community-Dwelling Older Adults and Physical Activity Recommendations: Patterns of Aerobic, Strengthening, and Balance Activities. *J Aging Phys Act*. 2021:1-13.
56. U.S. Department of Health and Human Services. Step It Up! The Surgeon General's Call to Action to Promote Walking and Walkable Communities. Washington, DC: U.S. Dept of Health and Human Services, Office of the Surgeon General. 2015.
57. Ewing R, Cervero R. Travel and the Built Environment: A Synthesis. *Transportation Research Record.* 2001;1780(1):87-114.
58. Creatore MI, Glazier RH, Moineddin R, et al. Association of Neighborhood Walkability With Change in Overweight, Obesity, and Diabetes. *JAMA.* 2016;315(20):2211-2220.
59. Glazier RH, Creatore MI, Weyman JT, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. *PLoS One.* 2014;9(1):e85295.
60. Jia P, Pan X, Liu F, et al. Land use mix in the neighbourhood and childhood obesity. *Obes Rev*. 2021;22 Suppl 1:e13098.
61. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. *BMJ Open.* 2016;6(2):e008878.
62. Rundle AG, Heymsfield SB. Can Walkable Urban Design Play a Role in Reducing the Incidence of Obesity-Related Conditions? *JAMA.* 2016;315(20):2175-2177.
63. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. *Health Place.* 2010;16(2):175-190.
64. Roe J, Mondschein A, Neale C, Barnes L, Boukhechba M, Lopez S. The Urban Built Environment, Walking and Mental Health Outcomes Among Older Adults: A Pilot Study. *Front Public Health.* 2020;8:575946.
65. Evans GW. The built environment and mental health. *J Urban Health.* 2003;80(4):536-555.
66. Berke EM, Gottlieb LM, Moudon AV, Larson EB. Protective association between neighborhood walkability and depression in older men. *J Am Geriatr Soc.* 2007;55(4):526-533.
67. Rachele JN, Sugiyama T, Davies S, et al. Neighbourhood built environment and physical function among mid-to-older aged adults: A systematic review. *Health Place.* 2019;58:102137.
68. Barnett DW, Barnett A, Nathan A, et al. Built environmental correlates of older adults' total physical activity and walking: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act*. 2017;14(1):103.
69. Cerin E, Nathan A, van Cauwenberg J, et al. The neighbourhood physical environment and active travel in older adults: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act*. 2017;14(1):15.

70. Sugiyama T, Neuhaus M, Cole R, Giles-Corti B, Owen N. Destination and route attributes associated with adults' walking: a review. *Med Sci Sports Exerc.* 2012;44(7):1275-1286.
71. Day K. Built environmental correlates of physical activity in China: A review. *Prev Med Rep.* 2016;3:303-316.
72. Troped PJ, Starnes HA, Puett RC, et al. Relationships between the built environment and walking and weight status among older women in three U.S. States. *J Aging Phys Act.* 2014;22(1):114-125.
73. Booth GL, Creatore MI, Luo J, et al. Neighbourhood walkability and the incidence of diabetes: an inverse probability of treatment weighting analysis. *J Epidemiol Community Health.* 2019;73(4):287-294.
74. Howell NA, Tu JV, Moineddin R, Chu A, Booth GL. Association Between Neighborhood Walkability and Predicted 10-Year Cardiovascular Disease Risk: The CANHEART (Cardiovascular Health in Ambulatory Care Research Team) Cohort. *J Am Heart Assoc.* 2019;8(21):e013146.
75. Braver NRd, Rutters F, Wagtendonk AJ, et al. Neighborhood walkability, physical activity and changes in glycemic markers in people with type 2 diabetes: The Hoorn Diabetes Care System cohort. *Health Place.* 2021;69:102560.
76. Boehmer TK, Lovegreen SL, Haire-Joshu D, Brownson RC. What constitutes an obesogenic environment in rural communities? *Am J Health Promot.* 2006;20(6):411-421.
77. Zhang X, Zhang M, Zhao Z, et al. Obesogenic environmental factors of adult obesity in China: a nationally representative cross-sectional study. *Environmental Research Letters.* 2020;15(4):044009.
78. Rutt CD, Coleman KJ. Examining the relationships among built environment, physical activity, and body mass index in El Paso, TX. *Prev Med.* 2005;40(6):831-841.
79. Troy AR, Bonnell LN, Littenberg B. Relationship Between the Built Environment and Body Mass Index in a Rural Context: A Cross-Sectional Study from Vermont. *Cureus.* 2018;10(7):e3040.
80. Bonnell LN, Troy AR, Littenberg B. Nonlinear relationship between nonresidential destinations and body mass index across a wide range of development. *Prev Med.* 2021;153:106775.
81. Crocker AM, Kessler R, van Eeghen C, et al. Integrating Behavioral Health and Primary Care (IBH-PC) to improve patient-centered outcomes in adults with multiple chronic medical and behavioral health conditions: study protocol for a pragmatic cluster-randomized control trial. *Trials.* 2021;22(1):200.
82. Buehler R, Pucher J, Merom D, Bauman A. Active travel in Germany and the U.S. Contributions of daily walking and cycling to physical activity. *Am J Prev Med.* 2011;41(3):241-250.

83. Pucher J, Buehler R, Merom D, Bauman A. Walking and cycling in the United States, 2001-2009: evidence from the National Household Travel Surveys. *Am J Public Health*. 2011;101 Suppl 1:S310-317.
84. Butler DC, Petterson S, Phillips RL, Bazemore AW. Measures of social deprivation that predict health care access and need within a rational area of primary care service delivery. *Health Serv Res*. 2013;48(2 Pt 1):539-559.
85. Rural Health Research Center (RHRC). Rural-urban commuting area codes (RUCAs), 2008. Available at: http://depts.washington.edu/uwruca/.
86. Khan S, Pinault L, Tjepkema M, Wilkins R. Positional accuracy of geocoding from residential postal codes versus full street addresses. *Health Rep*. 2018;29(2):3-9.
87. Royston P. Lowess Smoothing. *Stata Tech Bull Reprints*. 1991;1:41-44.
88. Moran P. Notes on continuous stochastic phenomena. *Biometrika*. 1950;37(1-2):17-23.
89. Anselin L, Syabri I, Kho Y. GeoDa: An Introduction to Spatial Data Analysis. In: Fischer MM, Getis A, eds. *Handbook of Applied Spatial Analysis: Software Tools, Methods and Applications*. Berlin, Heidelberg: Springer Berlin Heidelberg; 2010:73-89.
90. Jia P, Yu C, Remais JV, et al. Spatial Lifecourse Epidemiology Reporting Standards (ISLE-ReSt) statement. *Health Place*. 2020;61:102243.
91. Stierman B AJ, Carroll MD, Chen TC, Davy O, Fink S. National Health and Nutrition Examination Survey 2017–March 2020 prepandemic data files—Development of files and prevalence estimates for selected health outcomes. National Health Statistics Reports; no 158. Hyattsville, MD: National Center for Health Statistics. 2021.
92. Bassett DR, Jr., Tremblay MS, Esliger DW, Copeland JL, Barnes JD, Huntington GE. Physical activity and body mass index of children in an old order Amish community. *Med Sci Sports Exerc*. 2007;39(3):410-415.
93. Bassett DR, Schneider PL, Huntington GE. Physical activity in an Old Order Amish community. *Med Sci Sports Exerc*. 2004;36(1):79-85.
94. Roy B, Hajduk AM, Tsang S, et al. The association of neighborhood walkability with health outcomes in older adults after acute myocardial infarction: The SILVER-AMI study. *Prev Med Rep*. 2021;23:101391.
95. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. *Progress in Physical Geography: Earth and Environment*. 2007;31(5):471-479.
96. Le A, Judd SE, Allison DB, et al. The geographic distribution of obesity in the US and the potential regional differences in misreporting of obesity. *Obesity (Silver Spring)*. 2014;22(1):300-306.
97. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430-436.

98. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. Health Place. 2010;16(2):175-90.
99. Glazier RH, Creatore MI, Weyman JT, Fazli G, Matheson FI, Gozdyra P, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. PLoS One. 2014;9(1):e85295.
100. Muldoon KA, Duff PK, Fielden S, Anema A. Food insufficiency is associated with psychiatric morbidity in a nationally representative study of mental illness among food insecure Canadians. Social Psychiatry and Psychiatric Epidemiology. 2013;48(5):795-803.
101. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. BMJ Open. 2016;6(2):e008878.
102. Pan L, Sherry B, Njai R, Blanck HM. Food insecurity is associated with obesity among US adults in 12 states. J Acad Nutr Diet. 2012;112(9):1403-9.
103. Xu F, Jin L, Qin Z, Chen X, Xu Z, He J, et al. Access to public transport and childhood obesity: A systematic review. Obes Rev. 2021;22 Suppl 1:e12987.
104. Brown BB, Yamada I, Smith KR, Zick CD, Kowaleski-Jones L, Fan JX. Mixed land use and walkability: Variations in land use measures and relationships with BMI, overweight, and obesity. Health Place. 2009;15(4):1130-41.
105. Gunn LD, Mavoa S, Boulange C, Hooper P, Kavanagh A, Giles-Corti B. Designing healthy communities: creating evidence on metrics for built environment features associated with walkable neighbourhood activity centres. Int J Behav Nutr Phys Act. 2017;14(1):164.
106. Manisalidis I, Stavropoulou E, Stavropoulos A, Bezirtzoglou E. Environmental and Health Impacts of Air Pollution: A Review. Front Public Health. 2020;8:14.
107. Leaning J, Guha-Sapir D. Natural disasters, armed conflict, and public health. The New England journal of medicine. 2013;369(19):1836-42.
108. Alavanja MC, Sandler DP, McMaster SB, Zahm SH, McDonnell CJ, Lynch CF, et al. The Agricultural Health Study. Environ Health Perspect. 1996;104(4):362-9.
109. Gianfredi V, Buffoli M, Rebecchi A, Croci R, Oradini-Alacreu A, Stirparo G, et al. Association between Urban Greenspace and Health: A Systematic Review of Literature. Int J Environ Res Public Health. 2021;18(10).
110. Kellert SR, Wilson EO. The biophilia hypothesis: Island press; 1993.
111. Jimenez MP, DeVille NV, Elliott EG, Schiff JE, Wilt GE, Hart JE, et al. Associations between Nature Exposure and Health: A Review of the Evidence. Int J Environ Res Public Health. 2021;18(9).
112. Lin G, Spann S, Hyman D, Pavlik V. Climate amenity and BMI. Obesity (Silver Spring). 2007;15(8):2120-7.

113. Littenberg B, Bonnell LN, LeBruin AS, Lubetkin DA, Troy AR, Zia A. The Relationship Between Access to Natural Environmental Amenities and Obesity. Cureus. 2015;7(11):e377.
114. Bonnell LN, Troy AR, Littenberg B. Nonlinear relationship between nonresidential destinations and body mass index across a wide range of development. Prev Med. 2021;153:106775.
115. James P, Kioumourtzoglou MA, Hart JE, Banay RF, Kloog I, Laden F. Interrelationships Between Walkability, Air Pollution, Greenness, and Body Mass Index. Epidemiology. 2017;28(6):780-8.
116. Yin C, Yao X, Sun B. Population density and obesity in rural China: Mediation effects of car ownership. Transportation Research Part D: Transport and Environment. 2022;105:103228.
117. Crocker AM, Kessler R, van Eeghen C, Bonnell LN, Breshears RE, Callas P, et al. Integrating Behavioral Health and Primary Care (IBH-PC) to improve patient-centered outcomes in adults with multiple chronic medical and behavioral health conditions: study protocol for a pragmatic cluster-randomized control trial. Trials. 2021;22(1):200.
118. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. J Clin Epidemiol. 2010;63(11):1179-94.
119. Hays RD, Spritzer KL, Schalet BD, Cella D. PROMIS((R))-29 v2.0 profile physical and mental health summary scores. Qual Life Res. 2018;27(7):1885-91.
120. Natural Amenities Scale. Internet. U.S. Department of Agriculture. Economic Research Service. 1999. Available from: http://www.ers.usda.gov/data-products/natural-amenities-scale.aspx.
121. McGranahan DA. Natural Amenities Drive Rural Population Change. Agricultural Economic Report No. (AER-781). United States Department of Agriculture Economic Research Service. 1999, AER-781:.
122. Ratcliffe M, Burd C, Holder K, Fields A. Defining Rural at the U.S. Census Bureau, ACSGEO-1, U.S. Census Bureau, Washington, DC. 2016.
123. Royston P. Lowess Smoothing. Stata Tech Bull Reprints. 1991;1:41-4.
124. Bozdogan H. Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. Psychometrika. 1987;52(3):345-70.
125. Nieuwenhuijsen MJ, Khreis H, Triguero-Mas M, Gascon M, Dadvand P. Fifty Shades of Green: Pathway to Healthy Urban Living. Epidemiology. 2017;28(1):63-71.
126. Beyer KM, Kaltenbach A, Szabo A, Bogar S, Nieto FJ, Malecki KM. Exposure to neighborhood green space and mental health: evidence from the survey of the health of Wisconsin. Int J Environ Res Public Health. 2014;11(3):3453-72.

127. Grahn P, Stigsdotter UK. The relation between perceived sensory dimensions of urban green space and stress restoration. Landscape and Urban Planning. 2010;94(3):264-75.
128. Yang BY, Markevych I, Bloom MS, Heinrich J, Guo Y, Morawska L, et al. Community greenness, blood pressure, and hypertension in urban dwellers: The 33 Communities Chinese Health Study. Environ Int. 2019;126:727-34.
129. Dominski FH, Lorenzetti Branco JH, Buonanno G, Stabile L, Gameiro da Silva M, Andrade A. Effects of air pollution on health: A mapping review of systematic reviews and meta-analyses. Environ Res. 2021;201:111487.
130. Khan KM, Karnati J, Hamid I, Koceja D, Zahirul Islam M, Khan MA. Residential Proximity to Agricultural Fields and Neurological and Mental Health Outcomes in Rural Adults in Matlab, Bangladesh. Int J Environ Res Public Health. 2019;16(18).
131. Rentfrow PJ. Statewide differences in personality: toward a psychological geography of the United States. Am Psychol. 2010;65(6):548-58.
132. Rentfrow PJ. Geographical psychology. Curr Opin Psychol. 2020;32:165-70.
133. Rentfrow PJ, Gosling SD, Jokela M, Stillwell DJ, Kosinski M, Potter J. Divided we stand: three psychological regions of the United States and their political, economic, social, and health correlates. J Pers Soc Psychol. 2013;105(6):996-1012.
134. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. Progress in Physical Geography: Earth and Environment. 2007;31(5):471-9.
135. Druss B, Walker E. Mental Disorders and medical comorbidity THE SYNTHESIS PROJECT. Access June 18. 2011.
136. Wingood M, Bonnell L, LaCroix AZ, et al. Community-Dwelling Older Adults and Physical Activity Recommendations: Patterns of Aerobic, Strengthening, and Balance Activities. J Aging Phys Act 2021:1-13.
137. Ding D, Gebel K. Built environment, physical activity, and obesity: what have we learned from reviewing the literature? Health Place 2012;18:100-5.
138. Ewing R, Cervero R. Travel and the Built Environment: A Synthesis. Transportation Research Record 2001;1780:87-114.
139. Handy SL, Boarnet MG, Ewing R, Killingsworth RE. How the built environment affects physical activity: views from urban planning. Am J Prev Med 2002;23:64-73.
140. Barnett DW, Barnett A, Nathan A, et al. Built environmental correlates of older adults' total physical activity and walking: a systematic review and meta-analysis. Int J Behav Nutr Phys Act 2017;14:103.
141. Cerin E, Nathan A, van Cauwenberg J, et al. The neighbourhood physical environment and active travel in older adults: a systematic review and meta-analysis. Int J Behav Nutr Phys Act 2017;14:15.
142. Creatore MI, Glazier RH, Moineddin R, et al. Association of Neighborhood Walkability With Change in Overweight, Obesity, and Diabetes. JAMA 2016;315:2211-20.

143. Glazier RH, Creatore MI, Weyman JT, et al. Density, destinations or both? A comparison of measures of walkability in relation to transportation behaviors, obesity and diabetes in Toronto, Canada. PLoS One 2014;9:e85295.
144. Jia P, Pan X, Liu F, et al. Land use mix in the neighbourhood and childhood obesity. Obes Rev 2021;22 Suppl 1:e13098.
145. King TL, Bentley RJ, Thornton LE, Kavanagh AM. Using kernel density estimation to understand the influence of neighbourhood destinations on BMI. BMJ Open 2016;6:e008878.
146. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. Health Place 2010;16:175-90.
147. Center for Substance Abuse Treatment. Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders. Substance Abuse and Mental Health Services Administration (US). Treatment Improvement Protocol (TIP) Series, No. 54. Rockville (MD). 2012.
148. Schulz M, Romppel M, Grande G. Built environment and health: a systematic review of studies in Germany. J Public Health (Oxf) 2018;40:8-15.
149. Troy AR, Bonnell LN, Littenberg B. Relationship Between the Built Environment and Body Mass Index in a Rural Context: A Cross-Sectional Study from Vermont. Cureus 2018;10:e3040.
150. Sun B, Yao X, Yin C. An N-Shaped Association between Population Density and Abdominal Obesity. Int J Environ Res Public Health 2022;19.
151. Yin C, Cao J, Sun B. Examining non-linear associations between population density and waist-hip ratio: An application of gradient boosting decision trees. Cities 2020;107:102899.
152. Bonnell LN, Troy AR, Littenberg B. Nonlinear relationship between nonresidential destinations and body mass index across a wide range of development. Prev Med 2021;153:106775.
153. Bonnell LN, Troy AR, Littenberg B. Exploring non-linear relationships between neighbourhood walkability and health: a cross-sectional study among US primary care patients with chronic conditions. BMJ Open 2022;12:e061086.
154. Sarkar C, Webster C, Gallacher J. Association between adiposity outcomes and residential density: a full-data, cross-sectional analysis of 419 562 UK Biobank adult participants. Lancet Planet Health 2017;1:e277-e88.
155. Murphy M, Badland H, Jordan H, Koohsari MJ, Giles-Corti B. Local Food Environments, Suburban Development, and BMI: A Mixed Methods Study. Int J Environ Res Public Health 2018;15.
156. Park JH, Lai TF, Chang CS, Huang WC, Cho JS, Liao Y. A Nonlinear Association between Neighborhood Walkability and Risks of Sarcopenia in Older Adults. J Nutr Health Aging 2021;25:618-23.

157. James P, Kioumourtzoglou MA, Hart JE, Banay RF, Kloog I, Laden F. Interrelationships Between Walkability, Air Pollution, Greenness, and Body Mass Index. Epidemiology 2017;28:780-8.
158. Bonnell LN, Littenberg B. Nonlinear Relationships among the Natural Environment, Health, and Sociodemographic Characteristics across US Counties. Int J Environ Res Public Health 2022;19.
159. Bozdogan H. Model selection and Akaike's Information Criterion (AIC): The general theory and its analytical extensions. Psychometrika 1987;52:345-70.
160. Dark SJ, Bram D. The modifiable areal unit problem (MAUP) in physical geography. Progress in Physical Geography: Earth and Environment 2007;31:471-9.
161. Bodea TD, Garrow LA, Meyer MD, Ross CL. Explaining obesity with urban form: a cautionary tale. Transportation 2008;35:179-99.
162. Yin C, Yao X, Sun B. Population density and obesity in rural China: Mediation effects of car ownership. Transportation Research Part D: Transport and Environment 2022;105:103228.
163. Day K. Built environmental correlates of physical activity in China: A review. Prev Med Rep 2016;3:303-16.