

Transportation-related Environmental Mixtures and Diabetes Prevalence and Control in Urban/ **Metropolitan Counties in the United States**

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Abstract

Diabetes rates in the United States are staggering and climbing. Importantly, traditional risk factors fail to completely account for the magnitude of the diabetes epidemic. Environmental exposures, including urban and metropolitan transportation quality, are implicated as contributors to disease. Using data from the county-level Environmental Quality Index (EQI) developed for the United States, we analyzed associations between transportation and air quality environmental metrics with overall diabetes prevalence and control within urban/metropolitan counties in the United States from 2006 to 2012. Additionally, we examined effect modification by race/ethnicity through stratification based on the county-level proportion of minority residents. Last, we applied mixture methods to evaluate the effect of simultaneous poor transportation factors and worse air quality on the same outcomes. We found that increased county-level particulate matter air pollution and nitrogen dioxide along with reduced public transportation usage and lower walkability were all associated with increased diabetes prevalence. The minority proportion of the population influences some of these relationships as some of the effects of air pollution and the transportationrelated environment are worse among counties with more minority residents. Furthermore, the transportation and air quality mixtures were found to be associated with increased diabetes prevalence and reduced diabetes control. These data further support the burgeoning evidence that poor environments amplify diabetes risk. Future cohort studies should explore the utility of environmental policies and urban planning as tools for improving metabolic health.

Key Words: diabetes, transportation, walkability, public transportation, air pollution, particulate matter, nitrogen dioxide, commute time, endocrine disruptor, urban planning

Abbreviations: EPA, US Environmental Protection Agency; EQI, Environmental Quality Index; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; IHME, Institute for Health Metrics and Evaluation; NO_2 , nitrogen dioxide; PM, particulate matter.

Currently, an estimated 37.3 million people live with diabetes in the United States, and an additional 96 million adults with prediabetes are at high risk of developing the disease in the coming years [1]. Diabetes is the leading cause of adult blindness, kidney failure, and nontraumatic amputations; contributes to the development of cardiovascular disease; and is a major cause of mortality in the United States [2, 3]. Annual health costs associated with diabetes are estimated to be \$327 billion and rising [4]. Consequently, there is a desperate need to understand the drivers of diabetes risk and to use all available tools to address them, including efforts directed at diabetes risk factors that have been neglected both by clinical interventions and public policy.

It is clear that improving lifestyle factors by increasing physical activity and adhering to healthy diets decreases the likelihood of developing diabetes [5]. Less appreciated is evidence linking environmental factors with diabetes risk, including exposure to diabetogenic chemicals such as air pollution [6-9]. Moreover, the influence of urban design on the health behaviors of urban residents is often overlooked as a potential contributing factor. Urban counties in the United States have some of the highest diabetes rates. Specifically, major metropolitan regions including New York City, Chicago, Los Angeles, and Houston all have a diagnosed diabetes prevalence exceeding 20%, which is 8% higher than the national average [1]. Notably, urban areas are known to be regions with substantial air pollution, while urban planning decisions affect the availability and utility of various forms of transportation [10]. For multiple political and economic reasons, the United States struggles to promote active transportation and limit exposure to traffic-associated air pollution in urban areas [11]. Specifically, urban areas in the United States have been designed to favor motor vehicles as opposed to active transportation, such as walking, cycling, or public transportation [11]. This structural car dependency is reinforced by urban design choices and promotes negative health effects such as sedentary behavior, obesity, smoking, and exposure to air pollution. About 53 000 Americans die prematurely each year from particulate matter (PM) air pollution associated with roadways; indeed, on average 12 years of life are lost per premature death as a result of transportation-related air pollution [12]. Critically, the effect of traffic-related air pollution is disproportionately borne by those with low incomes and communities of color, potentially contributing to important health disparities experienced by these communities, including disproportionate rates and effects of diabetes [13].

Expanding evidence now implicates various environmental factors in the pathogenesis of diabetes [6-9], and our previous work has shown that total environments and various environmental domains are associated both with diabetes prevalence and diabetes control in the United States [14, 15]. However, the precise ways in which urban design influences diabetes status and control remain largely unknown, including sparse data on the effect of transportation infrastructure. To address this important knowledge gap, we conducted an ecological study to determine the associations between transportation, air pollution, and their mixture on diabetes prevalence and control in urban counties in the United States. This study fills data gaps regarding how discrete and mixtures of urban environmental features influence metabolic health and sheds light on how improved urban planning may serve to reduce the devastating burden of diabetes in the United States and globally.

Materials and Methods

Study Design and Data Sources

This ecological study examined the associations between transportation and air pollution environmental quality, both individually and as a mixture, with estimates of countylevel diabetes prevalence and control in metropolitan and urban counties in the United States. For outcome estimates, publicly available data were accessed through the Institute for Health Metrics and Evaluation (IHME) for the years 2006 to 2012 [16]. Additionally, exposure estimates were accessed through the US Environmental Protection Agency (EPA) Environmental Quality Index (EQI) for the years 2006 to 2010 [17]. The EQI is an index of cumulative environmental quality using data from air, water, land, built, and sociodemographic environmental domains constructed using principal components analysis. EQI data and IHME diabetes prevalence and control data were combined by name, state, and county Federal Information Processing Standards code after variable name differences were corrected. To understand the associations of transportation-related environmental quality within urban environments, analyses were restricted to only metropolitan (RUCC1) and nonmetropolitan urban counties (RUCC2) with a final analytical sample of 1473 US counties.

Outcomes

We used the IHME estimates of total diabetes prevalence that were calculated as the age-standardized proportion of individuals per county with a previous diabetes diagnosis or elevated glycated hemoglobin A_{1c} (HbA $_{1c}$) or fasting plasma glucose (FPG). Diabetes control was also estimated by IHME as the proportion of adults with a previous diabetes diagnosis who

currently do not have elevated FPG or HbA_{1c} . Elevated FPG and HbA_{1c} were defined as a FPG of at least 126 mg/dL or HbA_{1c} of at least 6.5%, respectively.

Exposures

All exposure variables were directly extracted from publicly available EQI data and referenced with the EQI technical report. Transportation and air quality variables were extracted from the individual built environment and air domains of the EQI; descriptions of each variable estimation can be found in the EQI technical report [18]. Transportation-related variables included county-level commute time, public transportation usage, and walkability. Commute time, derived from the 2010 census, was estimated as the average number of minutes an employed person spent commuting from home to work. Public transportation, estimated from the 2010 census, was defined as the percentage of county residents who used public transportation. Last, walkability scores were originally sourced from the EPA's National Walkability data, and the EQI walkability index was calculated as a weighted rank of employment type and housing both overall and by block groups, street intersection density, and predicted commuting modes. Air quality exposure variables included nitrogen dioxide (NO₂), PM less than or equal to 10 µm (PM₁₀), and less than or equal to $2.5 \, \mu m$ (PM_{2.5}). Air quality variables were gathered from the Air Quality System (AQS 2006-2010) and estimated from the average annual concentrations for each county at the county's center point for each year from 2006 to 2010. For positive built environment indices, including walkability and public transportation usage, variables were negatively coded so that higher values suggest poorer environmental quality. We used variable data either transformed or not transformed based on the EQI technical report. Air quality variables and public transportation usage were natural logtransformed, while commute time and walkability score remained in their untransformed format.

Covariates

County-level sociodemographic characteristics including average education level, household income, and unemployment rates were also extracted from the sociodemographic domain of the EQI and were used as covariates in the analysis. Additionally, to control for state-level geographical and policy differences, state was also included as a covariate in the analyses. Using 2010 census data, the proportion of the population that identified as non-White for each county was estimated. Counties were categorized as having a high proportion of minority inhabitants by dichotomizing at the median (>18.95%). To assess potential effect modification by proportion of minority population, a cross-product term was introduced into the models for each exposure. Results are presented both overall and stratified by high and low minority proportion. Last, while county level data on obesity and physical activity are available, these factors were not included in our primary analyses as they are likely within the causal pathway.

Statistical Analyses

Sociodemographic characteristics and outcome distributions were summarized for all 1473 counties included in the analysis. Correlation among transportation and air quality

Table 1. Characteristics of selected US counties (N = 1473)

Characteristics	Mean ± SD	
Prevalence of diabetes, %	13.77 ± 2.14	
Prevalence of diabetes control, %	46.87 ± 2.26	
Percentage of individuals with bachelor's degree or higher, %	14.57 ± 5.72	
Percentage of individuals who are unemployed, %	7.68 ± 2.50	
Median household income, \$	70212 ± 153725	
Percentage of minority residents, %	22.8 ± 16.11	

indices were assessed using Spearman rank correlation coefficients. Multivariable linear regression was used to assess the differences in diabetes prevalence and control estimates with worse transportation and air-related environmental quality. The multivariable models were adjusted for confounders established a priori, including education, unemployment, household income, and state [19]. Multicollinearity for each exposure variable was not detected based on variance inflation factors less than 1.5. Exposure variables were modeled as continuous exposures as documented in the EQI technical report [18]. To assess potential effect modification by countylevel minority ethnicity, a cross-product term was introduced into the models for each exposure with high/low county minority population proportion. Results are presented both overall and stratified by high and low minority proportion. Last, outcomes were log-transformed because of skewed distributions and regression coefficients were interpreted as percentage differences per unit increase in exposure using the following equation: $(e^{\beta} - 1) \times 100$. As a result, the coefficients from the linear models can be interpreted as percentage differences in either average county-level diabetes prevalence or control per increase in non-log-transformed exposure variables and per 2.7-fold increase in log-transformed variables. Despite considering obesity and physical activity to be within the causal pathway for the relationship between transportation, air quality, and diabetes, these factors are major predictors of diabetes risk. Consequently, we conducted a sensitivity analysis further adjusting both for county-level obesity and physical activity prevalence collected and estimated by IHME. The described analyses were performed using SAS software version 9.4 (SAS Institute Inc).

To evaluate the associations of the environmental quality mixture with the diabetes outcomes, quantile-based g computation (qgcomp) was used [20]. Although mixture approaches are typically used to evaluate chemical mixtures that drive health outcomes, we applied this approach to evaluate the association of a mixture of environmental quality factors on continuous diabetes outcomes. For the mixture analyses the exposure variables were distributed by quartile. Using generalized linear regression, the weights of each variable were evaluated along a Gaussian distribution for log-transformed diabetes outcomes. Specific variable weights were interpreted as the individual partial effect of that variable within the mixture. The transportation/air quality variables for each outcome were estimated using g-computation algorithms with a bootstrap of 1000 iterations. The sum of the regression coefficients was then applied and interpreted as the percentage difference in the log-transformed diabetes estimates as all indices increase by one quartile. To assess for mixture synergy, mixture associations were assessed both for air quality variables and transportation-related variables separately in addition to a joint transportation/air quality variable mixture association. The qgcomp R package was used to perform the described quantile-based g computation analysis in R version 3.0.2 (R Foundation for Statistical Computing).

Results

County Characteristics

After restricting our analyses to only urban and metropolitan US counties, 1473 counties were included in the final individual and mixture analyses. Descriptive characteristics of these counties are shown in Table 1. Estimated by IHME, diabetes prevalence was calculated as the age-standardized proportion of individuals per county with a previous diabetes diagnosis or HbA_{1c} or FPG based on the American Diabetes Association diagnostic criteria [21]. Diabetes control was estimated by IHME as the proportion of adults with a previous diabetes diagnosis who currently do not have elevated FPG or HbA_{1c} [15]. Among urban/metropolitan counties, the average diabetes prevalence was 14%, while the average prevalence of diabetes control was only 47%. On average, 15% of individuals had a bachelor's degree or higher, while the average percentage of people who were unemployed was 8%. Last, the median household income among these urban US counties was approximately \$70 000. Supplementary Table S1 depicts the Spearman correlation coefficients between the transportation and air quality indices [22]. There were weak to moderate correlations between factors, with the highest association between walkability and public transportation usage at 0.46.

Air Quality and Transportation Variables

After adjustment for average county education, employment, household income, and state, there were significant associations between air quality and transportation both with average diabetes prevalence and control. The estimated effects for transportation and air quality variables on average diabetes prevalence in urban and metropolitan counties stratified by minority proportion are shown in Table 2. Worse air quality, indicated by higher NO₂, PM₁₀, and PM_{2.5}, was associated with a 0.8%, 3.6%, and 3% higher diabetes prevalence per 2.7-fold increase in each exposure, respectively (P = .03; P < .0001; P = .03). Regarding transportation variables, less usage of public transportation was associated with a 1.1% increase in diabetes prevalence per 2-fold decrease in public transportation usage (P < .001). Furthermore, worse walkability was associated with 0.4% higher diabetes prevalence per point decrease in walkability score (P = .004). Conversely, higher commute times were associated with reduced diabetes prevalence (P < .001).

There was statistically significant interaction between PM_{10} , commute time, and walkability with high and low minority proportion within a county (see Table 2). Specifically, the association between PM_{10} increases to a 5.3% increase in diabetes prevalence for counties with a high minority population (P < .001). Furthermore, the association for commute time remains only among counties with a low minority population (P < .001). Last, the association for walkability on diabetes prevalence is consistent across both strata; however, the magnitude of the association is greater among counties with a low proportion of minority residents (P < .001).

Table 2. Percentage difference (95% CI) of average diabetes prevalence and control (2006-2012) in relation to Environmental Quality Index variable among urban counties in the United States (N = 1473)^{a,b,c,d}

Diabetes prevalence β (95% CI) P β (2000 CI) β (2000 CI		Overall		Low minority proportion $(n = 737)$	737)	High minority proportion (n = 736)	736)	Interaction
revalence 0.84 (0.10 to 1.58) 0.25 0.50 (-0.48 to 1.49) 0.315 1.22 (0.18 to 2.25) 3.60 (1.90 to 5.31) 3.03 (0.28 to 5.79) 3.03 (0.28 to 5.79) 2.029 3.52 (-0.07 to 7.13) 3.03 (0.28 to 5.90) 3.03 (0.29 to 1.48) 3.03 (0.29 to 1.48) 3.04 (0.69 to 1.48) 3.05 (0.69 to 1.48) 3.06 (1.90 to 5.31) 3.07 (-1.80 to 3.35) 3.52 (-0.07 to 7.13) 3.52 (-0.07 to 7.13) 3.52 (-0.07 to 7.13) 3.52 (-0.07 to 7.13) 3.53 (3.20 to 7.44) 3.03 (0.28 to 5.90) 3.52 (-0.07 to 7.13) 3.03 (0.28 to 5.90) 3.52 (-0.07 to 7.13) 3.04 (0.09 to 1.48) 3.05 (0.43 to 1.30) 3.05 (0.40 (-0.08 to 0.082) 3.05 (0.40 (-0.081 to 0.082) 3.05 (0.00 (-0.091 to 0.082) 3.05 (0.00 (-0.081 to 0.083) 3.05 (0.00 (-0.081 to 0.0077) 3.05 (0.00 (-0.081 to 0.083) 3.05 (0.00 (-0.081 to 0.093) 3.05 (0.00 (-0.081 to 0.0077)	Variable	β (95% CI)	Ь	β (95% CI)	Ь	β (95% CI)	Ь	Ь
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Diabetes prevalence							
3.60 (1.90 to 5.31) $<.001$ $.77 (-1.80 \text{ to } 3.35)$ $.556$ $5.32 (3.20 \text{ to } 7.44)$ $<.001$ 3.03 (0.28 to 5.79) 0.29 $3.52 (-0.07 \text{ to } 7.13)$ 0.56 $2.66 (-0.58 \text{ to } 5.90)$ sportation use $-0.13 (-0.21 \text{ to } -0.061)$ $<.001$ $-0.26 (-0.17 \text{ to } 0.033)$ $<.001$ sportation use $1.08 (0.69 \text{ to } 1.48)$ $<.001$ $1.13 (0.55 \text{ to } 1.71)$ $<.001$ $1.05 (0.57 \text{ to } 1.53)$ $<.006 (-0.17 \text{ to } 0.033)$ y $0.407 (0.13 \text{ to } 0.68)$ 0.049 $0.28 (0.43 \text{ to } 1.30)$ $<.001$ $1.05 (0.57 \text{ to } 1.53)$ $<.029 (-0.024 \text{ to } 0.58)$ nutrol $-0.46 (-0.88 \text{ to } -0.050)$ 0.29 $-0.44 (-1.00 \text{ to } 0.11)$ $0.29 (-0.024 \text{ to } 0.082)$ $<.029 (-0.024 \text{ to } 0.092)$ $-0.46 (-0.88 \text{ to } -0.050)$ 0.29 $-0.44 (-1.90 \text{ to } 0.90)$ $.461$ $-0.49 (-1.07 \text{ to } 0.082)$ $-0.83 (-2.33 \text{ to } 0.67)$ 0.29 $-0.44 (-1.90 \text{ to } 0.90)$ $.461$ $-0.33 (-0.077 \text{ to } 0.035)$ sportation use $-0.049 (-0.091 \text{ to } -0.072)$ 0.29 $-0.081 (-0.14 \text{ to } -0.021)$ 0.00 $-0.021 (-0.025 $	$Air NO_2$	0.84 (0.10 to 1.58)	.025	0.50 (-0.48 to 1.49)	0.315	1.22 (0.18 to 2.25)	.021	.307
time $-0.13 (0.28 \text{ to } 5.79)$ 0.29 $3.52 (-0.07 \text{ to } 7.13)$ 0.56 $2.66 (-0.58 \text{ to } 5.90)$ sportation use $-0.13 (-0.21 \text{ to } -0.061)$ 0.001 $0.21 (-0.21 \text{ to } -0.061)$ 0.001 0.001 $0.006 (-0.17 \text{ to } 0.033)$ sportation use $-0.13 (-0.21 \text{ to } -0.061)$ 0.001 0.001 0.001 0.001 0.000 0.001	${ m Air\ PM}_{10}$	3.60 (1.90 to 5.31)	<.001	.77 (-1.80 to 3.35)	.556	5.32 (3.20 to 7.44)	<.001	900.
inne $-0.13 (-0.21 \text{ to} -0.061)$ $<.001$ $-0.21 (-0.32 \text{ to} -0.11)$ $<.001$ $-0.066 (-0.17 \text{ to} 0.033)$ $<.001$ $1.08 (0.69 \text{ to} 1.48)$ $<.001$ $1.03 (0.55 \text{ to} 1.71)$ $<.001$ $1.05 (0.57 \text{ to} 1.53)$ $<.004$ $0.86 (0.43 \text{ to} 1.30)$ $<.001$ $0.29 (-0.0024 \text{ to} 0.58)$ $<.004$ $0.86 (0.43 \text{ to} 1.30)$ $<.001$ $0.29 (-0.0024 \text{ to} 0.58)$ $<.001$ $0.29 (-0.0024 \text{ to} 0.082)$ $<.001$ $0.29 (-0.0011)$ $0.29 (-0.0024 \text{ to} 0.090)$ $0.29 (-0.0924 \text{ to} 0.082)$ $<.001$ $0.29 (-0.0924 \text{ to} 0.090)$ $0.29 (-0.0924 \text{ to} 0.092)$ $0.29 (-0.0924 \text{ to} 0.090)$ $0.29 (-0.0924 \text{ to} 0.092)$ $0.29 (-0.0924 \text{ to} 0.090)$ $0.29 (-0.0924 \text{ to} 0.0924)$ $0.29 (-0.0924 \text{ to} 0.0927)$ $0.29 (-0.0924 \text{ to} 0.0927)$ $0.29 (-0.0924 \text{ to} 0.0927)$	Air PM _{2.5}	3.03 (0.28 to 5.79)	.029	3.52 (-0.07 to 7.13)	.056	2.66 (-0.58 to 5.90)	.107	.677
sportation use $1.08 (0.69 \text{ to } 1.48)$ $<.001$ $1.13 (0.55 \text{ to } 1.71)$ $<.001$ $1.05 (0.57 \text{ to } 1.53)$ $<.0024 \text{ to } 0.58)$ y $0.407 (0.13 \text{ to } 0.68)$ 0.04 $0.86 (0.43 \text{ to } 1.30)$ $<.001$ $0.29 (-0.0024 \text{ to } 0.58)$ $<.0024 \text{ to } 0.58)$ nutrol $-0.46 (-0.88 \text{ to } -0.050)$ $.029$ $-0.44 (-1.00 \text{ to } 0.11)$ $.121$ $-0.49 (-1.07 \text{ to } 0.082)$ $<.002 (-0.024 \text{ to } 0.082)$ $-1.67 (-2.59 \text{ to } -0.75)$ $<.001$ $-0.54 (-1.99 \text{ to } 0.90)$ $.461$ $-2.33 (-3.45 \text{ to } -1.22)$ $<.0.32 (-0.49 (-0.025 \text{ to } 0.02))$ cime $-0.83 (-2.33 \text{ to } 0.67)$ $.282$ $-3.24 (-5.14 \text{ to } -1.33)$ $.001$ $1.01 (-0.078 \text{ to } 0.035)$ sportation use $-0.049 (-0.091 \text{ to } -0.0072)$ $.022$ $-0.081 (-0.14 \text{ to } -0.021)$ $.002$ $-0.021 (-0.028 \text{ to } 0.035)$ y $-0.10 (-0.26 \text{ to } 0.053)$ $.195$ $0.16 (-0.088 \text{ to } 0.40)$ $.211$ $-0.17 (-0.34 \text{ to } -0.0077)$	Commute time	-0.13 (-0.21 to -0.061)	<.001	-0.21 (-0.32 to -0.11)	<.001	-0.066 (-0.17 to 0.033)	.189	.042
y $0.407 (0.13 \text{ to } 0.68)$ $0.86 (0.43 \text{ to } 1.30)$ $<.001$ $0.29 (-0.0024 \text{ to } 0.58)$ ontrol $-0.46 (-0.88 \text{ to } -0.050)$ 0.29 $-0.44 (-1.00 \text{ to } 0.11)$ 0.21 $-0.49 (-1.07 \text{ to } 0.082)$ $-1.67 (-2.59 \text{ to } -0.75)$ $<.001$ $-0.54 (-1.99 \text{ to } 0.90)$ 461 $-2.33 (-3.45 \text{ to } -1.22)$ $-0.83 (-2.33 \text{ to } 0.67)$ 2.82 $-3.24 (-5.14 \text{ to } -1.33)$ 0.01 $1.01 (-0.79 \text{ to } 2.81)$ sportation use $-0.049 (-0.091 \text{ to } -0.072)$ 0.22 $-0.081 (-0.14 \text{ to } -0.021)$ 0.08 $-0.021 (-0.078 \text{ to } 0.035)$ $0.16 (-0.088 \text{ to } 0.40)$ $0.16 (-0.088 \text{ to } 0.40)$ $0.16 (-0.088 \text{ to } 0.40)$ 0.11	Public transportation use	1.08 (0.69 to 1.48)	<.001	1.13 (0.55 to 1.71)	<.001	1.05 (0.57 to 1.53)	<.001	.814
nutrol $-0.46 \ (-0.88 \ \text{to} -0.050)$ $.029 \ -0.44 \ (-1.00 \ \text{to} \ 0.11)$ $.121 \ -0.49 \ (-1.07 \ \text{to} \ 0.082)$ $-1.67 \ (-2.59 \ \text{to} -0.75)$ $< .001 \ -0.54 \ (-1.99 \ \text{to} \ 0.90)$ $.461 \ -2.33 \ (-3.45 \ \text{to} \ -1.22)$ $< .083 \ (-2.33 \ \text{to} \ 0.67)$ $.282 \ -3.24 \ (-5.14 \ \text{to} \ -1.33)$ $.001 \ 1.01 \ (-0.079 \ \text{to} \ 2.81)$ $.001 \ 1.01 \ (-0.078 \ \text{to} \ 0.035)$ sportation use $-0.049 \ (-0.091 \ \text{to} \ 0.04)$ $.478 \ 0.30 \ (-0.025 \ \text{to} \ 0.63)$ $.070 \ -0.32 \ (-0.060 \ \text{to} \ -0.058)$ $.070 \ -0.32 \ (-0.060 \ \text{to} \ -0.058)$ $.016 \ (-0.26 \ \text{to} \ 0.053)$ $.195 \ 0.16 \ (-0.088 \ \text{to} \ 0.40)$ $.211 \ -0.17 \ (-0.34 \ \text{to} \ -0.0077)$	Walkability	0.407 (0.13 to 0.68)	.004	0.86 (0.43 to 1.30)	<.001	0.29 (-0.0024 to 0.58)	.052	.007
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Diabetes control							
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$Air NO_2$	-0.46 (-0.88 to -0.050)	.029	-0.44 (-1.00 to 0.11)	.121	-0.49 (-1.07 to 0.082)	.093	68.
time $-0.83 \ (-2.33 \ \text{to} \ 0.67)$ $-3.24 \ (-5.14 \ \text{to} \ -1.33)$ -0.01 $-0.021 \ (-0.079 \ \text{to} \ 2.81)$ $-0.049 \ (-0.091 \ \text{to} \ -0.0072)$ $-0.081 \ (-0.014 \ \text{to} \ -0.025 \ \text{to} \ 0.005 \$	${ m Air\ PM}_{10}$	-1.67 (-2.59 to -0.75)	<.001	-0.54 (-1.99 to 0.90)	.461	-2.33 (-3.45 to -1.22)	<.001	.046
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Air PM _{2.5}	-0.83 (-2.33 to 0.67)	.282	-3.24 (-5.14 to -1.33)	.001	1.01 (079 to 2.81)	.270	<.001
$-0.081 \ (-0.31 \ \text{to} \ 0.14) \qquad .478 \qquad 0.30 \ (-0.025 \ \text{to} \ 0.63) \qquad .070 \qquad -0.32 \ (-0.60 \ \text{to} \ -0.058) \\ -0.10 \ (-0.26 \ \text{to} \ 0.053) \qquad .195 \qquad 0.16 \ (-0.088 \ \text{to} \ 0.40) \qquad .211 \qquad -0.17 \ (-0.34 \ \text{to} \ -0.0077)$	Commute time	-0.049 (-0.091 to -0.0072)	.022	-0.081 (-0.14 to -0.021)	800°	-0.021 (-0.078 to 0.035)	.453	.15
$-0.10 \ (-0.26 \ \text{to} \ 0.053)$.195 $0.16 \ (-0.088 \ \text{to} \ 0.40)$.211 $-0.17 \ (-0.34 \ \text{to} \ -0.077)$	Public transportation use	-0.081 (-0.31 to 0.14)	.478	0.30 (-0.025 to 0.63)	.070	-0.32 (-0.60 to -0.058)	.017	.002
	Walkability	-0.10 (-0.26 to 0.053)	.195	0.16 (-0.088 to 0.40)	.211	-0.17 (-0.34 to -0.0077)	.040	.01

Abbreviations: NO2, nitrogen dioxide; PM, particulate matter.

^aAdjusted for county-level education, unemployment, household income, and state.

^bNatural log-transformed air quality indices and public transportation usage represent per 2.7-fold worsening.

^cCommute time associations are per minute increase.

^dContinuous negative walkability score association represents per unit increase in worsened walkability.

Table 3. Combined effects of domain mixtures on diabetes prevalence and control among urban and metropolitan counties in the United States (N=1473)^{a,b}

% change (95% CI)	Combined effect of domain mixture	P
Diabetes prevalence		_
Separate transportation	1.25 (0.29 to 2.23)	.011
Separate air quality	1.52 (0.81 to 2.24)	<.001
Joint mixture	2.65 (1.47 to 3.85)	<.001
Diabetes control		
Separate transportation	-0.21 (-0.71 to 0.30)	.425
Separate air quality	-0.62 (-1.06 to -0.17)	.007
Joint mixture	-0.69 (-1.31 to -0.07)	.030

^aAdjusted for education, unemployment, household income, and state.
^bAssociations correspond to a simultaneous increase in all domains by one

Table 2 additionally depicts the relationship between transportation and air pollution exposures with county-level diabetes control. The highest quartiles both of NO_2 and PM_{10} were associated with 0.5% and 1.7% lower diabetes control per 2-fold increase, respectively (P = .003; P < .001). Additionally, we found for each per minute increase in commute time there is a 0.5% reduction in diabetes control (P = .02).

There was statistically significant interaction between PM_{10} , $PM_{2..5}$, public transportation usage, and walkability with high and low minority proportion within a county (see Table 2). PM_{10} is associated with reduced diabetes control only among counties with a high proportion of minority residents (P < .001). Conversely, $PM_{2..5}$ is associated with reduced diabetes control only among counties with a low proportion of minority residents (P = .001). Last, reduced public transportation usage and worse walkability were associated with reduced diabetes control among counties with a high proportion of minority residents (P = .017; P = .040).

Transportation and Air Quality Mixture

The separate and joint estimates for the associations of transportation and air quality mixtures both with diabetes prevalence and control are shown in Table 3 and Fig. 1. There was a statistically significant association between both the transportation and air quality mixtures with increased diabetes prevalence (P < .001; P = .003). The joint mixture of transportation and air quality indices is approximately equal to the sum of the separate mixtures, indicating no synergy between the indices. Additionally, the air quality mixture is statistically significantly associated with 0.62% lower diabetes control (P < .001), but the transportation mixture is not. When combined, the total mixture is associated with reduced diabetes control, but this is primarily driven by the air quality factors. The specific mixture component weights are shown (Supplementary Figs. S1 and S2) [22].

Sensitivity Analysis

Following further adjustment for county-level obesity and physical activity prevalence, there is general conservation of the associations between air quality and transportation metrics with diabetes prevalence and control, both overall and by minority stratification (Supplementary Table S2) [22]. There is attenuation for the association between PM_{2.5} and

diabetes prevalence in addition to the associations between public transportation and walkability with diabetes control.

Discussion

This study is one of few to evaluate the associations between specific transportation-related, built environment factors and air pollution on diabetes prevalence and control in the United States, and it is also the first to assess these factors as a mixture. Using the EQI for urban and metropolitan counties in the United States, we found that counties with less public transportation usage and less walkability had a higher prevalence of diabetes. We also found associations for NO₂, PM₁₀, and PM_{2.5} with higher diabetes prevalence. Regarding diabetes control, we found that counties with higher air pollution had reduced diabetes control. These associations were heterogeneous as counties with a higher proportion of minority residents generally were more affected by these factors than counties with a lower proportion of minority residents. Last, the mixture analysis showed that the separate cumulative exposure of both less favorable transportation and worse air quality mixtures were positively associated with increased diabetes prevalence, while the overall mixture generally reflected the sum of the individual mixtures.

Our results are supported by previous studies that have found associations between active transportation or walkability with lower rates of diabetes. Specifically, a study using the National Health and Nutrition Examination Survey (NHANES) showed that active transportation was associated with reduced diabetes risk [23]. Furthermore, a health effect assessment study in the San Francisco Bay Area suggested that replacing short car trips with walking or cycling decreases the burden of diabetes [24]. Beyond the United States, studies conducted internationally have shown that active transportation is associated with reduced diabetes risk and improvements in other cardiovascular risk factors [25-34]. In addition to overall diabetes risk, studies have found positive associations between active transportation usage and improved glucose tolerance [35-38].

Collectively, the present study and the published literature suggest that promoting active transportation in urban areas has the potential to improve metabolic health and reduce diabetes risk. The primary mechanism for this benefit is likely through increased physical activity required for active transportation. This is supported by studies showing that increased active commuting reduces sedentary time [39]. Moreover, longer driving time has been shown to be associated with higher odds of smoking, decreased physical activity, decreased sleep, obesity, and worse overall physical and mental health [40]. It is speculated that simply eliminating automobile trips less than 8 km (0.6 miles) in metropolitan areas of the US Midwest has the potential to reduce mortality and health care costs [41]. Curiously, our data suggest that longer commute times are associated with a reduced prevalence of diabetes. We suspect that our county-level analysis likely captures individuals with extended commute times from more affluent residential communities in the periphery to jobs in the urban core, which is supported by the stratified analyses as the association persists only among counties with a low proportion of minority-identifying residents. Further analyses are required to delineate the precise effect of income on transportation-related outcomes, particularly in regions that exhibit marked spatial disparities in income, housing, and jobs.

^bAssociations correspond to a simultaneous increase in all domains by one quartile.

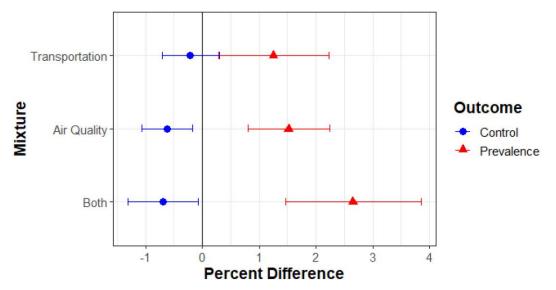


Figure 1. Differences and 95% bootstrap Cls, estimated with quantile g-computation, for diabetes prevalence and control. Adjusted for county-level education, unemployment, household income, and state. Figure corresponds to data in Table 3.

In addition to active transportation, there is evidence linking traffic-related air pollution with diabetes. In support of our results, numerous studies have shown positive relationships between PM and NO₂ with fasting glucose, diabetes prevalence, and diabetes incidence [42-47]. It is important to assess the potential consequences of air pollution with other related factors, specifically traffic-related built environments. As a result, we conducted a novel mixture analysis for the associations between air pollution factors and built environment factors with diabetes prevalence and control both individually and as a full mixture. These data indicate that the mixture of commute time, walkability, and public transportation usage is positively associated with county-level diabetes prevalence, effects that are primarily driven by public transportation and walkability factors. Furthermore, the mixture of air pollutants is also strongly associated with increased diabetes prevalence. The mixture summing all air pollution and built environment factors was equal to the sum of the individual mixtures. Very few studies have expanded mixture approaches to non-chemical exposures, and this study demonstrates that environmental quality mixtures have a significant association with county-level diabetes rates.

While this study contributes to our knowledge of how urban built environments affect chronic disease risk, it has several limitations. First, the study is limited by the fact that it is an ecological study examining populations at the county level. Consequently, interpretations are limited to populationlevel effects and cannot be applied to individuals. There are also unmeasured individual factors that are associated with diabetes prevalence and built environment exposures, increasing the risk of residual confounding. Such factors include individual anthropometrics, including body composition, as well as lifestyle factors such as diet and physical activity. Furthermore, counties are sizeable geographic units with large, intracounty variation in diabetes-associated risk factors. Future studies are required to interrogate these relationships with greater spatial resolution. Additionally, this study is cross-sectional as the evaluation of the EQI from 2006 to 2010 overlaps with the measurement of average diabetes prevalence from 2006 to 2012. This limitation increases the risk for reverse associations and lack of temporality, but inherent characteristics of our exposures make reverse associations unlikely.

Despite these limitations, this study addresses knowledge gaps pertaining to the relationships between features of urban environments and metabolic health. Our results show that urban and metropolitan counties with worse public transportation, walkability, and air quality have a higher prevalence of diabetes compared to other urban and metropolitan counties, especially counties with larger minority populations. As such, this study provides justification for future studies examining individual-level associations between transportation-related built environments and air pollution with diabetes risk using cohort designs. Importantly, such future studies should also assess temporal associations between air quality and diabetes outcomes, including the effect of air quality changes over time and across seasons. Overall, this study encourages improvements in urban planning and implementation of policies that positively influence the built environment to address the diabetes pandemic. With the burgeoning prevalence of diabetes and other chronic health conditions in the United States, there is an urgent need to heed this call and build urban environments that promote human health.

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Data Availability

Data generated and analyzed during this study are publicly available and included in data repositories listed in "References."

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