

Associations of Urban Environment Features with Hypertension and Blood Pressure across 230 Latin American Cities

Ione Avila-Palencia,¹ Daniel A. Rodríguez,^{2,3} J. Jaime Miranda,⁴ Kari Moore,¹ Nelson Gouveia,⁵ Mika R. Moran,⁶ Waleska T. Caiffa,⁷ and Ana V. Diez Roux¹

¹Urban Health Collaborative, Dornsife School of Public Health, Drexel University, Philadelphia, Pennsylvania, USA

²Department of City and Regional Planning, University of California, Berkeley, Berkeley, California, USA

³Institute for Transportation Studies, University of California, Berkeley, Berkeley, California, USA

⁴CRONICAS Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru

⁵Department of Preventive Medicine, University of Sao Paulo Medical School, Sao Paulo, Brazil

⁶Institute of Urban and Regional Development, University of California, Berkeley, Berkeley, California, USA

⁷Observatory for Urban Health, School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

BACKGROUND: Features of the urban physical environment may be linked to the development of high blood pressure, a leading risk factor for global burden of disease.

OBJECTIVES: We examined associations of urban physical environment features with hypertension and blood pressure measures in adults across 230 Latin American cities.

METHODS: In this cross-sectional study we used health, social, and built environment data from the SALud URBana en América Latina (SALURBAL) project. The individual-level outcomes were hypertension and levels of systolic and diastolic blood pressure. The exposures were city and subcity built environment features, mass transit infrastructure, and green space. Odds ratios (ORs) and mean differences and 95% confidence intervals (CIs) were estimated using multilevel logistic and linear regression models, with single- and multiple-exposure models adjusted for individual-level age, sex, education, and subcity educational attainment.

RESULTS: A total of 109,176 participants from 230 cities and eight countries were included in the hypertension analyses and 50,228 participants from 194 cities and seven countries were included in the blood pressure measures analyses. Participants were 18–97 years of age. In multiple-exposure models, higher city fragmentation was associated with higher odds of having hypertension (OR per standard deviation (SD) increase = 1.11; 95% CI: 1.01, 1.21); presence (vs. no presence) of mass transit in the city was associated with higher odds of having hypertension (OR = 1.30; 95% CI: 1.09, 1.54); higher subcity population density was associated with lower odds of having hypertension (OR per SD increase = 0.90; 95% CI: 0.85, 0.94); and higher subcity intersection density was associated with higher odds of having hypertension [OR per SD increase = 1.09; 95% CI: 1.04, 1.15]. The presence of mass transit was also associated with slightly higher systolic and diastolic blood pressure in multiple-exposure models adjusted for treatment. Except for the association between intersection density and hypertension, associations were attenuated after adjustment for country. An inverse association of greenness with continuous blood pressure emerged after country adjustment.

DISCUSSION: Our results suggest that urban physical environment features—such as fragmentation, mass transit, population density, and intersection density—may be related to hypertension in Latin American cities. Reducing chronic disease risks in the growing urban areas of Latin America may require attention to integrated management of urban design and transport planning. <https://doi.org/10.1289/EHP7870>

Introduction

High systolic blood pressure is a leading risk factor for global burden of disease and has been estimated to be responsible for >10 million deaths and >200 million disability-adjusted life years (GBD 2017 Risk Factor Collaborators 2018). In addition, high blood pressure has been identified as one of the most important modifiable risk factor for cardiovascular disease morbidity and mortality worldwide (Olsen et al. 2016). The population impact of high blood pressure is increasing because of longer life expectancy (Olsen et al. 2016).

A few studies have suggested that features of the urban physical environment may be linked to higher blood pressure and higher cardiovascular risk. Living in areas that are more walkable has

been found to be associated with lower levels of blood pressure or lower prevalence of hypertension in some (Chiu et al. 2016; Li et al. 2009) but not all studies (Müller-Riemenschneider et al. 2013). In addition, living in areas of higher population density has been linked to lower risk of coronary heart disease or cardiac death (Griffin et al. 2013). Walking for transportation may partly mediate these effects because it may be more common in high-density areas and has been associated with a lower likelihood of having hypertension compared with private transport (Lavery et al. 2013). Green space in urban areas has also been found to be associated with lower cardiovascular disease risk (Tamosiunas et al. 2014). A meta-analysis showed that living in greener areas was associated with lower cardiovascular mortality (Gascon et al. 2016). The mechanisms through which proximity to green space may reduce cardiovascular risk include increased physical activity levels, stress reduction, as well as reductions in air pollution and temperature (Nieuwenhuijsen 2018; Nieuwenhuijsen et al. 2016).

Very few studies have investigated the features of urban environments that may affect blood pressure or the risk of developing hypertension in rapidly urbanizing low- and middle-income countries. Most studies examining associations between urban physical environmental exposures and hypertension and related cardiovascular outcomes have been conducted in Europe and North America. Latin America, with its high levels of urbanization and diversity in urban environments (Greene and de Dios Ortúzar 2018) and its high and rising burden of hypertension and related cardiovascular disease (Miranda et al. 2019), presents a unique opportunity to investigate how urban environments are related to blood pressure and hypertension.

Address correspondence to Ione Avila-Palencia, Urban Health Collaborative, Dornsife School of Public Health, Drexel University, 3600 Market St., 717J, Philadelphia, PA 19104 USA. Telephone: (267) 359-6379. Email: ia384@drexel.edu

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The aim of this study was to examine how features of urban physical environments are related to the prevalence of hypertension and to blood pressure measures in adults across 230 Latin American cities. We hypothesized that living in less fragmented cities (cities with less interrupted urban landscape development), in cities with mass transit, in urban environments that have higher population density, higher intersection density, and higher levels of greenness would be associated with lower odds of hypertension and lower levels of systolic and diastolic blood pressure.

Materials and Methods

Study Design and Population

This cross-sectional study was based on data from SALUD URBana en América Latina (SALURBAL) project (Diez Roux et al. 2019). The SALURBAL project has compiled and harmonized data on health as well as social and built environment for all cities with >100,000 residents in 11 countries: Argentina, Brazil, Chile, Colombia, Costa Rica, El Salvador, Guatemala, Mexico, Nicaragua, Panama, and Peru (Quistberg et al. 2019). Cities were defined as a single administrative unit (e.g., *municipio*) or combination of adjacent administrative units (e.g., several *municipios*) that are part of the built-up area of the urban agglomeration as determined from satellite imagery. Each “subcity” is an administrative unit fully nested within a “city.” The subcity units were identified in each country as the smallest geographic administrative units for which health data was easily available. Approximately half of the cities included only one subcity unit. More details are available elsewhere (Quistberg et al. 2019).

Harmonized data on adults >18 years of age derived from national surveys was used to characterize the outcomes and individual-level covariates. Survey availability varied by year depending on the country as follows: Argentina (2013), Brazil (2013), Chile (2010), Colombia (2007), Guatemala (2002), Mexico (2012), Peru (2016), and El Salvador (2014). Surveys were generally conducted by government agencies in the different countries for purposes of risk factor surveillance, often using similar questions. A total of 124,742 adults ≥ 18 years of age linkable to SALURBAL cities responded to survey modules that collected information on self-reported hypertension and/or blood pressure. Of these, 11,350 participants (all from Brazil) were excluded because their subcity location was not identified. Another 51 participants were excluded because there was no information on subcity data on intersection density or educational attainment. In addition, 4,165 participants were excluded owing to missing or not available data on individual education level or hypertension, leaving a total of 109,176 participants for hypertension prevalence analyses (19.5% in Argentina, 24.2% in Brazil, 2.4% in Chile, 16.6% in Colombia, 1.4% in El Salvador, 1.2% in Guatemala, 23.8% in Mexico, and 10.9% in Peru). Of these, 50,228 participants (49.9% in Brazil, 4.9% in Chile, 11.2% in Colombia, 3% in El Salvador, 2.6% in Guatemala, 4.8% in Mexico, and 23.6% in Peru) had available blood pressure measures. No participants in Argentina were included in blood pressure analyses because continuous blood pressure was not measured in the Argentina survey. Further details on exclusions are shown in Table S1 and Figures S1–S9. Although there were some differences, included and excluded participants were generally approximately similar in key available covariates, as were samples included in hypertension and continuous blood pressure analyses (except for the exclusion of Argentina) (Table S1).

Exposures

The main exposures used in this study were defined at either the city or subcity level, depending on the hypothesized mechanism linking the exposure to the outcome and the presence of within-city variation. Table 1 provides complete details on each indicator.

City-level exposures included fragmentation of urban development and the presence of mass transit infrastructure. Both variables were defined at the city level given that they may affect the transportation behaviors of all residents regardless of what part of the city they live in. Fragmentation of urban development for the city was measured using patch density (Fan and Fan 2014; He et al. 2020; Ji et al. 2006; McGarigal et al. 2012; Tan et al. 2005; Tian et al. 2020; Zhang et al. 2017). An urban patch is an area of uninterrupted development, such as the area created by contiguous buildings, streets, and parking areas. Forests, water bodies, agriculture, and open space are types of land uses that interrupt the continuity of urban development. A city can be composed of few or many urban patches depending on the pattern of interrupted vs. uninterrupted development. For a given level of urban development, cities with less contiguous development will exhibit higher patch density (defined as the number of urban patches divided by the total area of the geographic unit) because the developed area is split into multiple patches and, therefore, is considered more fragmented. More fragmented cities raise the cost of providing urban infrastructure, may present more obstacles to traveling from one place to another, and are often characterized by longer trips and greater use of motorized transportation (e.g., automobile, motorcycles) (Liu and Meng 2020; Yuan et al. 2018). Long trips have been associated with higher air pollution emissions and lower active travel (Legrain et al. 2015; Nieuwenhuijsen and Khreis 2016; Novaco and Gonzalez 2009). In the present study, we identified urban patches using the satellite-based Global Urban Footprint (GUF) project, which defines urban footprints at a 12-m resolution for the years 2011 and 2012 (Esch et al. 2018).

Availability of mass transit infrastructure may also increase physical activity levels and decrease air pollution emissions, especially for cleaner transportation modes (Sallis et al. 2016). We measured the presence of mass transit infrastructure in the city with a dichotomous variable expressing whether the city has a mass transit system that relies on dedicated infrastructure (yes/no). The variable indicated the presence/absence of bus rapid transit (BRT) and/or subway in the cities included in the study. We focused on BRT and subway because of the availability of data for all the geographic units. The transit infrastructure data was collected in 2017.

Subcity-level exposures included population density, intersection density, and greenness. These were measured at the subcity level because it was hypothesized that exposures closer to the participants’ location of residence are more relevant to the hypothesized mechanisms linking our exposures of interest to hypertension risk. Higher population density and higher intersection density are related to indicators of greater walkability, which could affect hypertension through physical activity levels (Sallis et al. 2016). Greater exposure to greenness in the subcity could affect hypertension through higher levels of physical activity and its restorative effects (Kondo et al. 2018). Population density was defined as population per kilometer squared of all the built-up area inside the geographic boundary of the subcity. Density was measured for built-up areas because individuals tend to live in built-up areas and therefore density for built-up areas is a more accurate measure of actual population density where individuals live. The population density data was collected for every year between 2000 and 2020. For the analysis, each participant identifier (ID) received the data from the year of the survey of its country or the closest year. A higher value of population density indicates a denser urban

Table 1. Description of how each built environment exposure was defined.

Exposure	Data sources
Fragmentation [patch density ($n/100$ ha)]	Urban patches are defined based on the Global Urban Footprint (GUF) project that measures urban footprint at a 12-m resolution between 2011 and 2012 (Esch et al. 2018). We resampled GUF to a 30-m resolution and grouped connected urban pixels as urban patches using the Moore-Neighborhood rule (Weisstein 2022). We calculated fragmentation on the resulting set of patches as the number of urban patches over the administrative area using the FRAGSTATS (version 4.2) software package (McGarigal et al. 2012). In our analyses, fragmentation was measured at the city level.
Presence of mass transit (yes)	The data for BRT was collected in September 2017 from BRTData (https://brtdata.org) and OpenStreetMap. The data for subway presence was collected in December 2017 from official sources and OpenStreetMap. In our analyses, presence of mass transit was measured at the city level.
Population density (n/km^2)	Population per square kilometer in all the urban patches inside the geographic boundary and calculated based on Facebook's Population Density Maps. The data was collected for every year between 2000 and 2020. For the analysis, each participant ID received the data from the year of the survey of its country. There was one country (Guatemala: survey year 2002; population density year 2009) with population density missing data at the year of its survey, so those participants were assigned the population density values from the closest year from which there was population density data available. In our analyses, population density was measured at the subcity level.
Intersection density (n/km^2)	The data was collected in January 2018 from OpenStreetMap. In our analyses, intersection density was measured at the subcity level.
Greenness (median NDVI)	NDVI was calculated using a MODIS vegetation product, MOD13Q1.006. Permeant and seasonal water were further removed from the NDVI data set using the European Joint Research Council (JRC) Yearly Water Classification History data set. The data was collected for every year between 2000 and 2016. For the analysis, each participant ID received the data from the year of the survey of its country. In our analyses, greenness was measured at the subcity level.
Percentage of built-up urban area	The 2012 urban footprint data (in 30×30 m gridcells) comes from the Global Urban Footprint project. This variable is calculated based on 30×30 m gridcells using the FRAGSTATS (version 4.2) software package (McGarigal et al. 2012). In our analyses, percentage of built-up urban area was measured at the subcity level.

Note: BRT, bus rapid transit; ID, identifier; MODIS, Moderate Resolution Imaging Spectroradiometer; NDVI, Normalized Difference Vegetation Index.

development. Intersection density measures the amount of intersections (node density) per kilometer squared of area. The data was collected in January 2018. Higher values of intersection density mean higher street connectivity, which provides direct pathways for pedestrians and thus may enhance a shift from driving to

walking. Exposure to greenness was measured as the zonal median of annual maximum Normalized Difference Vegetation Index (NDVI), excluding water. Specifically, NDVI is the median value of all image pixels' NDVI within a subcity. This includes developed and undeveloped areas within each subcity. Subcity areas varied significantly in size, given that they are administratively determined, and they ranged from 0.30 to 53,182.88 km². NDVI appears to be a good proxy for area level greenness. NDVI ranges from -1 to 1, and a higher value indicates a higher level of vegetation greenness. The NDVI data was collected for every year between 2000 and 2016. For the analysis, each participant ID received the data from the year of the survey of its country.

All exposure variables were systematically assessed in each city and sub-city by collecting and processing publicly available Geographic Information System (GIS). A diversity of sources was used depending on the variable of interest.

Health Outcomes

We used three different measures as health outcomes: *a*) hypertension, *b*) objectively measured systolic blood pressure, and *c*) objectively measured diastolic blood pressure. Participants were defined as having hypertension if they reported that a physician had told them that they had hypertension and if they reported using medications "to lower blood pressure" or to control hypertension prescribed by a health care provider (i.e., both conditions had to be fulfilled). We chose to include medication use in the definition to increase specificity. In all countries except Chile, medication use was only asked among persons who reported that a physician had told them they had hypertension. Therefore, it was not possible to use a definition based on self-report or physician diagnosis or on medication use. Gestational hypertension was excluded except in Argentina and Guatemala, where the survey questions used did not exclude physician-diagnosed hypertension during pregnancy. This definition was used to incorporate data from as many countries as possible while maximizing comparability across countries. Systolic and diastolic blood pressure were measured by trained interviewers in subsets of participants in all countries except Argentina. The number of blood pressure measurements taken and conditions for the measurements varied by survey. The variables used were the average of all available measurements.

Covariates

We included a set of variables that may be confounders of our main associations of interest or may be important in interpreting other measures. Individual-level characteristics included age, sex, education level (in "Primary or less" and "Secondary or more" categories), household sanitation (defined as having access to a municipal sewage network), and household overcrowding (defined as having more than three people per room). Household sanitation and overcrowding were self-reported in the health surveys and examined in sensitivity analyses. A summary score of subcity education (summed *z*-score for the percentage of population ≥ 25 years of age that completed high school level or above, and the percentage of population ≥ 25 years of age that completed university level or above) was used as an indicator of subcity contextual socioeconomic status (SES). Higher score values signify better educational achievement in the population. A city-level social environment index was also used in sensitivity analyses. The social environment index is a summary of four variables: *a*) education (percentage population with at least completed primary education among those ≥ 25 years of age), *b*) water access (percentage households with access to piped water), *c*) sanitation (percentage households with access to a municipal sewage

network), and *d*) overcrowding (percentage households with more than three people per room). The social environment index is the sum of the *z*-scores of the four variables (reversing overcrowding) divided by 4 (assuming equal weighting of all variables). A higher value indicates a better social environment. We also included percentage of built-up area (at the city level), defined as the total built-up urban area divided by the total area of the geographic unit and multiplied by 100. This variable was used as an adjustment variable to account for the fact that some city and subcity units encompassed substantial surrounding nonbuilt-up areas. This adjustment is important when interpreting associations with fragmentation (patch density) because comparisons of fragmentation (patch density) are not meaningful if the percentage of area that is built up is not taken into consideration.

Statistical Analyses

We initially described the distribution of exposures of interest as well as covariates by hypertension status. We also examined the outcomes, exposures, and covariates by city size. In addition, we explored Spearman correlations between continuous exposures and distributions of continuous exposures across the presence of mass transit (Tables S2 and S3).

Multilevel logistic and linear regression models with random intercepts at the city and subcity level were used to evaluate the association between city and subcity characteristics and binary hypertension outcome and continuous blood pressure measures, respectively. The different associations were assessed running single- and multiple-exposure models. In the single-exposure models, only one exposure was used at a time, and in the multiple-exposure models, all different city and subcity characteristics were included in the model to allow assessing their independent effects. A total of three models were fitted for each outcome: *a*) single-exposure models adjusted for the confounders identified by a directed acyclic graph (Figure S10), which were individual age, sex, and educational level, and subcity educational attainment; *b*) multiple-exposure models adjusted for the confounders described in Model 1; and *c*) multiple-exposure models adjusted for the confounders described in Model 1 and for country as a fixed effect to account for any residual confounding effects of country. The country-adjusted models adjust for confounders associated with country but limit variability in exposures given that associations are estimated based only on within-country variability. Therefore, we discuss results based primarily on Model 2 but also comment on the impact of country adjustment.

All the blood pressure measures models were additionally adjusted for treated hypertension to estimate associations that are independent of treatment. Although treatment could partly mediate effects of urban environments on blood pressure, in these analyses of continuous blood pressure, we were interested in associations that persist after treatment differences are taken into account. All models were adjusted for percentage of built-up area in the city unit to appropriately interpret the urban patch density as a measure of fragmentation.

Sensitivity analyses were run adjusting the main models for additional socioeconomic characteristics (household sanitation and household overcrowding in one model, and city social environment index in another model). Interactions of each of the built environment exposures with sex (male, female), age (≤ 60 , >60 years of age), and education (primary or less, secondary or more) were examined using multiple-exposure models with interaction terms to generate the effect estimates and the interaction *p*-values. Each potential effect modifier (age, sex, education) was tested in a separate model.

All models were conducted with a complete case analysis. In all contrasts, a significance value of $p < 0.05$ was considered.

A *z*-score was used for every exposure variable [thus, odds ratios (ORs) and coefficients were derived using the standard deviation (SDs) as the exposure contrast]. All analyses were conducted in Stata (version MP 16.1; StataCorp).

Results

The study sample for hypertension analyses included 109,176 individuals distributed in 230 cities with a median of 343 respondents per city (minimum: 17, maximum: 3,901). The study sample for blood pressure analyses included 50,228 individuals distributed in 194 cities with a median of 68 respondents per city (minimum: 1, maximum: 3,278). Characteristics of survey respondents overall and by hypertension status are presented in Table 2. Overall, the median age of the study population was 40 y (minimum: 18 y, maximum: 97 y), 57.8% were females, and 49.1% had completed secondary school or more. Less than half of the sample (41.6%) lived in cities with mass transit infrastructure (i.e., BRT, subway). A total of 13% of individuals were classified as having hypertension based on self-report of diagnosis and use of antihypertensive medication (hereafter referred to as “individuals with hypertension” for simplicity). Individuals with hypertension were significantly older (median age = 61 vs. 37 y old) and had lower education levels than those who did not have hypertension. In addition, individuals with hypertension were also more likely to live in more populated cities, in cities with higher levels of fragmentation, in cities with a higher percentage of built-up area, and in cities with mass transit infrastructure (45.2% vs. 41.1%). Median subcity population density and amount of greenness were lower in individuals with hypertension compared with those without hypertension. Subcity intersection density, educational attainment, and percentage built-up area were higher for individuals with hypertension compared with those who did not have hypertension.

Table 3 shows selected characteristics across quartiles (Qs) of city size (city total population) because city size can be an important predictor of city and subcity characteristics. Compared with respondents living in smaller cities, respondents living in larger cities tended to be slightly older (Q1 = 39 y old vs. Q4 = 41 y old) and more educated (Q1 = 12.4% compared with Q4 = 15.7% had university education level), they also tended to have a higher prevalence of hypertension (Q1 = 11.4% vs. Q4 = 14.2%) and higher mean systolic and diastolic blood pressures (Q1 = 118.50/72.50 mmHg vs. Q4 = 122.67/76.50 mmHg). Larger city size was associated with higher levels of fragmentation, higher presence of mass transit infrastructure, higher city percentage of built-up urban area, higher subcity population density, higher subcity intersection density, and lower amount of greenness. Larger cities also tended to have higher subcity educational attainment.

Table 4 shows associations of city and subcity characteristics with hypertension and systolic and diastolic blood pressure measures. When each exposure was examined separately (Model 1), higher city fragmentation and the presence of mass transit infrastructure were associated with higher odds of having hypertension {OR = 1.11 [95% confidence interval (CI): 1.01, 1.22] and 1.25 (95% CI: 1.04, 1.49), respectively}. Higher subcity population density was associated with lower odds of having hypertension (OR = 0.93; 95% CI: 0.89, 0.98), and higher subcity intersection density was associated with higher odds of having hypertension (OR = 1.05; 95% CI: 1.01, 1.10). After mutual adjustment for all the city and subcity characteristics (Model 2), higher fragmentation and presence of mass transit infrastructure remained associated with higher odds of having hypertension [OR = 1.11 (95% CI: 1.01, 1.21) and 1.30 (95% CI: 1.09, 1.54), respectively]; higher population density remained associated with lower odds of having hypertension (OR = 0.90; 95% CI: 0.85, 0.94), and higher intersection density remained associated with

Table 2. Selected characteristics of the study population for the full sample of 230 cities and by self-reported hypertension from surveys from 2002 to 2016.

Characteristics	Total (<i>n</i> = 109,176)	Hypertension ^a		<i>p</i> -Value ^b
		No (<i>n</i> = 94,968)	Yes (<i>n</i> = 14,208)	
City characteristics				
Number of cities (<i>n</i>)	230	—	—	—
City size {total population [median (IQR)]}	930,101 (2,985,296)	930,101 (2,995,045)	1,064,891 (3,038,800)	<0.001
Fragmentation {patch density (<i>n</i> /100 ha) [median (IQR)]}	0.40 (0.54)	0.39 (0.53)	0.42 (0.59)	<0.001
Presence of mass transit {yes [<i>n</i> (%)]}	45,426 (41.6)	39,007 (41.1)	6,419 (45.2)	<0.001
Percentage of built-up urban area [median (IQR)]	6.28 (11.61)	6.25 (11.68)	7.01 (11.54)	<0.001
SE index { <i>z</i> -score [median (IQR)]}	0.32 (0.65)	0.32 (0.66)	0.32 (0.58)	0.027
Missing [<i>n</i> (%)]	1,654 (1.5)	1,424 (1.5)	230 (1.6)	—
Subcity characteristics				
Number of subcities (<i>n</i>)	672	—	—	—
Population density { <i>n</i> /km ² [median (IQR)]}	6,749.62 (6,103.64)	6,826.34 (6,312.94)	6,252.31 (5,927.50)	<0.001
Intersection density { <i>n</i> /km ² [median (IQR)]}	12.00 (44.43)	11.98 (44.43)	13.91 (54.34)	<0.001
Greenness [median NDVI (IQR)]	0.70 (0.33)	0.70 (0.33)	0.69 (0.32)	<0.001
Population educational attainment { <i>z</i> -score [median (IQR)]}	0.67 (2.07)	0.64 (2.07)	0.67 (2.09)	<0.001
Individual characteristics				
Age { <i>y</i> [median (IQR)]}	40 (25)	37 (21)	61 (18)	<0.001
Females [<i>n</i> (%)]	6,3123 (57.8)	53,768 (56.6)	9,355 (65.8)	<0.001
Education level [<i>n</i> (%)]	—	—	—	<0.001
Less than primary	18,855 (17.3)	14,261 (15)	4,594 (32.3)	
Primary	36,673 (33.6)	31,946 (33.6)	4,727 (33.3)	
Secondary	39,304 (36.0)	36,111 (38.0)	3,193 (22.5)	
University	14,344 (13.1)	12,650 (13.3)	1,694 (11.9)	
Household sanitation {access to a municipal sewage network [<i>n</i> (%)]}	82,362 (78.5)	71,405 (78.3)	10,957 (79.9)	<0.001
Missing [<i>n</i> (%)]	4,244 (3.9)	3,746 (3.9)	498 (3.5)	—
Household overcrowding {>3 people per room [<i>n</i> (%)]}	4,397 (4.3)	4,198 (4.7)	199 (1.5)	<0.001
Missing [<i>n</i> (%)]	6,910 (6.3)	6,055 (6.4)	855 (6.0)	—
Systolic blood pressure {mmHg [median (IQR)]} ^c	120.67 (21.67)	119.00 (19.67)	136.00 (26.33)	<0.001
Diastolic blood pressure {mmHg [median (IQR)]} ^c	75.00 (14.33)	74.33 (14)	80.33 (16.17)	<0.001
Country [<i>n</i> (%)]	—	—	—	<0.001
Argentina	21,286 (19.5)	17,561 (18.5)	3,725 (26.2)	
Brazil	26,398 (24.2)	22,034 (23.2)	4,364 (30.7)	
Chile	2,669 (2.4)	2,311 (2.4)	358 (2.5)	
Colombia	18,142 (16.6)	16,743 (17.6)	1,399 (9.8)	
El Salvador	1,495 (1.4)	1,192 (1.3)	303 (2.1)	
Guatemala	1,319 (1.2)	1,191 (1.3)	128 (0.9)	
Mexico	25,995 (23.8)	22,837 (24)	3,158 (22.2)	
Peru	11,872 (10.9)	11,099 (11.7)	773 (5.4)	

Note: —, not applicable; IQR, interquartile range; NDVI, Normalized Difference Vegetation Index; SE, social environment.

^aParticipants were defined as having hypertension if they reported that a physician had told them that they had hypertension and if they reported using medications to lower blood pressure or to control hypertension prescribed by a health care provider.

^bChi square test for categorical variables, Mann-Whitney *U* test for continuous variables. Comparing hypertension yes/no.

^cObjectively measured. Total sample size of individuals with blood pressure measures was 50,228. The subsample of blood pressure measures for individuals without hypertension was 43,878, and the subsample of measures for individuals with hypertension was 6,350.

higher odds of having hypertension (OR = 1.09; 95% CI: 1.04, 1.15). All associations became weaker after adjustment for country fixed effects (Model 3), and only the association with intersection density remained statistically significant (OR = 1.06; 95% CI: 1.01, 1.11).

The presence of mass transit was associated with slightly higher systolic and diastolic blood pressure, but only associations with diastolic blood pressure were statistically significant in the multiple-exposure model [mean difference = 1.32 (95% CI: -0.22, 2.86) for systolic blood pressure, and 1.87 (95% CI: 0.58, 3.15) for diastolic blood pressure]. All other associations of built environment characteristics with systolic blood pressure were weak (mean differences <1 mmHg) and were not statistically significant in single- or multiple-exposure models (Table 4). Higher fragmentation was associated with higher diastolic blood pressure in the single-exposure model (mean difference = 1.02; 95% CI: 0.27, 1.78), but this association became weaker in the multiple-exposure model (mean difference = 0.89; 95% CI: 0.14, 1.65). We observed a very weak (mean difference = 0.40; 95% CI: 0.04, 0.76), albeit statistically significant, association of more greenness with higher diastolic blood pressure in the single-exposure model, but the association was weaker and no longer

statistically significant in the multiple-exposure model. No substantial associations of built environment with systolic or diastolic blood pressure were present in the model with country fixed effects (all mean differences ≤1 mmHg). In models with country fixed effects, more greenness was weakly associated with lower systolic and diastolic blood pressure, but only the association with diastolic blood pressure was statistically significant (mean difference = -0.32; 95% CI: -0.62, -0.03).

In sensitivity analyses, results were generally similar in terms of directionality and patterns of associations for all three outcomes after additional adjustment for individual-level household sanitation and household overcrowding (Table S4), as well as after additional adjustment for the city-level social environment index (Table S5). We also examined heterogeneity in associations by age, sex, and education level. Although some tests for statistical interaction were statistically significant, no consistent patterns reflecting heterogeneity of associations by sex or education were observed (Tables S6 and S7). There was some evidence that the associations of higher fragmentation with higher hypertension prevalence and of higher population density with lower hypertension prevalence observed in the full sample were stronger in persons ≤60 years of age compared with those >60 years

Table 3. Selected characteristics of the study population by city size (total population) from 230 cities and surveys from 2002 to 2016.

Characteristics	City size (quartiles)				p-Value ^a
	Q1 (n = 27,823)	Q2 (n = 26,771)	Q3 (n = 27,826)	Q4 (n = 26,756)	
City characteristics					
Number of cities (n)	116	64	35	15	—
City size {total population (n) [median (IQR)]}	235,046.20 (158,043.90)	553,551.00 (321,236.20)	1,646,057.00 (1,092,551.00)	10,100,000.00 (10,700,000.00)	<0.001
Fragmentation {patch density (n/100 ha) [median (IQR)]}	0.11 (0.19)	0.19 (0.34)	0.61 (0.33)	0.57 (0.40)	<0.001
Presence of mass transit (yes) [n (%)]	0 (0.0)	2,689 (10.0)	15,981 (57.4)	26,756 (100.0)	<0.001
Percentage of built-up urban area [median (IQR)]	1.33 (2.92)	2.88 (5.64)	10.02 (7.08)	19.36 (10.16)	<0.001
SE index {z-score [median (IQR)]}	0.17 (1.14)	0.15 (0.71)	0.32 (0.84)	0.42 (0.15)	<0.001
Missing [n (%)]	589 (2.1)	208 (0.8)	97 (0.4)	760 (2.8)	—
Subcity characteristics					
Number of subcities (n)	183	165	119	205	—
Population density {n/km ² [median (IQR)]}	4,926.12 (3,922.71)	5,368.18 (4,075.07)	7,038.07 (7,511.73)	11,546.83 (9,471.08)	<0.001
Intersection density {n/km ² [median (IQR)]}	1.96 (5.32)	4.45 (8.58)	29.04 (46.39)	63.33 (53.18)	<0.001
Greenness {median NDVI [median (IQR)]}	0.76 (0.30)	0.78 (0.26)	0.7 (0.23)	0.54 (0.34)	<0.001
Population educational attainment {z-score [median (IQR)]}	-0.03 (1.40)	0.47 (1.60)	0.76 (1.64)	1.77 (1.60)	<0.001
Individual characteristics					
Age {y [median (IQR)]}	39 (24)	40 (24)	40 (25)	41 (25)	<0.001
Females [n (%)]	15,910 (57.2)	15,493 (57.9)	16,208 (58.2)	15,512 (58.0)	0.071
Education level [n (%)]	—	—	—	—	<0.001
Less than primary	4,506 (16.2)	4,836 (18.1)	5,321 (19.1)	4,192 (15.7)	
Primary	9,668 (34.7)	9,114 (34.0)	9,849 (35.4)	8,042 (30.1)	
Secondary	10,209 (36.7)	9,449 (35.3)	9,324 (33.5)	10,322 (38.6)	
University	3,440 (12.4)	3,372 (12.6)	3,332 (12.0)	4,200 (15.7)	
Household sanitation {access to a municipal sewage network} [n (%)]	21,106 (78.5)	19,385 (73.3)	18,738 (74.3)	23,133 (87.8)	<0.001
Missing [n (%)]	918 (3.3)	322 (1.2)	2,593 (9.3)	411 (1.5)	—
Household overcrowding {>3 people per room} [n (%)]	1,310 (5.1)	1,319 (5.0)	899 (3.6)	869 (3.4)	<0.001
Missing [n (%)]	2,331 (8.4)	661 (2.5)	2,717 (9.8)	1,201 (4.5)	—
Hypertension [n (%)] ^b	—	—	—	—	<0.001
No	24,647 (88.6)	23,459 (87.6)	23,909 (85.9)	22,953 (85.8)	
Yes	3,176 (11.4)	3,312 (12.4)	3,917 (14.1)	3,803 (14.2)	
Systolic blood pressure {mmHg [median (IQR)]} ^c	118.50 (21.50)	120.00 (21.00)	120.67 (21.33)	122.67 (21.50)	<0.001
Diastolic blood pressure {mmHg [median (IQR)]} ^c	72.50 (13.67)	74.50 (14.00)	75.67 (14.00)	76.50 (14.67)	<0.001
Country [n (%)]	—	—	—	—	<0.001
Argentina	7,982 (28.7)	5,534 (20.7)	3,869 (13.9)	3,901 (14.6)	
Brazil	1,578 (5.7)	4,975 (18.6)	9,805 (35.2)	10,040 (37.5)	
Chile	1,415 (5.1)	338 (1.3)	123 (0.4)	793 (3.0)	
Colombia	4,712 (16.9)	4,633 (17.3)	4,192 (15.1)	4,605 (17.2)	
El Salvador	500 (1.8)	0 (0.0)	995 (3.6)	0 (0.0)	
Guatemala	0 (0.0)	0 (0.0)	1,319 (4.7)	0 (0.0)	
Mexico	6,793 (24.4)	8,051 (30.1)	7,012 (25.2)	4,139 (15.5)	
Peru	4,843 (17.4)	3,240 (12.1)	511 (1.8)	3,278 (12.3)	

Note: The lower and upper range of values for each city size quartile: Q1 (minimum: 107,090.50, maximum: 364,877); Q2 (minimum: 369,899 maximum: 930,101); Q3 (minimum: 963,825.9, maximum: 3,350,173); Q4 (minimum: 3,379,292 maximum: 20,811,110). —, not applicable; NDVI, Normalized Difference Vegetation Index; SE, social environment.

^aChi square test for categorical variables, Kruskal-Wallis test for continuous variables. Comparing city size quartiles.

^bParticipants were defined as having hypertension if they reported that a physician had told them that they had hypertension and if they reported using medications to lower blood pressure or to control hypertension prescribed by a health care provider.

^cObjectively measured. Total sample size of individuals with blood pressure measures was 50,228. The subsample of blood pressure measures for Q1 was 10,244 for Q2 was 10,605 for Q3 was 14,359 and for Q4 was 15,020.

of age (Table S8), but these results should be interpreted with caution given the multiple comparisons performed.

Discussion

In this large survey sample spanning respondents in 230 cities in Latin America, we found that in multiple-exposure models

pooling across countries (Model 2) higher city fragmentation and presence of mass transit were associated with higher odds of having hypertension, higher subcity population density was associated with lower odds of having hypertension, and higher subcity intersection density was associated with higher odds of having hypertension. The presence of mass transit was also associated with slightly higher systolic and diastolic blood pressure in

Table 4. Odds ratios of self-reported hypertension and mean differences in measured blood pressure associated with differences in single- and multiple-exposure models after adjustment for different sets of covariates (samples from 2,30 cities and surveys from 2002 to 2016).

City and suburb characteristics (z-scores)	Category of exposure	Model 1			Model 2			Model 3		
		OR or mean difference (95% CI)	p-Value	OR or mean difference (95% CI)	p-Value	OR or mean difference (95% CI)	p-Value	OR or mean difference (95% CI)	p-Value	
Hypertension (<i>n</i> = 109,176) ^a										
Fragmentation [patch density (<i>n</i> /100 ha)]	Per SD (1 SD = 0.32)	1.11 (1.01, 1.22)	0.026	1.11 (1.01, 1.21)	0.031	1.01 (0.95, 1.09)	0.704			
Presence of mass transit	Yes	1.25 (1.04, 1.49)	0.015	1.30 (1.09, 1.54)	0.003	1.07 (0.95, 1.22)	0.267			
Population density (<i>n</i> /km ²)	Per SD (1 SD = 4881.69)	0.93 (0.89, 0.98)	0.004	0.90 (0.85, 0.94)	<0.001	0.96 (0.91, 1.01)	0.115			
Intersection density (<i>n</i> /km ²)	Per SD (1 SD = 35.21)	1.05 (1.01, 1.10)	0.030	1.09 (1.04, 1.15)	0.001	1.06 (1.01, 1.11)	0.016			
Greenness (median NDVI)	Per SD (1 SD = 0.23)	1.01 (0.97, 1.06)	0.581	1.02 (0.97, 1.07)	0.441	0.98 (0.93, 1.02)	0.256			
Systolic blood pressure (<i>n</i> = 50,228) ^b										
Fragmentation [patch density (<i>n</i> /100 ha)]	Per SD (1 SD = 0.36)	0.15 (-0.74, 1.03)	0.745	0.15 (-0.76, 1.06)	0.747	0.52 (-0.28, 1.32)	0.201			
Presence of mass transit	Yes	1.37 (-0.14, 2.89)	0.076	1.32 (-0.22, 2.86)	0.092	1.00 (-0.31, 2.31)	0.134			
Population density (<i>n</i> /km ²)	Per SD (1 SD = 4631.62)	0.11 (-0.24, 0.46)	0.555	0.01 (-0.37, 0.39)	0.958	-0.02 (-0.41, 0.37)	0.908			
Intersection density (<i>n</i> /km ²)	Per SD (1 SD = 39.58)	0.20 (-0.14, 0.53)	0.256	0.18 (-0.19, 0.55)	0.339	0.20 (-0.16, 0.56)	0.285			
Greenness (median NDVI)	Per SD (1 SD = 0.24)	0.04 (-0.43, 0.50)	0.874	0.04 (-0.45, 0.53)	0.866	-0.38 (-0.85, 0.08)	0.107			
Diastolic blood pressure (<i>n</i> = 50,228) ^b										
Fragmentation [Patch density (<i>n</i> /100 ha)]	Per SD (1 SD = 0.36)	1.02 (0.27, 1.78)	0.008	0.89 (0.14, 1.65)	0.021	0.45 (-0.06, 0.96)	0.082			
Presence of mass transit	yes	1.73 (0.41, 3.06)	0.010	1.87 (0.58, 3.15)	0.004	0.08 (-0.75, 0.91)	0.850			
Population density (<i>n</i> /km ²)	Per SD (1 SD = 4631.62)	-0.15 (-0.38, 0.07)	0.187	-0.19 (-0.43, 0.05)	0.122	-0.22 (-0.46, 0.02)	0.069			
Intersection density (<i>n</i> /km ²)	Per SD (1 SD = 39.58)	0.03 (-0.19, 0.25)	0.795	0.11 (-0.12, 0.34)	0.354	0.08 (-0.14, 0.30)	0.469			
Greenness (median NDVI)	Per SD (1 SD = 0.24)	0.40 (0.04, 0.76)	0.029	0.31 (-0.05, 0.68)	0.095	-0.32 (-0.62, -0.03)	0.030			

Note: Model 1: single-exposure model adjusted by age, sex, education, population educational attainment, percentage of built-up urban area at the city unit; city and suburb ID as random effects; all the blood pressure measures models were additionally adjusted for treated hypertension. Model 2: multiple-exposure model adjusted for Model 1 covariates with city and suburb ID as random effects. Model 3: multiple-exposure model adjusted for Model 1 covariates plus country, with city and suburb ID as random effects. CI, confidence interval; ID, identifier; NDVI, normalized difference vegetation index; OR, odds ratio; SD, standard deviation.

^aParticipants were defined as having hypertension if they reported that a physician had told them that they had hypertension and if they reported using medications to lower blood pressure or to control hypertension prescribed by a health care provider.

^bObjectively measured.

multiple-exposure models adjusted for treatment. Other associations of urban built environment features with continuous measures of systolic and diastolic blood pressure (adjusted for treated hypertension) were weak (mean differences <1 mmHg per SD) or absent. There was some evidence that associations of fragmentation and population density with hypertension prevalence may be stronger in younger persons, but no clear evidence of heterogeneity in these associations by sex or education was observed.

Our results regarding fragmentation and hypertension prevalence are in line with previous studies that reported a higher prevalence of hypertension in sprawling counties compared with compact counties in the United States (Ewing et al. 2003) and a higher risk of heart disease among women living in more compact communities compared with those living in less compact communities (Griffin et al. 2013). Although we are not aware of prior studies explicitly examining fragmentation and hypertension prevalence, we hypothesize that higher levels of fragmentation may make it difficult to go from one place to another by active travel modes, may create air pollution and noise by exacerbating reliance on motorized travel, and may decrease access to health services. There is some emerging evidence connecting fragmentation with walkability (Delso et al. 2017; Ortega et al. 2015). This is maybe because—holding other factors such as density, amount of development, and land-use mix constant—more fragmentation means longer distances, making walking less feasible and less attractive. At the same time, walkability has been shown to be associated with better cardiovascular health. For example, a meta-analysis of evidence mostly from high-income countries reported compelling evidence that greater walkability is linked to lower hypertension risk (Chandrabose et al. 2019). To our knowledge, our study is among the first to document links between higher fragmentation and higher hypertension prevalence across a large and diverse sample of cities of lower- and middle-income countries. Further research is needed to examine the mobility and behavioral consequences of high fragmentation.

We also found that higher population density was associated with lower odds of having hypertension. Residential density is one component of compactness that has been shown to be associated with health outcomes such as coronary heart disease event, myocardial infarction, or cardiac death (Griffin et al. 2013). Physical activity could be an important mediator of this association. Prior evidence suggests that a higher population density is associated with higher levels of physical activity (Sallis et al. 2016). When population and development density are high, travel distances tend to be shorter because destinations become closer to origins. Shorter travel distances are associated with less car use (Ewing and Cervero 2010) and with more walking and cycling trips (Grasser et al. 2013; Wang et al. 2016). Interestingly, in our results the associations of fragmentation (at the city level) and density (at the suburb level) with hypertension persisted after adjustment for each other.

An unexpected finding was that the presence of mass transit infrastructure in the city was associated with higher odds of having hypertension and higher levels of systolic and diastolic blood pressure. We hypothesized the opposite because mass transit has been associated with higher levels of physical activity (Sallis et al. 2016) and walking to transit (Gascon et al. 2019), which are known to be protective against high blood pressure (Chandrabose et al. 2019). It may be that the mere presence of mass transit infrastructure is not sufficient to affect active transport. Mass transit density and other factors, including the quality of mass transit, could have health implications (Eriksson et al. 2013; Sallis et al. 2016). Mass transit has been associated with user dissatisfaction resulting from delays, ride discomfort, or stressful interpersonal interactions (Eriksson et al. 2013), although the

implications of these experiences for blood pressure remain unclear. Those who use mass transit could be exposed to more road traffic air pollution and noise, which have been also associated with hypertension and higher blood pressure levels (Liang et al. 2014; van Kempen and Babisch 2012). Confounding by other city characteristics related to blood pressure could also play a role, although adjustment for city SES did not substantially modify results.

Subcity intersection density was also associated with higher odds of having hypertension. Intersection density is a subdomain of street connectivity, one of the key components of walkability (Frank et al. 2010). Neighborhood walkability has been shown to be beneficially associated with blood pressure outcomes, including hypertension (Sarkar et al. 2018), likely through increasing physical activity levels. Our unexpected results might be explained by other possible mechanisms. In prior studies, neighborhoods with high walkability were found to have high levels of traffic-related air pollution in Vancouver, Canada (Marshall et al. 2009), and significant interactions were identified between walkability and traffic-related air pollution on risk for hypertension in Ontario, Canada, such that the inverse association between walkability and prevalent hypertension was diminished at higher levels of traffic-related air pollution (Howell et al. 2019). Higher intersection density (without considering other factors, such as the presence or quality of sidewalks) could be representing more traffic rather than a walkable or cyclable environment. More traffic could result in higher levels of traffic-related air pollution, as well as heat and noise, which are other environmental exposures that have been linked to cardiovascular disease risk (Nieuwenhuijsen 2018).

Exposure to greenness has been linked to lower cardiovascular mortality in some studies (Gascon et al. 2016). Mechanisms through which greenness could affect blood pressure include increased physical activity levels, stress reduction, as well as reductions in air pollution and temperature (Nieuwenhuijsen 2018; Nieuwenhuijsen et al. 2016). However, we found no associations of greenness with hypertension prevalence. Higher greenness was associated with lower systolic and diastolic blood pressure, but associations were weak and only present in country fixed effects models (Model 3). Our metric of greenness was limited in that it did not capture exposures near the home, which may be the most relevant for some of the hypothesized mechanisms. It is also possible that any effects are weak and difficult to detect with measures such as self-reported hypertension prevalence or a single blood pressure measurement.

We included results using continuous blood pressure because it is objectively measured. However, several factors could explain the absence of clear associations with blood pressure measurements. Blood pressure measurements were only available on a subsample and were not standardized across countries. To make them complementary to analyses of hypertension prevalence (rather than duplicative), analyses of blood pressure included adjustment for treated hypertension. Detecting what are likely small effects of the built environment exposures on continuous blood pressure (over and above the effects on prevalence captured through treatment) is challenging.

Our study has several strengths. First, to our knowledge, with a sample size of >100,000 individuals for the hypertension measure and >50,000 individuals for the blood pressure measures, this is the largest study evaluating associations between built environment features and hypertension/blood pressure in Latin America. Second, we explored associations using data from 230 cities from eight countries for the hypertension measure and 194 cities from seven countries for the blood pressure measures, providing significant variability in exposures. Third, we used a

novel, data-driven measure of urban development fragmentation (Kaza 2013, 2020) rather than relying on population or job density as a proxy for fragmentation as has been done in other work (Hamidi and Ewing 2014). To our knowledge, urban patch density has not been used before to examine the prevalence of chronic conditions. Fourth, we defined exposures at different levels (city and subcity) on the basis of the construct and the hypothesized mechanisms linking it to blood pressure. Finally, we conducted single- and multiple-exposure analyses and were also able to adjust for individual-level confounders, including education and also a contextual measure of education at the subcity level. Multiple-exposure models may be more realistic given that they account for multiple elements to which city dwellers are exposed. Following common practice in many epidemiologic (including environmental epidemiology) studies, we did not adjust for multiple comparisons, but we reported all tests and emphasized point estimates and patterns of associations as opposed to only *p*-values when we described results. All *p*-values need to be considered in the context of the large number of tests we conducted. We were cautious in interpreting effect modification analyses because of the large number of comparisons and the very large sample size.

Our study has several limitations. The cross-sectional design and observational nature limits causal inferences. Confounding remains a possibility for some of the associations we observed (although finer adjustment for SES did not substantially modify results). Our hypertension measure is based on self-report and relies on having access to health care and treatment. Participants who reported a previous diagnosis of hypertension but did not report using medications to lower blood pressure and those who reported no previous physician diagnosis of hypertension were classified as not having hypertension in our analyses. The definition we used may have resulted in underestimating true prevalence. Such an underestimate could have resulted in biased estimates of associations, especially if access to health care is associated with the city characteristics we investigated. Although we had rich data, we did not have finer neighborhood or household exposure measures that could be relevant. Some of our subcity units were quite large and heterogeneous, possibly resulting in misclassification that could have biased estimates in any direction, although bias toward the null seems more likely. This may be especially relevant for some measures, such as greenness, but is not likely to be important for measures that are conceptualized at the city level, such as fragmentation. However, it is possible that for some of the constructs stronger associations would be observed with more refined measurement (e.g., better measures of access to mass transit) and better alignment of the measures with the spatial context most directly relevant to the hypothesized mechanism (density and green space measures for smaller areas). Similarly, the timing of the survey and urban environment measures was not always aligned, so we had to assume time invariance of the urban environment measures. This could have introduced bias, the direction of which is hard to predict.

Our measure of development fragmentation, despite its high spatial resolution, does not distinguish among the reasons for interrupted development. Some features causing development discontinuities may be health promoting, whereas others may not be. For example, even though the presence of a park or a lake interrupts development and results in fragmentation, it is also likely to have positive health impacts. There are also other features of urban development, such as how isolated the patches are from each other or their size, which we did not analyze but that may provide additional information on the construct of fragmentation. Accounting for multiple measures in future studies may help to better understand possible effects of urban fragmentation on chronic conditions.

Although we attempted to harmonize the survey measurements across countries, some heterogeneity may exist and affect our results. A challenge is accounting for country-level differences. If unmeasured country characteristics are associated with hypertension outcomes (or with measures of hypertension because of measurement differences), failure to adjust for country could result in confounded estimates. However, the inclusion of country fixed effects results in estimates being based only on within-country variability, which limits variability in exposures. In our analyses the inclusion of country fixed effects attenuated associations of fragmentation, presence of mass transit, and population density with hypertension. It is difficult to determine from our data whether this results from reduced variability in exposures or country-level confounding. Thus, although we consider the models without adjustment for country to be meaningful and have based our conclusions primarily on these models, we present results with and without country fixed effects.

In summary, we found that fragmentation, presence of mass transit, population density, and intersection density are associated with hypertension prevalence in Latin America cities. Additional research with more refined measures (including measured blood pressure, longitudinal data, and measures of environmental exposures for smaller areas) are necessary to draw firm conclusions. However, our results suggest that reducing chronic disease risk in the growing urban areas of low- and middle-income countries may require attention to integrated management of urban design and transport planning.

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