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Urban Scaling of Health Outcomes: a Scoping Review

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Abstract Urban scaling is a framework that describes how city-level characteristics scale with variations in city size. This scoping review mapped the existing evidence on the urban scaling of health outcomes to identify gaps and inform future research. Using a structured search strategy, we identified and reviewed a total of 102 studies, a majority set in high-income countries using diverse city definitions. We found several historical studies that examined the dynamic relationships between city size and mortality occurring during the nineteenth and early twentieth centuries. In more recent years, we documented heterogeneity in the relation between city size and health. Measles and influenza are influenced by city size in conjunction with other factors like geographic proximity, while STIs, HIV, and dengue tend to occur more frequently in larger cities. NCDs showed a heterogeneous pattern that depends on the specific outcome and context. Homicides and other crimes are more common in larger cities, suicides are more common in smaller cities, and traffic-related injuries show a less clear pattern that differs by context and type of injury. Future research should aim to understand the consequences of urban growth on health outcomes in low- and middle-income countries, capitalize on longitudinal designs, systematically adjust for covariates, and examine the implications of using different city definitions.

Keywords Urban scaling · City size · City growth · Urbanization · Urban health · Complex systems

Introduction

More than one half of the world population now lives in urban areas [1]. Cities present unique challenges for the well-being of their residents and their shared environment [2]. The United Nation's New Urban Agenda further highlights the importance of urban health research in achieving Sustainable Development Goals such as ending poverty, hunger, and creating sustainable cities [3, 4]. In a world undergoing rapid urbanization, understanding how city-level factors change with city size can be instrumental in the creation of a unified theory of city living: a predictive framework for how urbanization and city growth affects society and the environment [5–8]. This theory would allow, among other things, for a better understanding of how health

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outcomes vary across the continuum of city size, and how variations in these outcomes may be associated with city-level factors and underlying policies which are important to improve planetary health.

Cities are complex systems where the dynamics of population size and social interaction give rise to emergent phenomena known as urban scaling [9]. Urban scaling describes the processes by which urban features such as economic features, wealth, crime, pollution, consumption patterns, and energy expenditure vary with changes in city size (i.e., population growth) [6]. A *linear scaling* response indicates no relationship between the urban feature and city size. For example, the amount of energy consumption per household is relatively similar across cities of similar size [5, 7]. Some characteristics of cities, for example road infrastructure, show *sublinear scaling* which means that as cities grow in size, the amount of road length and gas stations, relative to population size, decreases [5, 7]. In contrast, other features of the urban environment such as the relative amount of wealth, innovation, crime, and pollution per capita increases as cities grow in size, a phenomenon known as *superlinear scaling* [5, 7]. The way cities grow is also relevant to the scaling phenomena. While often treated as a static feature of cities, city size is the result of dynamic processes that imply many different types and rates of growth [6–8]. Figure 1 shows an example of three scaling responses for three hypothetical types of causes of death.

A large body of literature has explored urban-rural differences in health and has originated the urban penalty and urban advantage theories which posit deleterious or positive overall impacts of urban living for population health [2, 10]. However, urban-rural comparisons are often limited by the fact that cities are heterogenous in many features, including city population size. Additionally, while the urban-rural framework can provide convenient comparisons, the urban penalty and advantage theories are limited by the complexity and diversity of cities, which tend to vary across the globe; suggesting the benefits and risk of urban living are not uniform [2]. Given the complex and diverse nature of cities, there is an inherent need for a framework to outline and characterize the dynamic relationship between city characteristics and health.

Current literature applying the concept of urban scaling to health is scarce, with most research focusing on the scaling properties of factors that are determinants of health [5, 7, 11–14]. Understanding urban population dynamics, and subsequent scaling laws, are the first steps toward developing theories that describe the relationship between city characteristics and population health, with many of these characteristics being meaningful policy levers in terms of sustainability, resource limits, and healthy governance [2–4]. In this study, we review the evidence pertaining to the urban scaling of health outcomes, that is, how health outcomes scale with city size.

Methods

The main objective of this scoping review was to map the existing evidence pertaining to the urban scaling properties of health outcomes. We followed the framework of the Joanna Briggs Institute (JBI) [15] and reported methods and results using the Preferred Reporting Items for Systematic Review and Meta-Analysis Extension for Scoping Reviews (PRISMA ScR) guidelines [16]. More details on the scoping review methodology can be found in the review protocol [17].

Search strategy and selection criteria

Briefly, we searched for empirical or review studies that investigated city or urban size, growth, or urbanization, in relation to any health outcome, health behavior, or risk factor including prevalence, incidence, and mortality. The structured search strategy was executed in English, Spanish, and Portuguese utilizing the MEDLINE (accessed via PubMed) and Latin American & Caribbean Health Science Literature (LILACS) databases, with no time restrictions. Duplicate studies were removed, and the remaining studies were then screened for inclusion by two members of the research team (EMM and UB), regardless of study design and research quality. We excluded studies such as commentaries, studies with other primary objectives, and studies written in languages other than English, Spanish, Portuguese. Full-text studies were reviewed in duplicate by four members of the research team (EMM, UB, PHM, and AFO), with discrepancies resolved by consensus.

The key exposure of interest was any measure of city size or growth. We defined city size as a simple count of individuals residing in a city at a given point in time, and growth was defined as a change in the number of individuals residing in a city over time. Although these two

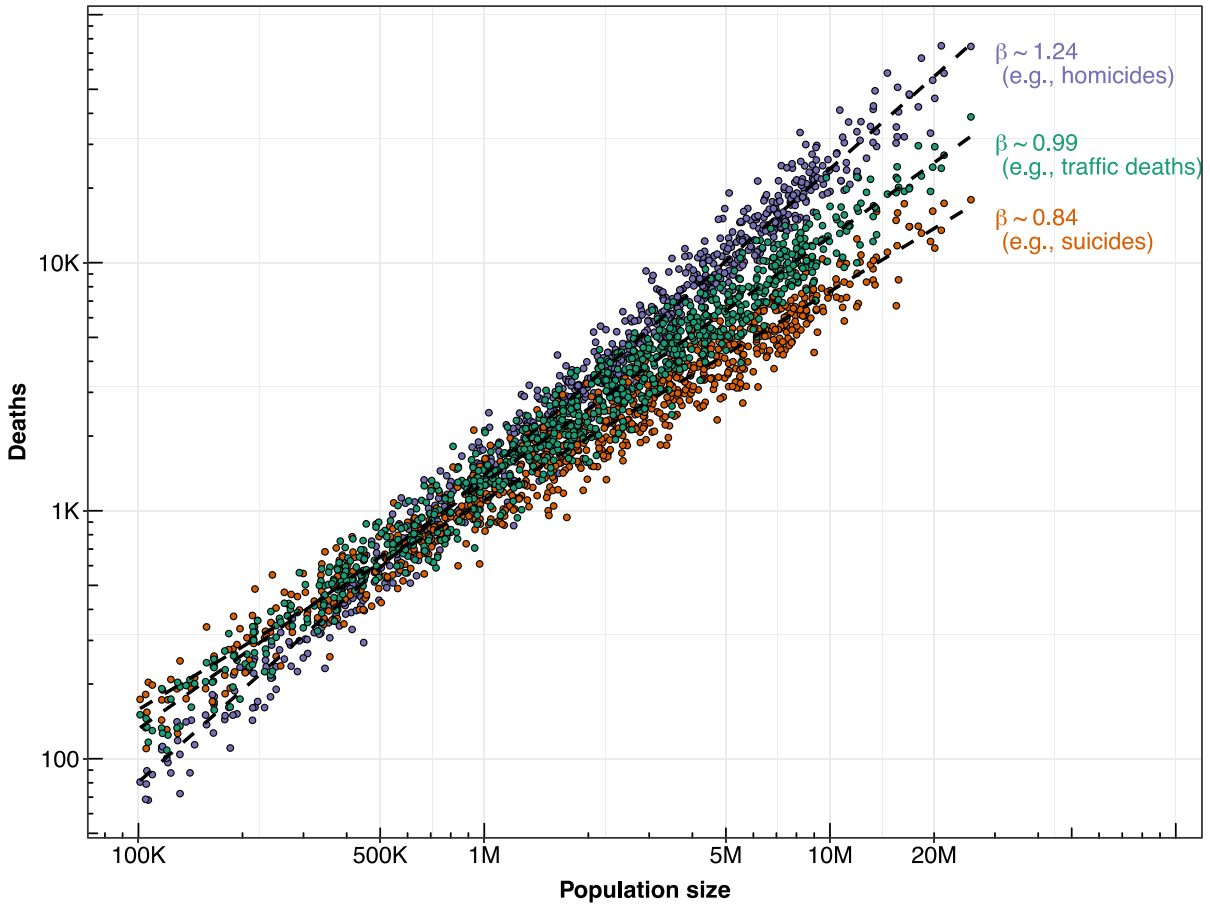

Fig. 1 Example of three urban scaling relationships (superlinear for homicides, linear for traffic deaths, and sublinear for suicides). *Footnote:* Data simulated using scaling coefficients from Melo et al. [89] for Brazilian cities

exposures are similar, differentiating between the two is critical in understanding any relationship between exposure(s) and outcome(s). Health outcomes were categorized according to the World Health Organization classification system for diseases and injuries [18] into: communicable, maternal, neonatal and nutritional conditions (CMNN), non-communicable diseases (NCDs) and their risk factors, and external causes or injuries. To determine which studies utilized an urban scaling framework, we identified scaling studies as those that specifically and explicitly presented findings in terms of an urban scaling response (i.e., sublinear, linear & superlinear scaling).

Presentation of results

We presented results by study inclusion/exclusion, study design, and methods, followed by key findings pertaining to the urban scaling of health outcomes for scaling and non-scaling studies in each category of health outcomes. We also summarized adjustment for covariates in scaling studies.

Role of the funding source

The funding sources had no role in study design, data collection, analysis, interpretation of data, writing, or in the decision to submit the manuscript. All authors had full access to all the data in the study and accept responsibility for the decision to submit the manuscript for publication.

Results

Study inclusion/exclusion

The PRISMA flowchart (Fig. 2) depicts the results of our review process. Our search yielded a total of

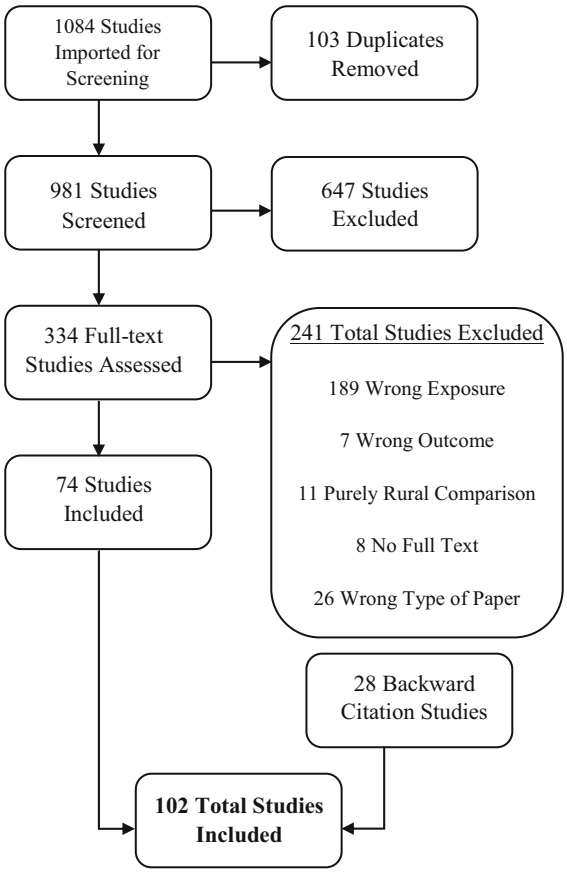

Fig. 2 PRISMA flowchart. *Footnote:* Wrong exposure refers to studies that do not have a city size or growth exposure. Wrong outcome refers to studies not using a health outcome. Wrong type of paper refers to editorials or opinion pieces. Purely rural comparison refers to studies that do not compare cities, but only urban and rural areas. Wrong setting refers to studies that were not set in cities

1084 studies. After title/abstract review, we found 334 studies eligible for full-text review, of which 74 were finally included. The most common reasons for exclusion were no exposure measure (e.g., city size or growth), commentaries, purely urban to rural comparisons (no comparison between cities), and no clearly defined health outcome. In addition to the 74 studies identified from the initial search, 28 additional studies were included through backward search of citations (cited by an included study), resulting in a total of 102 studies published from 1946 to 2019. A majority of the evidence was published in English (n = 98), and nearly 60% was published between 2010 and 2019. Only 15% of studies employed a scaling framework in their analyses (n = 15).

Study design and methods

Tables 1 and 2 describe overall characteristics of each non-scaling and scaling study, respectively. Ecological studies were the most common study design (n = 79), followed by individual level studies (n = 6), systematic reviews (n = 4), and simulation studies (n = 13). Around 90% of the studies used cross-sectional analyses (n = 93), and 9% used longitudinal analyses (n = 9). Roughly 73% of the studies were set in high-income countries (n = 75), and 17% in low- and middle-income countries (n = 17). A majority of the results were set in the Americas (n = 56), primarily in the USA (n = 42), and Brazil (n = 8), while the rest were set in Europe (n = 22) or Asia (n = 8). Additionally, 12 studies examined the urban scaling of health outcomes in numerous cities across more than one country.

The earliest studies were set in the nineteenth century in Scotland [19] and England [20], and the nineteenth and early twentieth century in the USA [21–23], while the majority were set in the twenty-first century (n = 56). The most commonly used city definitions were administrative units (n = 45) (e.g., counties, municipalities), followed by country-defined official metropolitan areas (n = 31), and other researcher-defined delineations (n = 21) that were based on satellite imagery data, relational classifications (e.g., core vs. fringe urban area), and arbitrarily assigned population size cut-points. Two studies did not present a clearly identifiable city definition, and three used several definitions concurrently.

The most common exposure among included studies was population size (n = 67), in which a simple count of the population living in the city was used, either as a continuous or categorical predictor. Other exposures included categorical predictors intended to capture levels of urbanicity (n = 23), population growth (n = 7), and study-specific measures of urbanization (n = 5). In all cases, these measures included at least one metric of city size, resulting in 95 studies using an exposure directly or indirectly based on city size, and only 7 studies using a population growth as the exposure. The most frequent class of health outcomes were, CMNN conditions (n = 49), followed by NCDs or their risk factors (n = 34), and injuries (n = 18). A few studies examined all-cause mortality (n = 7) and others had outcomes based on behaviors or health related perceptions (n = 5).

Table 1 Characteristics of Non-Scaling Manuscripts (n=84)

Characteristic		CMNN*		NCD*		EXTERNAL CAUSES/ INJURIES*		ALL-CAUSE MORTALITY*		OTHER*	
		N	Ref.	N	Ref.	N	Ref.	N	Ref.	N	Ref.
Exposure	Population Size	33	[21–23, 36-42, 44, 45, 50-57, 59-70, 116]	18	[23, 25, 41-43, 73, 74, 76, 85, 86, 88, 116-122]	4	[41, 42, 97, 123]	4	[19, 20, 24, 26]	1	[96]
	Population Size & Relative Location	5	[35, 46-49]	10	[72, 75, 77-80, 82-84, 124]	4	[94, 95, 98, 99]	0		1	[81]
	Population Growth	3	[33, 58, 103]	0		0		3	[27, 125, 126]	1	[127]
	Other	2	[34, 128]	4	[87, 128-130]	1	[128]	0		0	
Outcome Measure	Mortality Rates	14	[21, 23, 40, 41, 44, 46-52, 54, 57]	10	[23, 25, 41, 74, 75, 82-84, 120, 124]	3	[41, 98, 99]	6	[20, 24, 26, 27, 126, 127]	0	
	Prevalence	2	[35, 37]	11	[78-80, 85–88, 118, 120, 121, 130]	3	[94, 97, 122]	0		3	[81, 96, 128]
	Incidence	16	[22, 33, 36, 38, 39, 42, 45, 55, 58, 60, 61, 66, 67, 69, 70, 103]	5	[42, 72, 76, 116, 122]	1	[42]	0		0	
	Several	1	[128]	6	[43, 73, 77, 117, 128, 130]	2	[95, 128]	1	[19]	0	
	Other	10	[34, 53, 56, 59, 62-65, 68, 115]	0		0		0		0	
City Definition	Administrative Unit	19	[21–23, 33, 34, 38-42, 44, 50, 51, 56, 58, 59, 64, 69, 103]	16	[23, 25, 41-43, 72, 74, 76, 77, 85, 86, 88, 118, 120, 122, 130]	4	[41, 42, 98, 123]	5	[19, 20, 27, 125, 126]	1	[127]
	Official Metropolitan Area	7	[35–37, 46–49]	11	[75, 78-80, 82-84, 116, 117, 119, 124]	4	[94, 95, 97, 99]	1	[26]	2	[81, 96]
	Other	16	[45, 52–55, 57, 60–63, 65–68, 70, 115]	4	[73, 87, 121, 129]	0		0		0	
	Unclear	1	[128]	1	[128]	1	[128]	1	[24]	0	
Setting-Time*	2nd Half of 19th Century	2	[23, 103]	1	[23]	0		4	[19, 20, 24, 27]	0	
	1st Half of 20th Century	19	[21–23, 40, 41, 50–54, 60, 62, 63, 65, 66, 68–70, 103]	2	[23, 41]	1	[41]	3	[19, 26, 27]	0	
	2nd Half of 20th Century	20	[33, 34, 37–39, 44, 46, 57, 60–62, 64–70, 114, 128]	18	[25, 72–75, 82–85, 87, 88, 116, 118, 119, 120, 128–130]	6	[94, 95, 97, 99, 123, 128]	5	[20, 26, 27, 125, 126]	1	[127]
	21st Century	20	[33–36, 38, 39, 42, 44, 45, 47–49, 55-59, 64, 114, 127]	16	[42, 43, 76–80, 83, 86, 87, 117, 120, 121, 124, 128, 130]	6	[42, 97-99, 123, 128]	2	[27, 125]	2	[81, 96]
Setting-Location	Americas	21	[21–23, 34, 35, 39–42, 44, 46–49, 51, 53, 55–57, 59, 63]	18	[23, 25, 41, 42, 72, 74, 75, 78–80, 82–84, 86, 117, 119, 124, 130]	7	[41, 42, 94, 95, 97-99]	1	[26]	1	[81]
	Africa	3	[45, 64, 103]	0		0		0		1	[128]
	Europe	11	[37, 50, 58, 60-62, 65-69]	6	[73, 88, 116, 118, 120, 122]	1	[123]	3	[19, 24, 125]	1	[96]
	Asia	3	[33, 38, 115]	4	[43, 76, 77, 85]	0		1	[126]	0	
	Other	5	[36, 52, 54, 70, 128]	4	[87, 121, 128, 129]	1	[128]	2	[20, 27]	0	
Design-Type	Ecological	28	[21–23, 33–35, 37-42, 44-52, 54, 60, 62, 63, 67, 70, 103]	25	[23, 25, 41–43, 72, 74–80, 82–86, 88, 116, 118, 119, 122, 124, 130]	8	[41, 42, 94, 95, 97-99, 123]	7	[19, 20, 24, 26, 27, 125, 126]	1	[96]

Table 1 (continued)

Characteristic		CMNN*		NCD*		EXTERNAL CAUSES/ INJURIES*		ALL-CAUSE MORTALITY*		OTHER*	
		N	Ref.	N	Ref.	N	Ref.	N	Ref.	N	Ref.
	Experimental	13	[36, 53, 55-59, 61, 64-66, 68, 69]	0		0		0		0	
	Individual Level	1	[115]	3	[73, 117, 120]	0		0		2	[81, 128]
	Review	1	[127]	4	[87, 121, 128, 129]	1	[129]	0		0	
Design-Time	Cross-Sectional	40	[21-23, 34-37, 39-42, 44-70, 115, 128]	29	[23, 25, 41-43, 72, 74-80, 82, 85-88, 116-122, 124, 128-130]	9	[41, 42, 94, 95, 97-99, 124, 129]	4	[19, 20, 26, 127]	3	[81, 96, 128]
	Longitudinal	3	[33, 38, 103]	3	[73, 83, 84]	0		3	[24, 27, 126]	0	

Historical studies examining the urban penalty in high-income countries

We found a number of historical studies examining the urban penalty in the nineteenth or first half of the twentieth century in the UK and the USA, positing that urban living had adverse health impacts as a result of the unhealthy environments created by population concentration and industrialization [10]. The studies focused on the nineteenth century showed lower life expectancy in larger cities [19, 24]. Results from the early twentieth century in the USA were complex, with higher mortality in smaller cities immediately following the 1918 influenza pandemic, followed by a change in the burden of mortality from infectious disease mortality to NCD mortality in larger cities [23]. By the middle of the twentieth century NCD rates in larger cities began to stabilize and decrease over time [25], while mortality remained highest in metropolitan areas with populations greater than 50,000, except for accidents and suicides [26]. Worldwide, studies focused on the early twentieth century described rapid post-war population growth in cities linked to low urban wages and the rise of poor mega-cities [27].

Communicable, maternal, neonatal, nutritional conditions and infant mortality

We found 49 studies that examined the association between city size or growth and rates of CMNN conditions. Six of these specifically employed a scaling framework (Table 2). In general, for cities in the USA, Brazil, and Sweden, the incidence of human immunodeficiency virus (HIV), influenza, meningitis, dengue fever, leprosy, and hepatitis A, B, and C scaled superlinearly with city size [28]. This superlinear scaling behavior was also observed for the incidence of sexually transmitted infections (STIs), specifically chlamydia, syphilis, and gonorrhea [28–31], indicating that infections of this type are more common in large cities. Two studies examined the incidence of acquired immunodeficiency syndrome (AIDS) as a function of population size, finding a superlinear behavior [7, 32]. However, a few diseases (hantavirus and leprosy) were more common in medium-sized cities [33, 34]. There was only one study looking at infant and child mortality in US and Brazilian cities, which found higher rates of infant and child mortality in small cities [28]. Overall, these

Table 2 Characteristics of Scaling Manuscripts (n=15)

Characteristic		CMNN*		NCD*		EXTERNAL CAUSES/ INJURIES*		OTHER*	
		N	Ref.	N	Ref.	N	Ref.	N	Ref.
Exposure	Population Size	4	[7, 28, 31, 32]	1	[28]	9	[7, 12, 13, 28, 89–93]	1	[28]
	Population Size & Relative Location	2	[29, 30]	1	[71]	0		1	[131]
Outcome Measure	Mortality Rates	0		1	[71]	7	[12, 13, 89–93]	0	
	Prevalence	0		0		0		1	[131]
	Incidence	5	[7, 29–32]	0		1	[7]	0	
	Several	1	[28]	1	[28]	1	[28]	1	[28]
City Definition	Administrative Unit	2	[28, 32]	2	[28, 71]	3	[28, 90, 91]	1	[28]
	Official Metropolitan Area	3	[29–31]	0		2	[12, 92]	1	[131]
	Administrative Unit & Official Metropolitan Area	1	[7]	0		4	[7, 13, 89, 93]	0	
Setting-Time*	2nd Half of 20th Century	3	[7, 28, 32]	2	[28, 71]	6	[7, 12, 28, 89, 91, 93]	2	[28, 131]
	21st Century	6	[7, 28–32]	2	[28, 71]	8	[7, 12, 13, 28, 89, 90, 92, 93]	2	[28, 131]
Setting-Location	Americas	4	[29–32]	1	[71]	7	[12, 13, 89–93]	1	[131]
	Other	2	[7, 28]	1	[28]	2	[7, 28]	1	[28]
Design-Type	Ecological	6	[7, 28–32]	2	[28, 71]	9	[7, 12, 13, 28, 89–93]	2	[28, 131]
Design-Time	Cross-Sectional	6	[7, 28–32]	2	[28, 71]	9	[7, 12, 13, 28, 89–93]	2	[28, 131]

**Note:* Citations belonging to more than 1 subcategory are listed multiple times across every applicable subcategory

studies did not adjust for covariates, except those focused on STIs, which explored the role of several city-level covariates (age distribution, racial/ethnic composition, income, education) in the generation of scaling patterns [29, 30].

We found 43 studies examining the relationship between CMNN conditions and city size without a scaling framework, most of them finding higher rates in larger cities (Table 3). In Europe and the USA, larger cities had a higher prevalence of HIV and AIDS cases [35, 36], and other STIs [37]. The incidence of vector-borne diseases such as dengue fever in Singapore and leishmaniasis in Brazil was found to be higher in larger cities compared to smaller cities [38, 39]. Additionally, mortality from tuberculosis in the USA was higher in larger cities during most of the twentieth century [40, 41]. A few diseases followed inverted u-shapes with population size (more common in medium-sized cities), including the incidence of hantavirus in China [33], or leprosy in Brazil [34]. Finally, hospitalizations due to communicable disease in Brazil and South Korea were lower in large cities [42, 43]. Aside from communicable diseases, there were several non-scaling studies of infant mortality, maternal, and neonatal conditions (n = 10), however, these findings are heterogenous and appear to vary by health outcome and geographic context. In Mexico, under 5 mortality due to birth defects was more prevalent in larger cities [44], while under 5 mortality rates were higher in smaller cities of Sub-Saharan Africa [45]. In the USA perinatal [46], infant [46–48], and child mortality rates were higher in smaller cities [49].

Two epidemic diseases have frequently been linked to population size: influenza and measles. We found a total of 11 studies that examined the relationship between influenza and city size, one using a scaling framework [21]. Six of these examined the 1918 influenza pandemic, finding that while mortality was generally higher in urban areas as compared to rural areas [50], there was either a weak correlation with city size [51–53], or slightly higher mortality in smaller cities [21, 50, 54]. These results were consistent with the five studies examining seasonal influenza, finding that geographic location matters more than city size [55–57], although population growth [58] and size [59] may play a role in shaping seasonal flu epidemics.

We found a total of 11 studies examining the relationship between measles and city size, two of them using a scaling framework [60, 61]. All measles studies

Table 3 Scaling Relationships

Classification	Scaling Relationship	Health Outcome	Setting- Location	Setting- Time	Citation(s)	Year
Communicable, Maternal, Neonatal, and Nutritional Conditions (CMNN)	Linear (No Relationship with City Size)	Hepatitis B	Brazil	2007	[28]*	2015
		Influenza	Brazil	2010		
	Sublinear (More Common in Small Cities)	Dengue	Brazil	2001		
		Infant & Child Mortality	Brazil	2012		
		Leprosy	Brazil	2001, 2002		
		Infant & Child Mortality	United States	2000-2009		
	Superlinear (More Common in Large Cities)	Infant & Child Mortality	Brazil	1981		
		Influenza	Brazil	2009		
		Hepatitis B	Brazil	2012		
		Dengue	Brazil	2012		
		AIDS cases	Brazil	1980-2012		
		HIV	Brazil	1990, 2012		
		Meningitis	Brazil	2001, 2012		
		Hepatitis A	Brazil	2007, 2012		
		Hepatitis C	Brazil	2007, 2012		
		Chlamydia	United States	2011		
		HIV	United States	2000-2009		
		Chlamydia Gonorrhea Syphilis	United States	2007-2011	[29]	2018
		Chlamydia Gonorrhea Syphilis	United States	2007-2011	[30]	2015
		Chlamydia Syphilis	United States	2007-2011	[31]	2018
		AIDS cases	United States, China, Germany	1990-2003	[7]*	2007
Non-Communicable Diseases (NCD)	Linear	Cerebrovascular Accident Mortality	Brazil	2012	[28]*	2015
		Colon Cancer Mortality	Brazil	2012		
	Sublinear	Colon Cancer Mortality	Brazil	1981		
		Diabetes Mortality	Brazil	2012		

Table 3 (continued)

Classification	Scaling Relationship	Health Outcome	Setting- Location	Setting- Time	Citation(s)	Year
		Diabetes Mortality	Sweden	2008-2012		
		Heart Attack Mortality	Sweden	2008-2012		
		Lung Cancer Mortality	Sweden	2008-2012		
		Chronic Respiratory Insufficiency Mortality	Sweden	2008-2012		
		Obesity	Sweden	2010-2013		
		Obesity	United States	2010		
	Superlinear	Diabetes Mortality	Brazil	1996		
		Cerebrovascular Accident Mortality	Brazil	1996		
		Heart Attack Mortality	Brazil	1981, 2012		
		Lung Cancer Mortality	Brazil	1981, 2012		
		Chronic Respiratory Insufficiency Mortality	Brazil	1981, 2012		
		Cancer Cardiac Disease Respiratory Disease Endocrine Metabolic Disease	United States	1999-2010	[71]	2018
External Causes/Injuries	Linear	Pedestrian Mortality	United States	1994-2011	[93]*	2016
		Traffic Accident Mortality	United States & Brazil	2003-2007	[89]*	2014
	Sublinear	Rape	Brazil	2009	[28]*	2015
		Traffic Accident Mortality	Brazil	2012		
		Suicide	Brazil	1981, 1995		
		Suicide	Brazil	2005-2014	[90]*	2018
		Suicide	Sweden	2008-2012	[28]*	2015
		Drug Poisoning	United States	2000		
		Suicide	United States & Brazil	1992-2009	[89]*	2014
	Superlinear	Traffic Accident Mortality	Brazil	1981	[28]*	2015
		Homicide Mortality	Brazil	2000	[91]	2013
		Homicide Mortality	Brazil	2010	[13]	2014
		Rape	Brazil	2012	[28]*	2015
		Homicide, Traffic Accident Mortality	Brazil	2005-2014	[90]*	2018
		Homicide Mortality	Several	2003-2009	[92]	2012
		Rape	Sweden	2013	[28]*	2015

Table 3 (continued)

Classification	Scaling Relationship	Health Outcome	Setting- Location	Setting- Time	Citation(s)	Year
		Homicide Mortality	United States	1969-2006	[12]	2010
		Non-Pedestrian Mortality	United States	1994-2011	[93]*	2016
		Excessive Alcohol Consumption	United States	2006-2012	[28]*	2015
		Violent Crimes	United States	2009-2011		
		Homicide Mortality	United States & Brazil	1992-2009	[89]*	2014
		Homicide Mortality	United States, China, Germany	1990-2003	[7]*	2007
Other	Linear	Organ Donation	United States	1995-2008	[131]	2011
	Sublinear	Physical Inactivity	United States	2010	[28]*	2015

**Note:* Citations with health outcomes belonging to multiple classifications are listed multiple times across applicable classifications

characterized how city size affected the shape of epidemics, including the intensity and frequency of fadeouts. This started with the works of Bartlett [62, 63], who characterized a critical community size (CCS) threshold of 300–400,000 persons, above which cities do not experience fadeouts in measles incidence, the temporary disappearance of measles from a population. This CCS threshold is influenced by birth rates and, nowadays, by vaccination coverage [64, 65]. Several studies suggested that in populations below the critical size, the probability of fadeouts increase as population size decreases [60, 62–70]. A second critical aspect of the measles dynamics is the presence of a spatial hierarchy, where epidemics of measles move from larger "donor" cities to nearby smaller "recipient" towns [69, 70], this phenomenon scales superlinearly with donor city size, so that larger cities are more likely to be the source of regional epidemics [61]. Last, the incidence of pertussis, another frequent but vaccine-preventable childhood disease, follows a pattern similar to measles [22].

Non-communicable diseases

Of the 34 NCD studies identified in the review, there were only 2 scaling studies (Table 3). In a study of four major classes of NCDs in large urban US counties, the authors found a superlinear scaling behavior for deaths due to cancer, circulatory, respiratory, endocrine, nutritional and metabolic diseases [71]. However, the authors found that this superlinear behavior was sensitive to the size of included counties, as the relationships turned sublinear when only the largest countries were included, possibly indicating higher mortality in mid-sized cities. In a study with multiple outcomes in US, Brazilian and Swedish cities [28], the NCD results varied by context. For example, heart attack mortality, lung cancer, and respiratory insufficiency, scaled superlinearly in Brazil and sublinearly in Sweden [28]. Additionally, in the USA and Sweden, obesity scaled sublinearly. This same study suggested that physical inactivity scaled sublinearly, and excessive alcohol consumption scaled superlinearly in US cities [28]. Only one of these studies explored the effects of adjustment for covariates by including covariates of income and population density [71].

We found 32 non-scaling studies that examined the relationship between city size or growth and NCDs. The association between city size and cancer varied by type and location. The incidence of acute lymphocytic leukemia was higher in large US cities [72], while in Europe and the USA lung cancer and its major risk factor, smoking, were more common in larger than in smaller cities in the second half of the twentieth century [73, 74], a pattern consistent with higher mortality by other cancer types with increasing urbanization levels [75]. In South Korea thyroid and colorectal cancers were more common in larger cities, but gastric and lung cancers more common in smaller cities [76]. The prevalence of cardio-metabolic conditions varied by city size and location. Larger cities in China had a higher prevalence of obesity [77], while in the USA the prevalence of obesity was lower in large cities [78–80], a result consistent with higher rates of physical inactivity in less urbanized areas [81]. Several findings indicate that coronary heart disease mortality in the USA used to be more prevalent in larger cities, compared to their smaller counterparts [41, 82–84]. Last, the prevalence of psychiatric disorders such as clinical depression and anxiety disorder increased with city size [85–88].

External causes/injuries

Health outcomes classified as external causes and injuries are among the health outcomes more frequently studied from a scaling perspective (n = 9, Table 3). Overall, these findings largely suggested that homicides scale superlinearly with city size [89–92], but a study in Brazil suggested that this result may not be linear, with potential for mid-sized cities to have higher homicide rates [13]. Aside from homicides, one study found that other violent crimes such as rape and domestic physical violence scaled superlinearly [28]. Suicide mortality in US and Brazilian cities scaled sublinearly [89, 90]. Studies on traffic-related injuries displayed linear [89], superlinear [28, 90], and sublinear behaviors [28]. These differences may be related to the type of traffic-related mortality, as a study in US cities found that pedestrian fatalities scaled sublinearly with population size, and non-pedestrian fatalities displayed a superlinear scaling response [93]. For the most part, these scaling studies did not adjust for any covariates; except for two studies, which adjusted for educational attainment [31] and income per capita [93], respectively.

We found 9 non-scaling studies of injuries. Among these non-scaling studies, homicide was more common in larger cities compared to smaller cities [41, 94, 95]. Levels of perceived insecurity were also found to be higher in larger cities than in smaller cities [96]. A few studies suggested that other injuries, such as those from

motor vehicle accidents and suicide are more common in less populated areas [97, 98]. Out-of-hospital injury related mortality rates were higher in less urbanized areas [43], while injury hospitalization rates in Brazil were highest in mid-sized cities [42]. Last, in a small study using data from 18 cities in New Mexico, USA, the rate of unintentional drug overdoses was higher in larger cities than in smaller cities [99].

Discussion

In this scoping review, we mapped evidence regarding the associations between city size or growth and health outcomes, with a focus on studies with an explicit scaling framework. We highlight five key findings. First, we found a diverse literature from many different geographical and temporal settings and outcomes, that included heterogeneous city definitions and different operationalizations of city size (e.g., continuous, as is the case for all scaling studies and some non-scaling studies, as well as categorical). Second, we found evidence of an urban penalty with higher mortality and worse health outcomes in larger cities of high-income countries, at least during the nineteenth century, that shifted in the early twentieth century toward lower mortality in larger cities. Third, we found that two key diseases with an epidemic component, measles, and influenza, are influenced by city size in conjunction with other factors like geographic proximity and transmission potential, while other communicable diseases such as STIs, HIV, and dengue tend to occur more frequently in larger cities. Fourth, we found that NCDs show a heterogeneous pattern that depends on the specific outcome and context. Fifth, homicides and other crimes are more common in larger cities, suicides are more common in smaller cities, and traffic-related injuries show a less clear pattern that may differ by context and type of injury.

A majority of the studies in this review were set in high-income countries (75 out of 102, 74%). While we captured a few studies from low- and middle-income countries (LMIC), such as Brazil and Mexico, the absence of evidence examining the urban scaling in other settings is a clear gap in the literature. This lack of evidence is especially worrisome for low-income countries, where poor sanitation, inequalities in resource availability, and overcrowding are especially prevalent in urban areas and may have a large influence on scaling patterns [100]. Furthermore, most future urban population growth is expected to occur in LMICs, specifically in Latin America, Asia, and Africa, and understanding the consequences of urban growth in these settings is key to achieving the Sustainable Development Goals [101] and should be a priority of future research.

One key aspect of being able to compare cities is having a clear definition of their boundaries [102]. In this scoping review, we found large heterogeneity in the way cities are defined. There is no single universally accepted definition of a city, and more often than not, the way cities are defined varies across countries and regions. While administrative units were the most used city definition, their primary purpose is administrative, and they may not represent actual city boundaries. Understanding the consequences of different city definitions on the scaling properties of health outcomes is a key direction of future research, as previous studies have highlighted that the scaling laws of some city features may vary systematically by city definition [11]. In a small number of studies we were not able to even identify what the authors referred to as "city", which creates issues for reproducibility. Future research on urban health should clearly define what is meant by "city" and how boundaries are defined.

Our second key finding is that an urban penalty was present in the nineteenth and early twentieth century for studies set in what are now high-income countries [19, 22–27, 103], with a shift occurring during the first half of the twentieth century toward lower mortality, especially due to communicable diseases, in larger cities of high-income countries [23]. The shift in mortality is likely attributable to changes in both rural and urban areas [2]. However, the heterogeneity in outcomes observed for cities of similar size in most scaling studies points to other city characteristics that are driving health. The emergence of these characteristics depends not only on size, but also on differences in geographic context, connectivity, resource availability, and economic growth, among many other factors [2]. Aside from being complex, city populations are among the most diverse; and while urbanization can affect health, these effects are heterogeneous for different populations, resulting in inequities at multiple levels [104]. Additionally, the observed shift in mortality may be related to changes in the urbanization processes [2, 27], evident in present day LMICs where rapid urbanization and development may contribute to unsafe settlement conditions and poor access to services, which can further exacerbate the

urban penalty [105]. Whether the shifts in disease burden that originally occurred in cities of high-income countries are being replicated currently in LMIC cities has yet to be studied, precluding a complete understanding of this phenomenon, so future studies should leverage cross-national comparisons of cities to understand the dynamic associations between urbanization and health in countries at different stages of development [106].

Our third finding identified complex associations of city size and growth with certain diseases such as measles and influenza, and superlinear associations with city size for other commonly studied communicable diseases such as STIs, HIV, and dengue fever. A number of studies examined the 1918 influenza pandemic, with mixed evidence regarding the role of city size, consistent with studies on seasonal influenza. On the other hand, for measles, city size has a clear effect on the size and shape of epidemic waves [69, 70], as factors such as the critical community size, spatial hierarchies, and fadeout probabilities are all related to city size [68]. Last, STIs follow a consistent superlinear scaling pattern [30], but the scaling behavior of specific STIs is heterogenous and may depend on variability in disease transmission [29]. The effect of transmission variability on disease dynamics has been reported before [107, 108], and currently represents a potential avenue of future research in understanding the dynamics of large outbreaks such as the COVID-19 pandemic [109, 110].

Our fourth finding was that NCDs show a heterogenous pattern which varies based on health outcome, geographic context, developmental stage, and other factors. This is evident in the findings that cardiometabolic conditions scaled differentially in cities of the USA, Brazil, and China, where the USA tends to display a sublinear behavior (outcomes more common in smaller cities) while other countries display superlinear behaviors (outcomes more common in larger cities). While NCDs were the second most common class of health outcome in the review, there is limited evidence about the urban scaling of NCDs to date.

Our fifth key finding, is that the scaling properties of injuries were mostly consistent, indicating that homicides and other serious crimes were more common in larger cities, and suicides were more common in smaller cities. However, the scaling properties of road-traffic injuries were less clear and seemed to vary by type of injury (e.g., pedestrian vs. other road users) [93]. This may also be due to underestimation resulting in relatively low counts of injuries, compared to broader causes of death, which may lead to statistical issues in estimating scaling coefficients when a number of cities have zero counts of a specific injury [92].

Our review identified a few directions for future research on the urban scaling of health outcomes. We found very little research examining population growth as an exposure. The study of population growth in longitudinal study designs allows better inferences regarding the possible causal link between city size and health than cross-sectional analyses of city size. Drawing inferences regarding the links between city size and city outcomes from cross-sectional analyses of city size relies on an important assumption: the absence of confounding by other factors associated with city size (i.e., differences between cities of different sizes are equivalent to differences associated with changes in city size for a given city over time, which holds at least time invariant city factors constant). This is also known as the assumption of ergodicity (i.e., lack of path dependence), or no impact of how the city arrived to that population number [111]. Recent studies have challenged this assumption, finding that the longitudinal scaling properties of urban features may differ from the cross-sectional properties [112–114]. Better understanding of the links between city size and health requires longitudinal analyses that examine population growth within cities over time as well as attention to the type of city growth and the processes driving growth.

While scaling studies aim to describe changes in city outcomes with changes in city size, the scaling framework also allows for the differentiation between size-related and place-specific effects, as proposed by Bettencourt, Lobo, Strumsky & West [12]. This is achieved through the mapping and examination of regression residuals from the basic scaling equation, which contain deviations from the empirically estimated scaling power law. These residuals are dimensionless indicators, independent of city size, that can provide quantitative information about the performance of urban areas and allow for calculation of correlations with other city-level predictors. These other city-level predictors include city-level policies,

social environment features (e.g., levels of poverty, inequality, segregation, etc.), and physical and built environment characteristics (e.g. climate, air pollution, urban landscape, street design, etc.), among others. The key contribution of a scaling analysis that includes an exploration of residuals would be the joint interpretation of both size-related patterns (e.g., a scaling coefficient above 1 indicating a higher homicide rate in larger cities) and city-specific effects derived from other city features independent of city size (e.g., cities with higher income inequality having a higher homicide rate).

Finally, all studies included in this review have a common objective of examining the relationship between city size and some health outcome(s); features characteristic of the urban scaling framework. However, we found heterogeneity in how these studies were conducted, in terms of definitions, operationalizations of city size, and the presence of (or lack thereof) adjustment variables. For example, we only found a few studies that examined how introducing adjustment variables changed scaling patterns [29–31, 39, 71, 93]. Future research should be transparent about the inclusion of relevant covariates, as adequately controlling for these covariates can influence the scaling response and also provide meaningful evidence on the relationship between covariates (e.g., income, education, population density) and health in cities. For example, given the important role of age in driving mortality, studies of the scaling of deaths with city size should consider how adjusting for age may change scaling coefficients.

We acknowledge some limitations. First, our search strategy may have missed some studies on city size/growth and health, especially if they were published in journals not indexed in the databases we searched. This may be especially important for studies published in the early twentieth century, which may not be entirely captured in these databases. However, in order to increase the scope of the review, we also used a backwards search to identify references cited by included studies. Second, we did not complete a forward search (i.e., a search for papers citing included studies). Consequently, we may have missed studies relevant to our objectives. Additionally, the decision to search only two databases (PubMed and LILACS) may have excluded relevant studies. Last, given the broad scope of our review, we could not present the results of each study in detail. However, as is the goal of scoping reviews, our main objective was to map the available evidence and identify gaps for future research. We have also provided in Appendix Table 4 the full scope of our review, detailing all reviewed studies. We also acknowledge several strengths. This scoping review has provided an initial comprehensive map of evidence on the urban scaling of health outcomes. We reviewed 102 studies in total, drawing attention to several factors that may contribute to inconsistencies between studies, including exposure, and city definitions. The scoping review was not limited to a single language and was able to capture evidence in English, Spanish, and Portuguese.

Conclusions

In this scoping review, we have identified a rich and complex evidence landscape on the urban scaling of health outcomes and the relationship between city size and health. However, we have identified several gaps that merit future research, including a paucity of research in LMICs urban areas and across a variety of countries in different settings, along with a lack of clarity and consistency in city definitions, and how different definitions may lead to changes in inferences. We also identified several aspects where current research in scaling may help in understanding disease dynamics, including the exploration of the complexity of transmission of epidemic diseases, the recognition of the importance of studying population growth (i.e., longitudinal population size), the use of deviations from the scaling law to study predictors of health outcomes, and greater transparency about decisions regarding adjustment for important covariates. With growing urban populations worldwide, the continuous challenge of non-communicable diseases, the importance of injury mortality in premature mortality, and the (re-)emergence of infectious diseases, understanding the consequences of our urban world seems key in the design and planning of interventions to address unmet public health needs.

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Author contribution EMM and UB conceptualized the study, executed the search and screening of studies, and drafted the first version of the manuscript. EMM, UB, PHM and AFO reviewed all studies. All authors contributed to the interpretation of results and editing of the final manuscript.

Declarations

Conflict of interest The authors declare no competing interests.

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