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Scaling patterns of human diseases and population size in Colombia

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ABSTRACT

Colombia has had one of the largest numbers of internally displaced populations in the world and in 2016 entered a period of post-conflict. These socio-ecological and geopolitical processes and trends have increased the migration of people towards cities and accordingly are affecting the distribution and occurrence of tropical diseases in its urban and peri-urban areas. Studies have suggested that anthropogenic phenomena such as urbanization scale according to the size of human populations regardless of cultural context. But, other studies show that health epidemics such as malarial and human immunodeficiency virus infections, follow a scale-free distribution in terms of urban population size and density. Here, we explore these relationships and dynamics in a tropical context using statistical analyses and available geospatial data to identify the scale relationships between urban growth processes and disease transmission in Colombia. Our results show that the dynamics of rural populations and certain diseases were characterized by power-laws that are indeed observed in urbanization studies. However, as opposed to these other studies, we found that malaria presented a higher intensity of infection in human settlements with less than 50,000 individuals and in particular for ethnic, indigenous populations. Results indicate that disease and urbanization relationships in Colombia do indeed follow scales; findings that differ from previous epidemiological studies such as those for malarial infection. Additionally, we identified trends showing that malarial infections become endemic in peri-urban areas. This approach using few, but robust and readily available, data is key for managing public health issues and understanding the spatial distribution of environmental impacts in the urbanizing tropics.

1. Introduction

As the world is becoming increasingly urbanized, there is growing attention and uncertainty as to the potentially positive and negative effects of the urban population related growth processes on the health of human populations. Of particular concern in middle- and low-income tropical countries is that urban planning and public policies are seldom developed, or informed, by evidence-based health information that is relevant to the population (Daniels et al., 2014). Another limitation in such countries lacking resources and information are monitoring approaches and techniques that can readily assess trends in infectious and non-communicable diseases across space and human settlements (Eckert and Kohler, 2014; Neiderud, 2015). Numerous complex pathways connecting urbanization processes, environmental impacts, and human health have received growing interest from researchers and policy makers alike (Giles-Corti et al., 2005; Landrigan et al., 2018). However, there is limited understanding of some structural drivers of disease distribution across spatial and temporal scales. Taking advantage of simple and readily available data such as population size and administrative units could make for more efficient and effective public health planning and environmental management efforts and research at both national and regional scales (Goodchild, 2011; Hui, 2009).

Evidence to inform the management of limited public health resources is crucial in contexts with rapid and unplanned urbanization and where the potential negative effects of urbanization and population size on human health are exacerbated. Moreover, the effects of population size on human disease may not be equally distributed across different

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populations, particularly in low- and middle-income countries with high levels of forced internal and external migration. One such socio-ecological context to explore the effects of population size and unplanned urbanization across geographies and administrative levels is Colombia. The country, for example, has several complex and ongoing public health challenges including: communicable, non-communicable, environmental, and vector-borne diseases, and a rapidly emerging environmental and demographic transitions. Although 75% of its population currently lives in cities, this number is projected to increase in the near future (Green et al., 2018).

Colombia has multiple large urban centers with a diverse range of population sizes, and high population mobility between mid-sized cities (Camargo et al., 2020). These multiple social, environmental, and economic challenges have been exacerbated by recent events. The country has one of the largest internally displaced populations in the world and the displacement rate is currently increasing (IDMC, 2020; UNHCR, 2021a, 2021b). Also, after more than 50 years of war between the government and The Revolutionary Armed Forces of Colombia guerrilla (FARC), the two parties signed a peace treaty in 2016 that has further influenced internal displacement patterns. Moreover, in the midst of the Covid-19 pandemic, Colombia became the largest receiver of refugees and immigrants from neighboring Venezuela (UNHCR, 2021a). In addition to other socio-ecological and geopolitical factors, these population dynamics are interconnected with processes such as urbanization, deforestation, and other land use-cover change (Sánchez-Cuervo and Aide, 2013).

This urbanization process and increased presence of displaced and recently arrived people in urban and peri-urban areas of Colombian cities is characterized by highly disturbed environments, poor infrastructure, and marginalized conditions (Green et al., 2018). As such, taking advantage of available data on: population size and density, mobility patterns, urban morphology, and other socio-ecological factors in cities is key for the study of infectious disease in rapidly changing environments (Santos-Vega et al., 2016). In Colombia, previous research showed that these factors affect public health and lead to increased vulnerability to disease burden particularly in peri-urban locations and among recently arrived ethnic minorities (Feged-Rivadeneira et al., 2018). Even though our understanding of the connection between urbanization and population health in rapidly changing countries like Colombia is still in its early stages, it is likely that simple linear associations do not offer an adequate description of how disease burden distribution in different populations varies across human settlements and their population size and ethnic diversity (Santos-Vega et al., 2016). Population size, in particular, is a readily available Census variable that is used for determining political representation and administrate units, allocating resources, and for understanding and differentiating rural versus urban human settlements and their inherent dynamics (Daniels et al., 2014; Feged-Rivadeneira et al., 2018). For example, while sparsely populated, rural human settlements in early stages of the urbanization process are experiencing active disturbances such as illegal mining and deforestation, leading to higher than average risks for malaria disease occurrence; improved infrastructure and populations size in later stages of urbanization (i.e. more and improved infrastructure) can reduce morbidity rates resulting from this infection (Feged-Rivadeneira et al., 2018). Thus, a further exploration that accounts for the complex relation between morbidity dynamics and how they change across different population sizes and demographics is needed.

One emergent approach is the application of scaling dynamics analyses to better understand organisms and their metabolic rates, but it can also be applied to study other phenomena, such as cities, organizations, social networks and overall sustainability (Brenner and Schmid, 2015; Gandy, 2004; Lefebvre, 2003, 1991; West, 2017). While analyzing urban phenomena using relationships akin to those of living organisms and metabolic rates is not novel (Gandy, 2004), such approaches have varying acceptability in the field of urban studies (Brenner and Schmid, 2015; Lefebvre, 2003, 1991). For example, studies on urbanization using scaling dynamics have found that human phenomena can scale according to population size (Bettencourt, 2013; Bettencourt et al., 2007; Brenner and Schmid, 2015; Noulas et al., 2012). We refer to "scale" as the geographical and areal extent or dimensions of an area of interest or phenomena, while "scaling" is the process of measuring, locating, and understanding these dimensions and phenomena across the continuum of geographical and areal extents.

Similarly, an emergent body of literature has also focused on the growth processes and spatial distribution of cities according to certain patterns and scales. For example, studies have found that such patterns - regardless of cultural context and political ecologies - are bounded by factors such as population growth, energy transformation and biogeochemical cycles (Bettencourt, 2013; Bettencourt et al., 2007; Glazier, 2005). Therefore, understanding the scaling relationships between population size and disease processes is necessary for identifying the spatial patterns of occurrence and improving public health interventions across urbanization and administrative levels to reduce morbidity in growing urban and peri-urban areas in the tropics (Pou et al., 2017; Wen et al., 2016). Another body of literature has also found contrasting relationships among urban population size, urbanization rates, and infectious disease occurrence such as malaria or dengue (Hay et al., 2005; Hay and Snow, 2006; Ng et al., 2017; Snow et al., 2005; Wen et al., 2016). While some research suggests that urbanization leads to better access to health care and niche reductions for transmission factors, thus reducing morbidity (Hay et al., 2005; Hay and Snow, 2006; Snow et al., 2005), other studies concluded that disease occurrence might increase due to urbanization and other socio-ecological disturbance processes, as documented for disease incidence in sub-Saharan Africa (Donnelly et al., 2005; Keiser et al., 2004).

Scaling relationships have also been used to analyze several epidemic processes and their relationship to population size (Goldstein et al., 2004; Hochachka and Dhondt, 2000; Newman, 2002; Rhodes et al., 1996). For example, measles virus infection has been reported to follow a power-law in isolated populations, and available epidemiological models have failed to predict pathogen dynamics on a wider spatial scale (Newman, 2002). Other studies have documented how the structure of social contacts, often described as scale-free networks, can actually determine the behavioral characteristics of an epidemic (Eubank et al., 2004; Salathé et al., 2013). This is the case of sexually transmitted diseases where studies have shown that the distribution of sexual contacts, scales according to population size and density (Beyrer et al., 2012; Leventhal et al., 2014). However, the relationship between population size and disease occurrence is not yet fully understood and results may vary depending on the health outcome of interest. While some studies have found that the relationship is inverse (i.e., as population increases, the disease burden fades) (Hay et al., 2005; Hay and Snow, 2006), other studies have concluded that population size increase and disease burden occurrence are proportional (Bettencourt, 2013; Bettencourt et al., 2007). Previous studies in Colombia, (Feged-Rivadeneira et al., 2019, 2018; Feged-Rivadeneira and Evans, 2019) have shown that the epidemiology of malarial infection presents a distinct distribution among indigenous groups in cities with less than 50,000 inhabitants. When looking at infectious diseases, other research has found that population size is only one of a number of factors that determine the size of epidemics for multiple species and pathogens (Bouma et al., 1995; Bronner et al., 2015; Cruz Espinoza et al., 2016; Gandon and Michalakis, 2002). Although recent studies on the scaling of biological phenomena continue to present consistent findings across a wide variety of species that in general organisms conform to such distributions (Brown et al., 2004; Gillooly et al., 2001); some argue the need for approaches to include other physical, chemical, and ecological factors to explain disease distribution.

Specifically, power-laws and scale-free networks are two approaches for describing scaling dynamics in urbanization and disease related processes and phenomena (Bettencourt, 2013; Bettencourt et al., 2007). Such power-laws, or scale-free distributions, are defined as a distribution of the form: y(x) ∝ x –λ for × > x0 (Stumpf and Porter, 2012), where scalar invariance produces the characteristic linear relationship between y and × variables in log–log scales. In such scale-free distributions (Fig. 1), extreme observations are far more likely than in other types of distributions (i.e., "heavy tails'') and they often lack a well-defined mean value (Stumpf and Porter, 2012). Therefore, power-law analysis provides one means to address issues of scale in spatial analyses such as: spatial interpolation (e.g., Kriging), regionalized variables, spatial autocorrelation, and spectral analysis, modifiable unit areal problems (MUAP), and ecological fallacies (Goodchild, 2011). For theoretical background and specific applications and examples of these see Goodchild (2011).

Such scalar relationships between human and natural phenomena have analyzed: wages, jobs, walking speed, infectious diseases spread, and how they vary in relation to population size (Bettencourt, 2013; Bettencourt et al., 2007; Harris and Benedict, 1918; Kleiber, 1932). It is important to highlight that adequate statistical tools (e.g., maximum-likelihood analysis versus ordinary least square test) are needed to properly identify power-law distributions, as relationships between variables could be misclassified (Goldstein et al., 2004). Such incorrectly fitted power-law distributions can overestimate the occurrence of large and rare observations (i.e., "heavy-tails").

Thus, there is growing interest in better understanding the relationships among scaling, urbanization, population size, and disease in populations undergoing rapid land use changes and socio-political issues. Such information could be used to assess the relationships between the morbidity (e.g., malarial infection, chemical intoxication) of certain demographic groups, urbanization patterns, and population size-densities in urbanizing areas of the tropics. Moreover, there is emergent work exploring the scaling dynamics of infection (Stroud et al., 2006), and diseases such as dengue (Massad et al., 2008) and more recently COVID-19 (Singer, 2020); thus showing the potential for applying this analytic approach to understand other public health issues and inform policies and interventions.

In this study we explore the role of scale and its application to better understand the relationship between population size and disease in Colombia. To analyze such scaling patterns, we test whether population size and epidemic characteristics have similar scales that follow a conventional power-law distribution. In addition, to exploring the nuances of scaling patterns for particular diseases, we use malaria as a case study to further assess the relationship between population growth and disease occurrence. We test for these objectives with an integrated approach using likelihood ratios and hypotheses tests. We also discuss how this approach and information can be used to better understand the increasing trend in malaria cases and the effectiveness of policies such as Colombia's National Malaria Control Program goal of eliminating malaria in urban areas by 2021.

2. Materials and methods

2.1. Study area

Colombia is one of the most biodiverse countries in the world with a wide range of socio-ecological contexts due to a diversity of biomes, elevations, temperature, precipitation regimes, and other socio-ecological factors (Sánchez-Cuervo and Aide, 2013). Accordingly, we use municipality as the unit of analysis and include all 1,222 Colombian municipalities, or the second administrative level or division after Departments, in our study. The country is located in northern South America and by 2018 had a population of approximately 50 million inhabitants, most of whom are settled in the mountainous and Caribbean areas in the western and northeastern regions of the country (Camargo et al., 2020). Seven metropolitan areas surpass 1 million inhabitants, and 70% of its population lives in urban areas (Camargo et al., 2020). Municipal capital areas grew at a rate of 2% per year over the period 1993–2005, while rural populations decreased at a rate of 0.09% (Camargo et al., 2020). Forced displacement due to the armed conflict has been documented to be among the main factors behind the rapid urbanization rate of the country (Camargo et al., 2020). Please see Section 2.3 for the definition of urban and rural as applied in Colombia.

By 2003, approximately 6.6% of the population identified as afro-colombian (afrodescendent, "mulato" or palenquero), 2% as indigenous, and less than 1% as "raizal del archipiélago" (Bernal and Cárdenas, 2005). Minorities are regionally concentrated in the Pacific (54% is afro-colombian, indigenous or raizal), San Andrés y Providencia (46.79%) Valle del Cauca (20.3%), and the Atlantic regions (13.1%) (Bernal and Cárdenas, 2005). Population with no ethnic denomination was labeled "No-ethnic designation" (ND) in this study. By 2003, 49.4% of the population belonging to these ethnic minorities lived in the lowest strata of socioeconomic conditions and their average household size was 4.38, compared to the 25.6% of the rest of the population with a household size of 3.85 (Bernal and Cárdenas, 2005). People living without access to healthcare among minorities was 48%, compared to 31% among the rest of the population (Bernal and Cárdenas, 2005).

A recent multidimensional classification of municipalities has been implemented by the National Planning Department of Colombia (NDP),

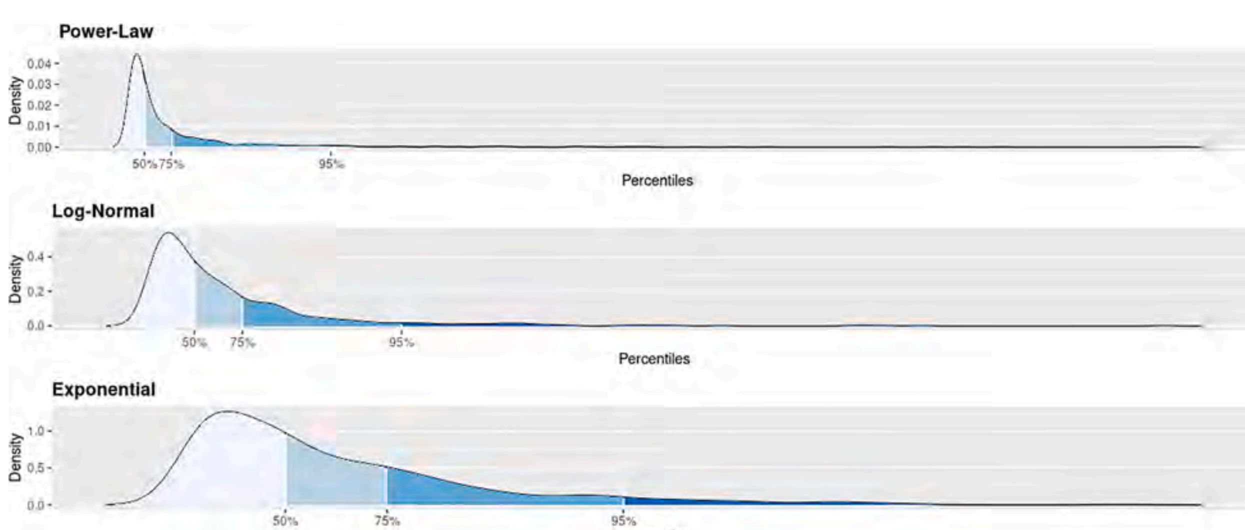

Fig. 1. Examples of the power-law, log-normal and exponential distributions. Selected percentiles are included to show the distribution's tails. Note the difference in the position of the 0.5 percentile relative to the distribution, making the power-law distribution the most likely to show high, atypical values.

where they are classified into a gradient of 7 distinct categories using urban-regional characteristics, living conditions such as multidimensional poverty, economic indicators, environmental variables, institutional indicators, and security (Carmona Sanchez et al., 2014). There were 6.2% of the municipalities included in the Robust Development category (divided into two subcategories), 64.7% comprise the Intermediate Development category (divided into 3 subcategories), and 29.1% are classified as Incipient Development (Parés-Ramos et al., 2013).

Despite land consumption being relatively low in Colombia, urban density in some cities is among the highest in the world, and there is a tendency to urbanize environmentally hazardous areas (Green et al., 2018; Parés-Ramos et al., 2013). The dynamics related to urbanization and other land cover changes such as deforestation are complex and include a number of factors, such as national and local level governance and governability issues, socio-political instability, climate change effects, inequities, and on-going low level armed conflict (Parés-Ramos et al., 2013; Sánchez-Cuervo and Aide, 2013). This long history of social conflict, inequitable distribution of wealth, lack of land tenure, poverty, and lack of governability in the country have led to decades of armed conflict and subsequent socio-political unrest. Nevertheless, with the 2016 signing of a peace accord with the FARC guerrilla, there is speculation as to what will happen in terms of land use and cover changes such as deforestation, urbanization, and population-demographic shifts.

2.2. Data

We used case report data from the National Health Institute (INAS in Spanish) for all 74 diseases reported in the national surveillance system during 2007–2015, as well as available population data for 1,122 different municipalities from the National Department of Statistics (DANE, acronym in Spanish). All 2,455,617 compiled case reports specify: type of disease, occurrence locations at the municipality level, and demographic variables such as age and self-reported ethnicity. Individual-level case reports were not available; however, aggregated anonymous data (n = 2,455,617) were obtained from a cube-query system maintained by the Social Health Protection Ministry. We aggregated cases at the municipality scale according to ethnicity and age, since the burden of disease has been reported to vary across different ethnicities, with indigenous populations mostly living in the per-iurban areas of small and middle size cities (1000 to 50,000 thousand inhabitants) and are more vulnerable to diseases (Feged-Rivadeneira et al., 2019; Feged-Rivadeneira and Evans, 2019). The three following ethnic groups were analyzed: Afro-Colombian (AFRO), Indigenous (IND), and No-ethnic designation (ND). The ND designation can be construed as the population category conformed by mixed ethnicities (*mestizo* in Spanish), and generally describes people who do not identify with a minority. We focused on these populations as they represent over 99% of the total case reports and we categorized disease events as: chronic transmission, vector-borne or environmental subgroups. We note that some diseases are associated with more than 1 event such as malaria and complicated malaria. In the subsequent analyses we focused on the events that are associated with four different diseases types (Table 1).

2.3. Population, epidemics and power-law distribution scales analysis

We tested our objective using the Kolmogorov-Smirnov (KS) statistic to calculate the difference among observed, theoretical, and truncated distributions. A truncated distribution finds the value of Xmin such that the observed distribution minimizes the value of the KS statistic (Lai, 2016). The KS test also simulated numerous data sets and compared each occurrence with the observed distribution. We used a significance level of 0.10, performed the test on each simulated distribution, and counted the number of instances when the null hypotheses were rejected (H_o: two data sets came from the same distribution). We determined the power-law to be a good fit for the observed data if the null hypothesis was rejected in less than 10% of the simulations. To examine if the other distributions also fit the data, we performed KS tests for three distributions (i.e., power-law, exponential, log-normal) for both population and disease incidence separately, and we subsequently combined them. The KS test was also performed independently for each of the three analyzed ethnic groups.

The main parameter of a power-law distribution is the alpha exponent, which in this case indicates the rate at which burden of disease decreases given a specific population size: a larger value of alpha indicates the disease burden decreases more rapidly. Prevalence was calculated using the total number of events divided by the total population of each municipality (Case reports events/Total Population). We also used 'intensity of disease' (cases less than 5 years-old/total cases), which is a relevant disease occurrence metric that is used to understand the heterogeneity of malaria distribution and describes the varying degree of household or community transmission across populations (Feged-Rivadeneira et al., 2018). Urban populations in this study are defined by DANE as those inhabiting locations with increased infrastructure, transportation network and building density, and availability of public services; while rural populations are defined as those living in low housing densities, lacking infrastructure and where agricultural activities, pasture and forest land uses predominate (Camargo et al., 2020). All statistical tests and spatial mapping procedures were analyzed using the distribution test code in the R statistical software package (Rader and Wash, 2008; R Core Team, 2018).

Table 1
Examples of events for different disease types in Colombia and analyzed in this study.

Disease Type	Events
Environmental	Snakebite, exposure to flour, adverse event following vaccination, aggression by animal potentially infected by rabies, acute respiratory infection, rare acute respiratory infection, intoxication with pesticides, intoxication with drugs (medications), intoxication with methanol, intoxication with heavy metals, intoxication with solvents, intoxication with other substances, intoxication with carbon monoxide and other gasses, intoxication with psychoactive substances, injury by explosive artifacts, injury by fireworks, congenital anomalies, domestic violence
Non-Communicable	Low birth-weight, death due to malnutrition, congenital malformations, congenital hypothyroidism, acute lymphoid pediatric leukemia, acute myeloid pediatric leukemia, typhoid and paratyphoid fever, infant cancer, maternal mortality, perinatal and neonatal mortality, mortality due to acute diarrhea 0–4 years old, mortality due to acute respiratory infection,
Communicable	Hepatitis A, B and C, Leprosy, leptospirosis, meningitis (meningococcica), meningitis (Haemophilus influenzae), meningitis (pneumococcus), meningitis (tuberculosa), meningitis (bacterial), parotitis, measles, acute diarrhea due to rotavirus, congenital syphilis, gestational syphilis, pertussis, tuberculosis (extra-pulmonary), tuberculosis (pulmonary), tuberculosis (resistant), chickenpox, human immunodeficiency virus (HIV)
Vector-Borne	Chagas disease, dengue, complicated dengue, chikungunya, cutaneous Leishmaniasis, mucosal Leishmaniasis, visceral Leishmaniasis, malaria (mixed), malaria (P. falciparum), malaria (P. vivax), malaria (P. malariae), malaria (complicated), mortality due to malaria, mortality due to dengue, epidemic typhus transmitted by lice, endemic typhus transmitted by fleas

3. Results

3.1. Population size, epidemics and power-law scale distributions

A total of 2,455,617 case reports were analyzed for the period 2007–2015. Table 2 shows the distribution of total case reports by year

Table 2
Case reports in Colombia for 2007–2015 by ethnicity and year. Note that the total cases for the Indigenous (Indig.), Afro-Colombian (Afro) and Other (N.D.) comprise over 99% of the total case reports.

Year	Afro	Indig.	N.D	Palenquero	Raizal	Rom	Total
2007	12,991	2999	66,627	17	210	161	83,005
2008	19,438	4924	118,113	44	1336	492	144,347
2009	20,418	6297	187,411	114	1379	594	216,213
2010	31,342	8948	276,671	149	2421	662	320,193
2011	23,050	6490	181,823	181	670	320	212,534
2012	24,229	10,783	268,433	276	728	358	304,807
2013	27,892	12,496	314,429	262	592	217	355,888
2014	31,145	13,065	343,884	189	694	1918	390,895
2015	38,038	18,600	368,483	132	707	1775	427,735
Total	228,543	84,602	2,125,874	1364	8737	6497	2,455,617

and ethnicity. Fig. 2 illustrates the time trend for the four disease types showing that some disease events increase over time, likely following the country's population growth trends (population time series data were not available for a further assessment). Within each category, chicken pox, newborn mortality, and dengue presented a relatively high number of cases during the study period, while for environmental events several diseases had relatively high counts. Fig. 3 shows the spatial distribution of diseases by category, where chronic disease events per thousand people are higher among the most densely populated areas of the country, and diseases classified as transmission events present a higher rate along the Pacific Coast, the Caribbean Coast, and the Amazon Basin.

Based on the KS test for power-law distribution, we found that the total population (x_{min} = 14784; alpha = 2.15, KS-test rejection = 2.80%), urban population (x_{min} = 8425; alpha = 1.86, KS-test rejection = 0.80%) and rural population (x_{min} = 18252; alpha = 3.53, KS-test rejection = 1.52%) scaled according to the power-law distribution. However, our test also showed that both total and urban populations follow an exponential distribution while rural populations had a log-normal distribution. The complete table of results is included in the supplementary materials.

3.2. Ethnicity, diseases, and power-law scale distributions

When applying the KS test for the prevalence (Case reports events/ Total Population) for all the diseases included in this study, we found they scale according to a power-law (x_{min} = 0.05; alpha = 2.78; KS-test rejection = 1.68%). In addition, the test results according to ethnic groups, showed that total disease prevalence and ethnic population followed a power-law for the ND (x_{min} = 0.06; alpha = 3.2; KS-test rejection = 2.04%) and AFRO group (x_{min} = 0.00; alpha = 1.64; KS-test rejection = 2.56%). However, it was not the case for the IND group (x_{min} = 0.00, alpha = 1.45; KS-test rejection = 25.8%). Interestingly, this group did show a power-law distribution when focused only on the rural population (x_{min} = 0.01, alpha = 2.00; KS-test rejection = 1.04%). The calculated alpha values for the ND group was the highest, followed by the IND class, and then the AFRO group which had the lowest alpha. This suggests that as populations scale, the ND population has the largest reduction in overall disease prevalence, followed by the IND population (in the rural population), and the AFRO with the least effect associated with population growth.

A further analysis of scaling relationships was also conducted for the four established disease categories (i.e., communicable, non-communicable, environmental, and vector-borne). Fig. 4 illustrates the power-law alpha values compared to the prevalence of the four disease types and malaria, by ethnic class. The KS test showed that communicable diseases for the ND ethnic class scaled according to the power-law distribution (x_{min} = 0.02; alpha = 4.40; KS-test rejection = 1.32%), and did not scale according to exponential and log-normal distributions (both KS-test rejection = 0.0%). In contrast, communicable diseases did not scale for IND and AFRO classes. For non-communicable diseases, we found that the total population (x_{min} = 0.00; alpha = 5.51; KS-test rejection = 2.32%), ND (x_{min} = 0.00; alpha = 5.39; KS-test rejection = 3.80%) and AFRO (x_{min} = 0.00; alpha = 3.4; KS-test rejection = 0.90%) scaled according to a power-law distribution, while the test showed that this was not the case for log-normal and exponential distribution. The IND ethnic class showed a similar trend (x_{min} = 0.02; alpha = 3.2; KS-test rejection = 1.00%). In line with the results for the total of diseases analyzed, the ND category presented the highest alpha value, showing that this population experiences a greater reduction of non-communicable diseases as population grows.

The KS test results for environmental diseases show evidence that the prevalence of environmental diseases for the total population scaled and followed a power-law distribution (x_{min} = 0.02; alpha = 5.54; KS-test rejection = 0.70%) and did not follow a log-normal or exponential distribution (KS-test rejection close to zero percent). We found that environmental diseases among the ND population scaled according to a power-law (x_{min} = 0.01; alpha = 4.43; KS-test rejection = 2.52%) and did not follow either a log-normal or an exponential distribution. In contrast, there is no evidence that this is the case for AFRO (x_{min} = 0.00; alpha = 1.68; KS-test rejection = 75.7%) and IND populations (x_{min} = 0.00; alpha = 1.60; KS-test rejection = 36.9%). For vector-borne diseases, the KS test showed clear evidence that the total population (x_{min} = 0.03; alpha = 2.25; KS-test rejection = 2.4%), IND (x_{min} = 0.00; alpha = 1.46; KS-test rejection = 2.88%), AFRO (x_{min} = 0.00; alpha = 1.54; KS-test rejection = 2.08%), and ND (x_{min} = 0.04; alpha = 2.75; KS-test rejection = 1.96%) classes, scaled according to a power-law distribution. Moreover, the tests for log-normal and exponential distributions, for the total population and across ethnic classes, were far below our KS test rejection percentage. Consistent with these findings for the other disease groups, the ND class presented the highest alpha among ethnic classes, thus providing evidence to support that larger human settlements are associated with more reduction in vector-borne diseases for ND populations when compared to the AFRO and IND ethnic classes.

In general, all of the diseases included in this study scaled as a power-law, with leukemia and domestic violence having the highest rejection values (7%). Fig. 5 shows the alpha values for the power-law tests compared to the disease prevalence, for all diseases and public health issues considered. It is worth noticing the effect of population size varies depending on the disease. For example, malaria is the least affected disease and public health issue according to increases in population size as indicated by low alpha, mean prevalence and KS rejection values. The case of malaria burden and population size is presented to further explore this finding. A limited effect of population size on specific disease events was also found for Changas, diarrhea, leptospirosis, and leishmaniasis. In contrast, newborn mortality, dengue, chickenpox, intoxication and AIDS, presented the highest alpha values, thus showing a relatively high effect of population size on disease prevalence when compared to other event cases (Fig. 5).

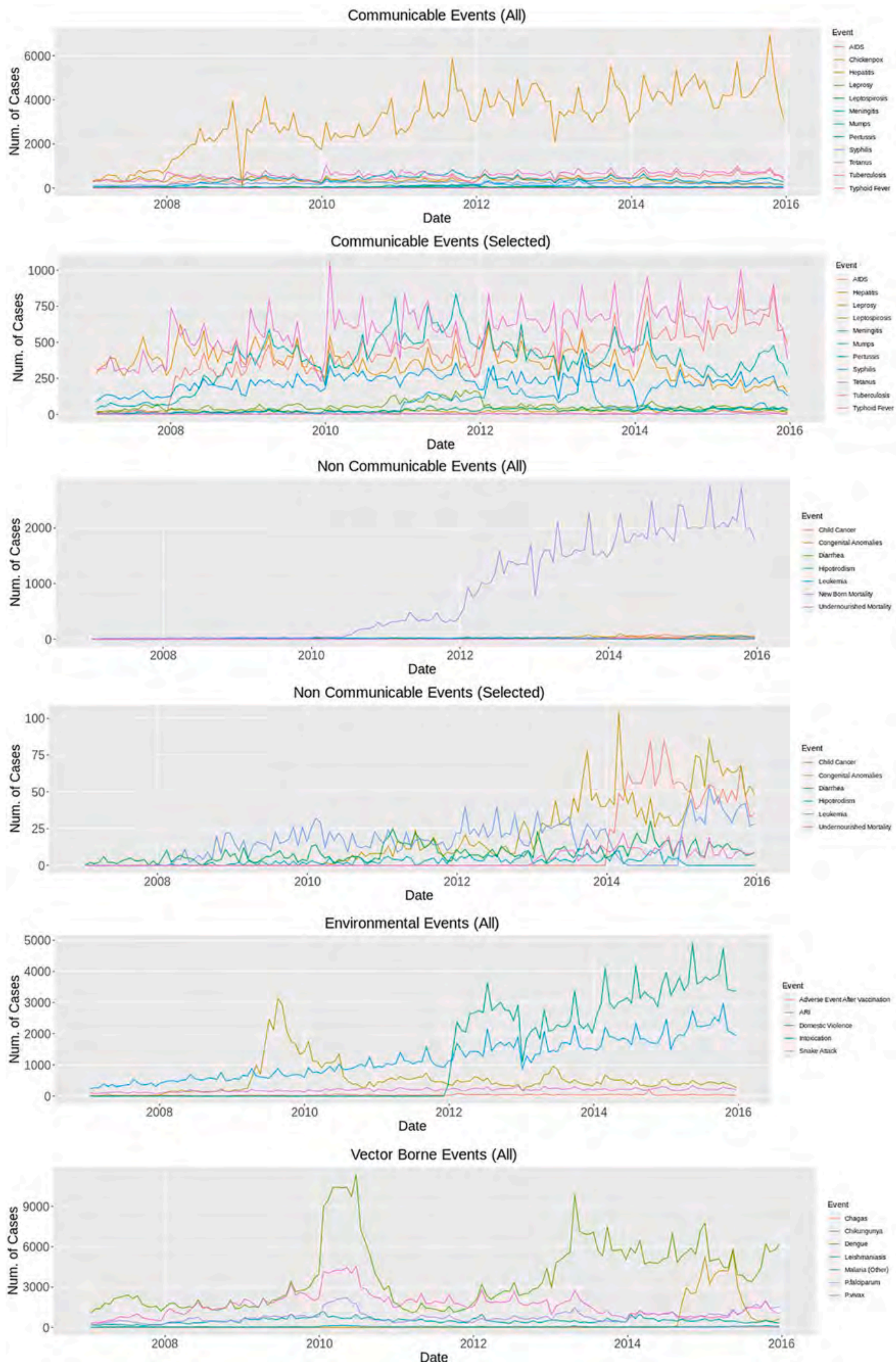

Fig. 2. Case reports events by week and disease type over the study period in Colombia. Note, Num = number; AIDS = Acquired immunodeficiency syndrome. Case reports for some events, such as domestic violence, were not available for the whole period because surveillance for such events began during the study period.

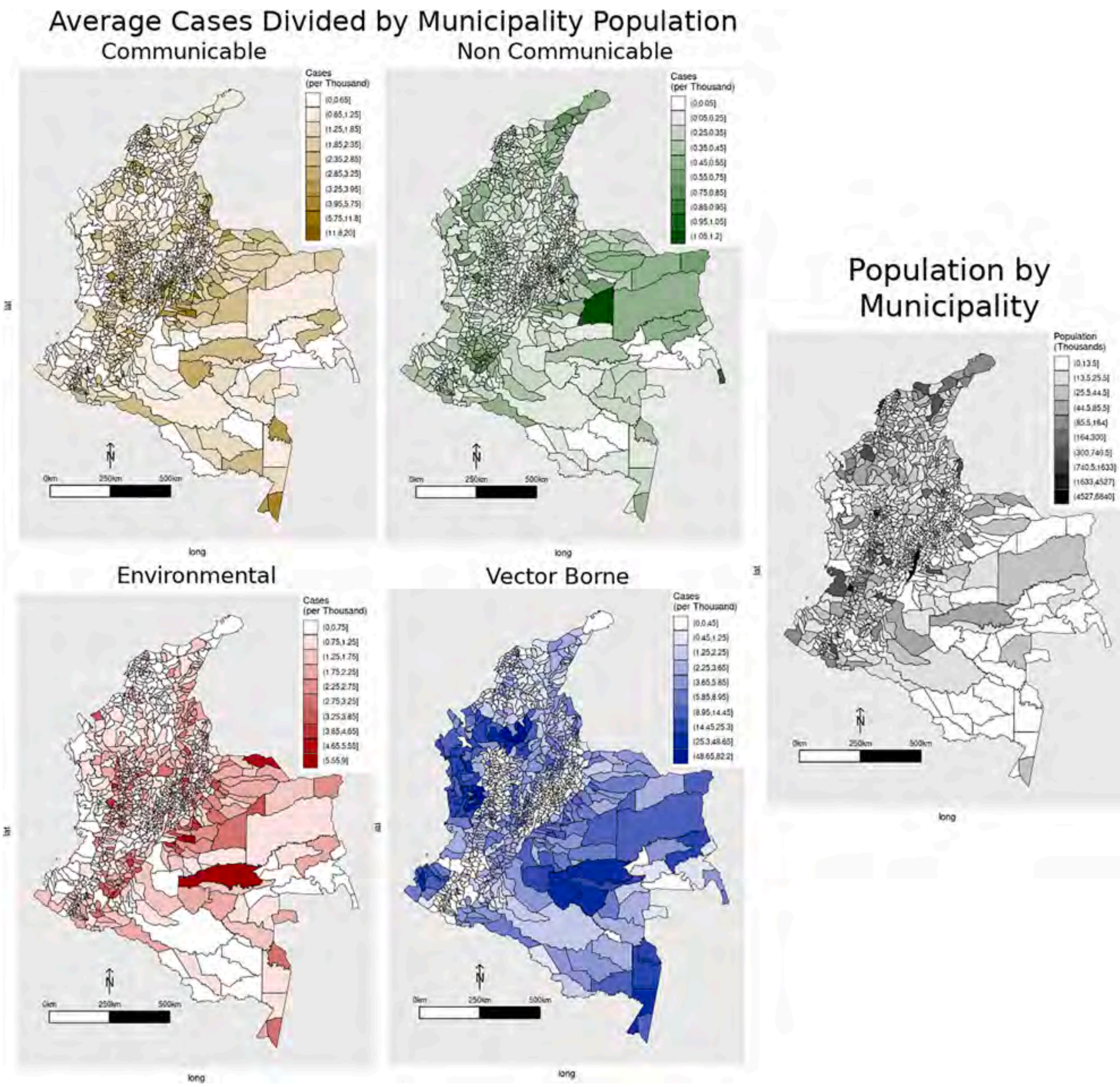

Fig. 3. Average case reports events divided by municipality population in Colombia. Events have been aggregated into categories for the purpose of visualization (i.e. communicable, non communicable, environmental, and vector borne).

3.3. Population size, urbanization levels, ethnicity, and malaria

To further explore how disease occurrence might be associated with population size and possibly urbanization processes, an analysis using population size - as a proxy for urbanization and administrative levels- and ethnicity was conducted for malaria infection. In recent years, the increasing trend in malaria cases has raised concern among researchers and public health authorities and is jeopardizing the goals of the National Malaria Control Program of eliminating urban malaria by 2021 (Feged-Rivadeneira et al., 2018; Knudson et al., 2020; Ministerio de Salud y Protección Social, 2012). Hence, we conducted a series of KS tests for malaria prevalence and found evidence of disease events scaling and following a power-law distribution for the total population (x_{min} = 0.00; alpha = 1.43; KS-test rejection = 4.48%), the AFRO ethnic class (x_{min} = 0.00; alpha = 1.36; KS-test rejection = 3.88%) and the ND (x_{min} = 0.00; alpha = 1.54; KS-test rejection = 3.48%). Moreover, we found no evidence that malaria prevalence follows a log-normal or exponential distribution for the total population and each of the ethnic categories. When conducting the KS test for malaria intensity we found a greater effect of population on events occurring for the total population (x_{min} = 0.02; alpha = 2.41; KS-test rejection = 1.40%) realtive to our scaling relationships for malaria prevalence results. The ND (x_{min} = 0.00; alpha = 1.80; KS-test rejection = 1.84%), and IND (x_{min} = 0.12; alpha = 3.37; KS-test rejection = 3.20%) ethnic classes also showed evidence that malaria intensity scales to a power-law distribution, while the AFRO class was just below the 5% rejection percentage (x_{min} = 0.01; alpha = 2.32; KS-test rejection = 6.20%). There is no statistical evidence that malaria intensity scales following a log-normal or exponential distribution for the ethnic classes analyzed.

Overall, our results also indicated an association between malarial intensity and population size (Fig. 6). We found specific ranges in population size where malaria prevalence (i.e., intensity) actually increased. Fig. 6 shows that there is an interval in population size (0–100,000) where indigenous populations experience a statistically significant greater malaria intensity when compared to ND and AFRO ethnic classes. The IND group also experienced the most acute increase in malaria

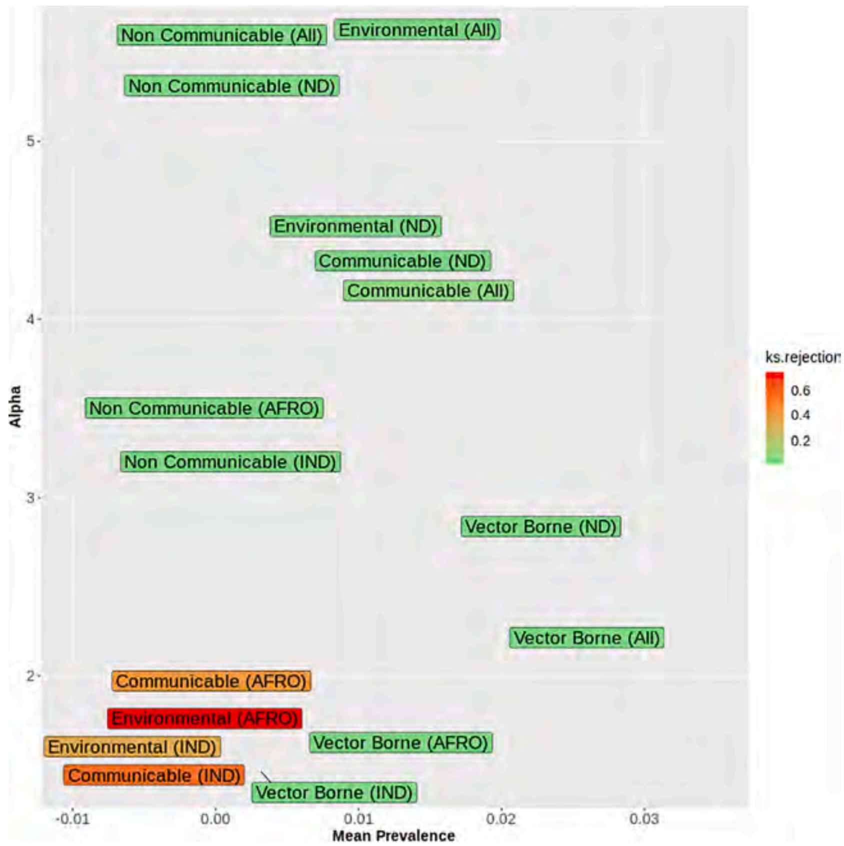

Fig. 4. Alpha values for the power-law tests and prevalence values for different diseases and public health issues in Colombia, grouped by type and ethnicity.

intensity relative to the other two ethnic groups (Fig. 6).

4. Discussion

This study explored the scaling relationships between population size and disease via power-law distributions. Using malaria as a case study, we further assessed the relationship between population growth and disease occurrence. Case reports during the study period presented different trends across the four disease categories used in this study (Fig. 2). Similarly, the spatial distribution of case report incidences for these categories sheds some light on specific areas of public health concern, and how they varied according to different types of disease. For example, a noticeable spatial pattern of average case reports of vector-borne disease can be identified with three major geographic areas: the Pacific Coast and Antioquia (west), Amazon region (south), and the Eastern Plains (east) (Fig. 3). Thus, using spatio-temporal scan statistics, a comparable distribution was confirmed by other studies in the case of malaria outbreaks in Colombia between 2007 and 2015 (Feged-Rivadeneira et al., 2018). We note that the Eastern Plains region presents consistently high rates across the four disease categories (Fig. 3).

Overall, we found that the prevalence of case reports in Colombia scale following a power-law distribution among the total population. When looking at different types of diseases across ethnic classes, the ND ethnic class consistently scaled following a power-law distribution. Moreover, the ND group presented the highest alpha among ethnic classes for total, non-communicable, and vector-borne diseases. Therefore, the effects of population size on the reduction of disease prevalence may be stronger for populations that do not identify as Indigenous or Afrocolombian. In fact, environmental and communicable diseases for the IND and AFRO ethnic classes did not scale with population size, suggesting that the effects of larger urban centers on disease prevalence reduction, may not be present for these particular populations. One potential explanation is that these populations tend to live, or settle following internal migration, in urban and peri-urban areas where access to infrastructure and health care is limited, and environmental and communicable diseases drivers are not controlled or may be exacerbated (Feged-Rivadeneira et al., 2019; Feged-Rivadeneira and Evans, 2019). Other social, cultural, and economic factors could impact the accessibility of these populations to safe housing and infrastructure conditions (Feged-Rivadeneira et al., 2019; Feged-Rivadeneira and Evans, 2019). Further studies should be conducted to assess the distribution of disease across ethnic classes in smaller administrative units including an assessment of differences between urban, peri-urban, and rural settlements.

For the other disease types (i.e., vector-borne, non-communicable), the AFRO and IND populations did show evidence of a reduction in disease prevalence, however we found a more moderate decrease than for the ND group. This sheds light on potential health equity issues where the benefits of health care facilities and other services provided in larger settlements do not have the same positive effect on IND and AFRO populations as it has among the ND group. This finding should be further explored in order to determine causal pathways, although some preliminary studies have highlighted a number of barriers these populations must face to access health care and how these populations are segregated to neighborhoods with precarious sanitation and infrastructure (Espinosa et al., 2018; Hurtado-Saa et al., 2013; Noreña-Herrera et al., 2015; Sandes et al., 2018). In regard to non-communicable disease risk factors, there is evidence that income inequality and socioeconomic status in Colombia are associated with hypertension and cardiovascular and metabolic risk (Lucumi et al., 2017a, Lucumi et al., 2017b). Although there is some evidence that cardiovascular and metabolic risk is not associated with ethnicity after accounting for socioeconomic status, overall ethnic differences in non-communicable diseases still remain understudied in Colombia (Lucumi et al., 2017a).

For most of the individual health outcomes analyzed, disease prevalence and population size in Colombia do scale according to power-law

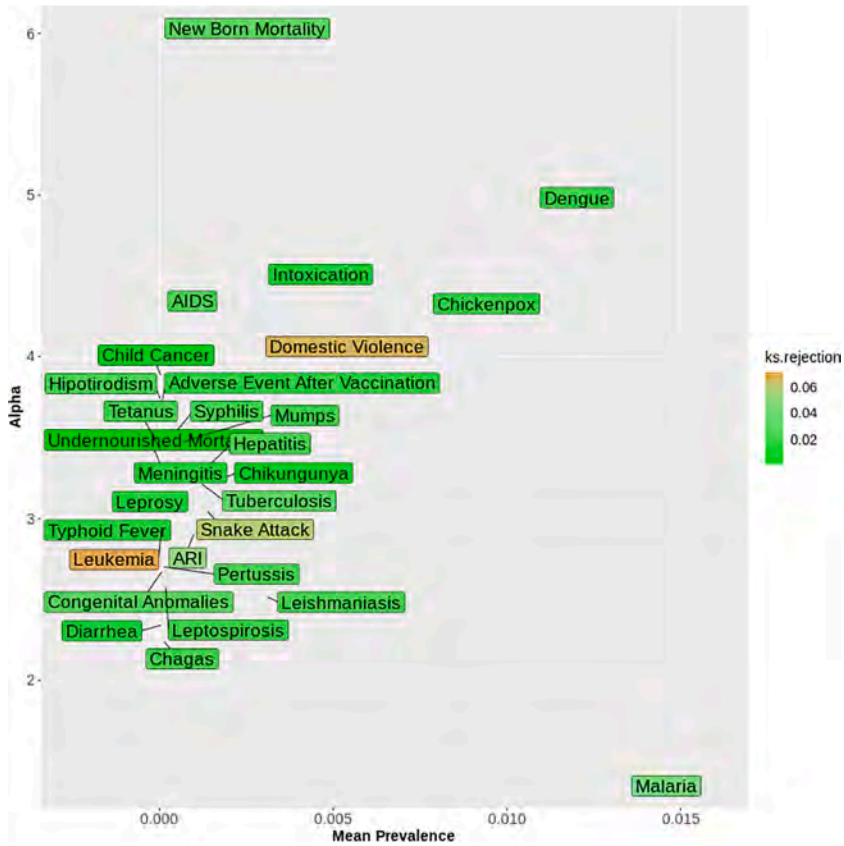

Fig. 5. Alpha values for the power-law tests and prevalence values for different diseases and public health issues in Colombia. Note: ARI, Acute respiratory infections; AIDS,Acquired immunodeficiency syndrome.

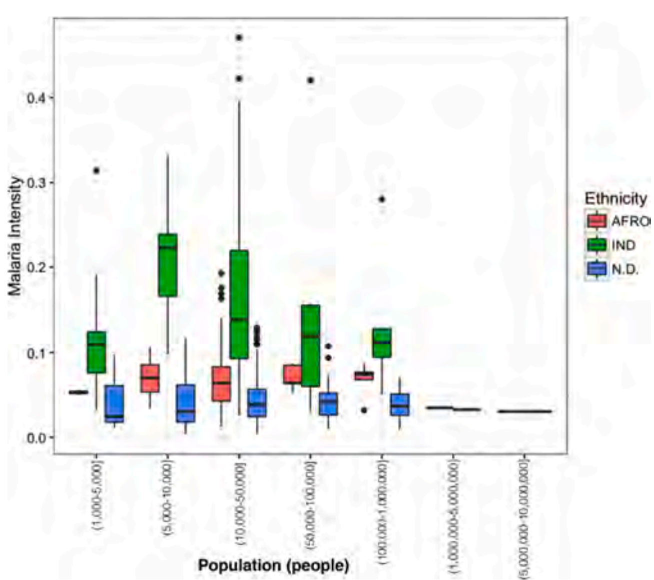

Fig. 6. Malaria intensity (cases < 5 years-old/total cases) and population size, divided by ethnic groups. The graph shows that there is an interval in population size (5000–100,000) when indigenous populations experience a significantly higher malaria intensity realtive to the other ethnic groups. Note, AFRO, Afro-Colombian, IND, Indigenous, N.D. other.

properties (Fig. 5). This decrease in disease burden according to population size has also been observed in previous studies by Keiser et al. (2004) and Feged-Rivadeneira and Evans (2019). Indeed, the effect of population on disease prevalence varies across diseases and public health issues, as well as disease metrics. For example, population size seems to have a limited effect over diseases like dengue, chikungunya, respiratory infections, typhoid, and whooping cough, while tetanus, leishmaniasis, and maternal mortality showed a more pronounced decrease as population size increases (Fig. 5). Moreover, some disease burden metrics, that are relevant for specific health outcomes, provide complementary information about the relationship of disease with other socio-ecological factors. In our study, we found that the malaria intensity provided additional evidence of the scaling relationships of the disease, showing a stronger association between population size and disease for the total population and across ethnic groups than for disease prevalence. Thus, in order to assess the broader scaling dynamics of a particular disease, other relevant metrics of disease occurrence that expand our understanding of the disease burden should be explored.

We do note that analyzing the relationships between population size and disease might require a more nuanced analysis, since the effect of population on disease may be mediated by other factors beyond the size of a population. Although our results indicated an association between malaria intensity and population size (Fig. 6), previous ethnographic work (Feged-Rivadeneira et al., 2019; Feged-Rivadeneira and Evans, 2019) suggested a consistent pattern across Colombia where population growth in urban areas is associated with a reduction in malaria infection; a pattern that was later assessed using spatiotemporal surveillance tools (Feged-Rivadeneira et al., 2018). However, this study showed specific ranges in population size where malaria infections actually increased for Indigenous populations (Fig. 6). Specifically, we found that in the interval between 5,000 and 50,000 inhabitants, Indigenous populations presented a greater disease burden than expected by their population size (Fig. 6). This may be related with Indigenous populations residing in peri-urban areas – where an intricate network of interactions occurs. Although Indigenous populations might present some reduction in disease occurrence when living in human settlements with larger populations, it is crucial to assess the absence of this reduction within this population size range for malaria infection.

Therefore, establishing a robust health surveillance system to monitor disease across different administrative and urbanization levels, and vulnerability in these populations, is warranted in order to prevent a niche of malarial transmission infection by the parasite becoming endemic. Moreover, a further understanding of the distribution of disease in peri-urban areas across ethnic groups is needed, as some research has already shown that social-ecological factors in peri-urban areas may exacerbate health issues such as malaria and parasite infections in children among Indigenous populations (Bermúdez et al., 2013; Feged-Rivadeneira et al., 2019; Quintero et al., 2015).

Several potential limitations should be considered when interpreting our results. First, we are exploring aggregated data of a diverse nature in very complex socio-ecological systems across multiple socio-political scales in communities that are often resource poor. Second, there is a high degree of heterogeneity in reporting the occurrences of various diseases and thus, observed differences may be the result of reporting or data quality and increased surveillance. For example, while some diseases must have a report card to access treatment (i.e., malaria or Leishmaniasis), others such as the Zika virus might have large underreporting due to the fact that many infected individuals do not seek medical treatment and are thus never reported. Even though reporting to the surveillance system is mandatory for the included events, each case report is subject to specific characteristics and pathogen bionomy. Also, our analysis includes social phenomena such as domestic violence, intoxications, and pathogens that affect human health. Therefore, our analysis should be construed as both an analysis of scaling properties of social phenomena that affect human wellbeing, as well as a depiction of the surveillance system itself. Third, our use of population sizes might vary in terms of settlement patterns (e.g., population densities, administrative levels). Finally, observed trends could change if disease surveillance and reporting were to be improved. This is particularly important in the case of highly vulnerable populations since smaller populations might be underestimated if a few number of cases were not reported.

That said, our integrated statistical-spatial approach to analyzing our data in an aggregated manner, should be robust to underreporting and issues of scale. And as mentioned in our Introduction, it can also be used to address cross-scale interference issues such as MUAP and ecological fallacy problems frequently encountered in public health and environmental policies.

Overall, our findings show that in the rapidly changing socio-political and demographic environment of Colombia, factors associated with urbanization such as population size as well as ethnicity and socio-ecological contexts can create the necessary conditions and niches for disease transmission as has been reported in other studies (Bouma et al., 1995; Gandon and Michalakis, 2002). This could be the case of other low- and middle income countries, particularly in tropical areas of the Global South. Other studies have documented how epidemic characteristics of pandemics such as communicable and vector-borne diseases change due to modifications of host populations (Bettencourt, 2013; Bettencourt et al., 2007). But, the approach and findings presented in this study can be used as a means to understand and create awareness of the importance of specific municipalities receiving large populations in peri-urban areas, to be cognizant and prepared for the possible impacts of urbanization-related process on disease occurrence in contexts with highly dynamic occurring natural and anthropogenic disturbances (Bronner et al., 2015; Cruz Espinoza et al., 2016; Green et al., 2018). Similarly, using population size and diseases as proxies for urbanization, administration types and levels, and environmental impacts; we show how two accessible, but robust, variables can be used to feasibly analyze the spatial dynamics of anthropogenic change in data poor contexts while accounting for issues of scale (Goodchild, 2011).

5. Conclusions

Findings from this study have potential implications for public health and environmental planning and research in countries such as Colombia. Most importantly, it provides a spatially explicit approach for simplified, policy relevant analyses that can be implemented using two variables from free, publicly available data sets. Such an approach could be used to design more cost-effective public health and surveillance systems while addressing issues of MAUP and ecological fallacies. Our study can also be used as a framework by planners and researchers to better understand the relative effectiveness and efficiency of urban public health policies and the national and regional level epidemic profiles of a country. For example, analyzing case reports according to their population size - using our approach- can be a simple indicator or metric for the evaluation of policies aimed at reducing disease burden. As pointed out by one of our reviewers, our findings regarding peri-urban areas and indigenous populations are highly relevant in that they highlight inadequate and often inaccessible public health services in these areas and for these disenfranchised communities.

Researchers, for example, can also use publicly available geospatial and disease occurrence data to quantify relationships that have been documented elsewhere in the world. Such data-driven quantitative analyses have some advantages over other more complex and expensive studies depending on site-specific and multiple disease transmission data based on extensive clinical and field work (e.g., trapping mosquito populations and estimating disease incidence in each location). The relationship identified in this study between population size and disease occurrence can also be used to more readily map, understand and predict the impact of land use and cover changes (i.e., deforestation), and explore the distribution of health outcomes in urban and peri-urban settings.

Colombia, with its ongoing post-peace treaty process, accelerated deforestation rates, urbanization processes, and history of displaced peoples and their movement to cities, presents a novel context for better understanding these relationships. Therefore, this type of research is a way forward in a country where the migration of populations to cities due to internal displacement and current environmental change (e.g., climate change) might exacerbate population health issues. In terms of public health intervention, planning, and surveillance applications, we have documented that peri-urban locations of both small and large urban settlements have higher disease occurrence, while at the same time large populations in urban centers experience lower burden of disease. Our findings also suggest that public health intervention units should vary according to their epidemiologic characteristics in terms of ethnic groups, population characteristics, and disease as these have specific scaling and epidemic properties.

CRediT authorship contribution statement

Alejandro Feged-Rivadeneira: Conceptualization, Methodology, Software. **Federico Andrade-Rivas:** Conceptualization, Writing - review & editing. **Felipe González-Casabianca:** Data curation, Writing – original draft, Visualization, Investigation. **Francisco J. Escobedo:** Conceptualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gloenvcha.2022.102546.

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