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Association of green areas, spatial metrics and urban configuration with prevalence of chronic diseases: An ecological study in Tuscany, Italy

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ABSTRACT

Urban green spaces are consistently associated with health benefits, but evidence is limited for Southern European compact cities. The relationship between urban structure, green areas, and chronic disease prevalence was examined in the 273 municipalities of Tuscany, Italy.

This ecological cross-sectional study used exposure data from remote sensing and land use datasets. Exposure variables included the Normalized Difference Vegetation Index (NDVI), percentage of impervious surfaces, and urban spatial metrics. Municipality-level health outcomes, collected from Tuscany's health data portal, were diabetes mellitus, ischemic heart disease, heart failure and dementia point prevalence. Cluster analyses were conducted and prevalence ratios with 95% confidence intervals were estimated using robust Poisson regression models adjusting for potential confounders, i.e. spatial autocorrelation, urbanicity and socio-demographic factors.

We found suggestive evidence of an inverse association between NDVI and ischemic heart disease prevalence (PR 0.985, 95% CI: 0.958–1.013 per 0.1 NDVI increase). Greater landscape compactness (LCPI) was associated with lower prevalence of ischemic heart disease and dementia per IQR increase. Conversely, higher edge density was associated with increased ischemic heart disease prevalence (PR 1.035, 95% CI: 1.009–1.061). Polycentric municipalities showed higher ischemic heart disease prevalence compared to sprawling areas (PR 1.041, 95% CI: 1.014–1.070). Moderate-density semi-structured municipalities (good green coverage, moderate presence of built-up areas, moderate fragmentation), had lower prevalence of ischemic heart disease (PR 0.959, 95% CI: 0.928–0.992) and diabetes (PR 0.964, 95% CI: 0.941–0.989) compared to low-density fragmented municipalities.

Strategic urban and greenspace planning may help reduce the burden of chronic diseases in Tuscany and similar settings.

1. Background

Climate change is an extremely urgent public health challenge globally. The WHO estimates an excess mortality of 250,000 deaths per year between 2030 and 2050 due to its effects, with an economic impact of $2–4 billion by 2030 (World Health Organization, 2023). Consequences include food system disruptions, increased spread of infectious diseases, massive migrations and rising risks for non-communicable diseases and mental health (Intergovernmental Panel On Climate Change, 2023).

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Urban areas are particularly vulnerable, being exposed to the urban heat island effect, poor air quality and scarce green spaces, and consequently suffer from relevant public health impacts (UN-Habitat, 2024; Yang et al., 2024).

Green areas offer significant health benefits through mitigating harmful environmental exposures (e.g., improving air quality) and promoting health (e.g., encouraging physical activity and reducing stress). Long-term exposure to green spaces is associated with lower rates of cardiovascular and cerebrovascular diseases (Liu et al., 2022). These benefits are more pronounced in low-income populations, where green spaces mitigate urban heat islands and provide relief in areas with limited access to air conditioning (Rigolon et al., 2021). Urban planning that considers these factors can reduce health inequalities, ensuring that all residents, regardless of their socioeconomic background, can benefit from recreational and green areas, which are vital for physical and mental health (UN-Habitat, 2025).

Most evidence comes from North America and Northern Europe (Liu et al., 2022; Xie et al., 2024), but Italian cities have peculiar characteristics, especially medium-small cities, which are predominant in the country. More localized research is needed to understand the specific health effects of green spaces in these settings.

Welfare and health are strongly related to the urban spatial configuration, and in the early 1800s spatial planning emerged as a cooperating factor in the construction of a democratic community (Benevolo, 1971), particularly in addressing the public hygiene problems caused by the new industrial cities. Nowadays, urban planning — in the shaping of the modern city — also assumes a key role in this context, as the relationship between the built environment and health is strong and complex. Beyond the quantity of green spaces, the spatial configuration of urban areas—including their morphological patterns, connectivity, and fragmentation—may significantly influence population health outcomes. Landscape metrics such as edge density, patch size, and connectivity indices provide quantitative measures of urban form that capture how built environments are organized spatially, offering insights into accessibility, walkability, and exposure to environmental stressors (Wan et al., 2023). Urban configurations (i.e. monocentric, polycentric, or sprawling) and connectedness of built areas may be among the pathways through which cities affect cardiovascular and metabolic health beyond simple vegetation coverage.

Tuscany, located in central Italy between the Apennine mountains and the Tyrrhenian Sea, is home to approximately 3.6 million inhabitants and 273 municipalities. The region boasts a rich landscape of hills, forests, and a vast system of protected areas, including 3 national parks, 3 regional parks, and over 50 nature reserves. Major cities include Florence, Pisa, and Siena, alongside vibrant medium-sized towns like Arezzo, Grosseto, and Lucca. Tuscany's spatial configuration, a mix of coastal areas, rural countryside, and mountainous zones, plays a key role in shaping wellbeing and accessibility, intended as good connectivity and ease of access. Its ecological networks and cultural heritage contribute to a high quality of life and a model of sustainable, inclusive development (Alberti et al., 2022; Colavitti et al., 2018; Istituto Nazionale di Statistica, 2024; Scaramuzzi et al., 2023).

The Health and Urban Green (HUG) project, through the "City Atlas" Work Package, aims to analyze the relationship between urban structure, green areas distribution, and public health outcomes. The objective of this study is to quantify the associations between municipality-level environmental exposures—specifically greenness (NDVI) and urban spatial configuration metrics (Edge Density, Largest Class Patch Index, and Residual Mean Patch Size)—and the overall prevalence of four chronic diseases (ischemic heart disease, heart failure, diabetes, and dementia) across 273 municipalities in Tuscany, Italy in 2024. We examine: (1) associations of NDVI with disease prevalence, (2) associations of landscape metrics with disease prevalence while adjusting for NDVI as a co-exposure, (3) effect modification by urbanicity and income levels, (4) disease patterns across different urban morphologies (monocentric, polycentric, and sprawling configurations), and (5) health outcomes associated with municipality clusters defined by the simultaneous consideration of NDVI, imperviousness percentage, ED Index, LCPI, and RMPS.

2. Methods

2.1. Study design

An ecological cross-sectional study was carried out. Exposure, health and covariate data at the municipality level in the Italian region of Tuscany were gathered.

Out of 273 Tuscany's municipalities with an average surface area of 84.19 km^2 (SD 68.73), 2.6% of them belongs to the highest urbanicity category (i.e. cities, characterized by at least 50% of the population living in one or more urban centers), 36% to the intermediate category (i.e. towns and suburbs, characterized by less than 50% of the population living in rural grid cells and at least 50% of the population living in an urban cluster), and 61% to the lowest one (i.e. rural areas, characterized by more than 50% of its population living in rural grid cells), according to the classification provided by Eurostat, based on population size and population density thresholds (European Commission, Food and Agriculture Organization of the United Nations, et al., 2021).

2.2. Exposure assessment

2.2.1. NDVI

The NDVI (Normalized Difference Vegetation Index) is the most commonly used index for analyzing vegetation. In this study, it was employed to quantify and qualify vegetation across different municipalities, assuming a direct correlation between the index and the presence of natural, semi-natural, and agricultural areas. The NDVI was calculated using multispectral remote sensing imagery obtained from the Sentinel-2 satellite mission by the European Space Agency (ESA).

The Sentinel-2 satellites have a temporal resolution of 5 days and are equipped with the MSI (MultiSpectral Instrument), capable of capturing 4 bands in the visible and near-infrared spectrum with a spatial resolution of 10 m, 6 bands in the infrared with a resolution of 20 m, and 3 bands with a resolution of 60 m (one in the blue spectrum and two in the infrared). Among the 13 available bands, the NDVI is calculated using the red band (Band 4) and the near-infrared band (Band 8), both with a geometric resolution of 10 m.

The NDVI is computed as the ratio of the difference to the sum of the spectral reflectance measurements acquired in the near-infrared (NIR) and red (RED) regions, using the following formula: NDVI = (NIR - RED) / (NIR + RED). The resulting values range from −1 to 1, where values between −1 and 0 typically indicate anthropogenic areas or water bodies, and values between 0 and 1 are characteristic of areas with varying levels of vegetation.

In this study, Level-2 Sentinel-2 images were imported into Google Earth Engine. Only images with a cloud pixel percentage below 10% within the timeframe from January to December 2023 were selected. To account for the annual data coverage and the broad territorial scope of acquisitions, additional preprocessing steps included applying cloud and snow masks to exclude areas affected by clouds, their shadows, or snow, which could distort NDVI results in many areas.

Following this preprocessing, the NDVI formula was applied to each pixel of every image in the dataset. The resulting values were then aggregated to create a single composite image representing average NDVI values. For municipality-based aggregated statistics, a zonal statistics operation was performed, generating a CSV file containing the average NDVI for each municipality.

2.2.2. Imperviousness and landscape metrics

To estimate impervious surface areas, the CLC+ Backbone map was used, which provides 11 land cover classes at a resolution of 10 × 10 meters. Each pixel is assigned to the predominant class within that specific area. Among these classes is the "sealed" category, which directly represents the footprint of urban settlements. This class includes all artificial surfaces and structures, such as roads and railways, but excludes quarries and other permeable anthropogenic surfaces (European Environment Agency, 2022).

To calculate the percentage of impervious surface at the municipal level, a zonal statistics operation was performed in a GIS software, overlaying the CLC + Backbone map with the municipal boundaries of the relevant regions.

To further analyze the urban-rural continuum, metrics from Landscape Ecology were employed to evaluate the morphological characteristics of urban areas (Marinosci et al., 2023). The following indicators were used in this study:

- Edge Density (ED): The ratio of the total perimeter of urban polygons (in meters) to their total area (in hectares). This metric describes landscape fragmentation in terms of edge density, with higher values reflecting increasingly irregular and fragmented urban boundaries.
- Largest Class Patch Index (LCPI): The percentage of the largest contiguous urban area relative to the total urban area within the reference boundary (administrative limit).
- Residual Mean Patch Size (RMPS): The average size of urban polygons, excluding the largest polygon.

The Edge Density (ED) indicator reflects urban dispersion, while the compactness and spread of built-up areas can be further assessed using LCPI and RMPS.

The calculation of these indicators was not based on the CLC + Backbone classification because it does not provide the degree of imperviousness relative to the pixel area. Instead, the Imperviousness High Resolution Layer (Copernicus) was used, which identifies all artificial surfaces partially or fully covered with impermeable material and calculates their degree of imperviousness relative to the pixel area.

To delineate urbanized areas, a threshold of 20% imperviousness was applied. Areas exceeding this threshold were considered built-up, and a 51 × 51 pixel kernel was used to smoothen the results and minimize the influence of isolated houses or linear elements (e.g., roads).

2.2.3. Urban fabric type

Urban structure classification is based on the ISPRA Methodology for urban fabric description (Marinosci et al., 2015). Urban areas are classified into the following five categories:

i) Municipalities with a predominantly compact, monocentric urban fabric, with two subcategories:
   a. Compact urban areas that cover or exceed the boundaries of the entire municipal territory;
   b. Compact urban areas that occupy only a portion of the territory and are entirely or mostly contained within the municipal boundaries.
ii) Municipalities with a predominantly monocentric urban fabric showing tendencies toward sprawl at the urban edges.
iii) Municipalities with a dispersed urban fabric.
iv) Municipalities with a polycentric urban fabric.

Given the limited number of dispersed monocentric municipalities in Tuscany ($n = 4$), this category was combined with the compact monocentric category.

2.3. Outcome assessment

Data on non-communicable disease prevalence at the municipality level were extracted from the dedicated open-access platform of Tuscany (ARS Toscana - Agenzia Regionale di Sanità & Regione Toscana, 2026; Profili et al., 2020). Among the available outcomes, we selected those that are associated with greenspaces exposure according to previous literature, with varying degrees of evidence certainty (Xie et al., 2024), i.e. ischemic heart disease, dementia, diabetes and heart failure. We used crude point prevalence calculated on January 1, 2024. The criteria to consider a case as prevalent are outlined in Table S1.

2.4. Covariates

The choice of confounders was based on previous literature. Data on covariates were retrieved from official sources. By consulting the Italian National Institute for Statistics (ISTAT), we retrieved the following demographic characteristics at the municipality level from the 2021 Italian census: percentage of females, percentage of people with upper secondary or tertiary/higher education attainment, percentage of people aged 15–64 who are employed, percentage of foreign residents, percentage of people aged 70 or older. Urbanicity categorization was obtained from ISTAT, as well, obtaining a variable with 3 levels: cities (1), towns and suburbs (2), and rural areas (3) (ISTAT, 2024). Open data from the Italian Ministry of Economy for tax year 2022 were used to calculate the average income for each municipality.

2.5. Statistical analysis

Multivariable Poisson generalized additive models (GAMs) were used to estimate associations between exposures and observed chronic disease prevalence. The outcome variable was the observed count of prevalent cases, with the natural log of municipality population included as an offset term. This formulation is equivalent to modeling the log-prevalence proportion directly, while retaining the count-based likelihood of the Poisson family. We employed robust standard errors to return unbiased estimates even under assumption violations scenarios (W. Chen et al., 2018; Tsou, 2006). Models were adjusted for proportion of females, high school graduates, foreigners, people older than 70, employment rate, urbanicity and average income as fixed linear terms. Spatial autocorrelation was accounted for by means of a bivariate thin plate spline of the municipality centroid's geographic coordinates (Kasdagli et al., 2021). In a GAM using splines, the degrees of freedom are determined through effective degrees of freedom (EDF) rather than nominal degrees of freedom. This allows for automatic smoothness selection: the model, once provided with an upper bound on the complexity of the smooth, can effectively adjust the wiggliness of the curve by optimizing a penalty term that trades off between fit and smoothness. Modeling crude prevalence proportions and adjusting for age as a covariate has been shown to return unbiased estimates (Grisotto et al., 2010; Rosenbaum & Rubin, 1984), which led us to choose this analytical approach rather than modeling age-standardized prevalence proportions as the outcome variable. NDVI single- and bi-exposure models are presented, as models 2 and 3 include landscape metrics as independent variables in addition to NDVI, i.e. LCPI and RMPS in models 2 and ED Index in models 3. The choice on which co-exposures to include was based on the correlation matrix of all exposures, avoiding to use in the same model exposures that were too highly correlated.

Effect measure modification on the multiplicative scale was assessed by adding product terms to the single exposure, multivariable models and obtaining stratum-specific estimates by urbanicity and income. In the analysis stratified by urbanicity, all towns, suburbs and cities were considered as urban areas.

Additionally, we ran models with urban fabric type classification as the exposure variable, with and without adjusting for NDVI as co-exposure, while maintaining the remaining set of adjustment variables.

Lastly, cluster analyses were conducted. The following variables were considered: NDVI, percentage of impervious surface, LCPI, RMPS, ED Index. We selected the number of clusters based on the silhouette width and the elbow methods. We ran a spatially constrained cluster analysis, by computing a spatial distance matrix and combining it with a feature distance matrix (using a weighting factor for spatial influence of 0.3). The partitioning around medoids algorithm was used for the clustering procedure. Clusters were then used as the exposure variable in GAMs, adjusting for the same set of covariates as in previous models: age, sex, education, employment, foreigners, urbanicity, income, and spatial autocorrelation. We further conducted a spatially unconstrained k-means cluster analysis, for sensitivity purposes.

Results are presented as prevalence ratios (PRs) with 95% confidence intervals. PRs for NDVI correspond to increments of 0.1 in NDVI. All analyses were conducted in R version 4.2.0.

3. Results

The study sample included 273 municipalities, with 167 (61.2%) classified as rural and 106 (38.8%) as urban. Descriptive statistics of exposure and outcome variables are shown in Table 1. In rural areas, the median prevalence per 1000 inhabitants was 47.38 (Q1: 41.41, Q3: 54.25) for ischemic heart disease, 26.26 (Q1: 21.19, Q3: 31.91) for heart failure, 75.56 (Q1: 69.84, Q3: 84.89) for diabetes, and 15.88 (Q1: 13.29, Q3: 19.15) for dementia. In urban areas, the corresponding values were 41.58 (Q1: 38.77, Q3: 45.10) for ischemic heart disease, 21.93 (Q1: 19.66, Q3: 25.56) for heart failure, 70.58 (Q1: 67.57, Q3: 75.72) for diabetes, and 13.95 (Q1: 12.10, Q3: 15.85) for dementia. Regarding exposure variables, urban areas showed a median built-up area of 8.59% (Q1: 5.33, Q3: 15.46) and LCPI of 61.80 (Q1: 48.11, Q3: 81.88), while rural areas had a median built-up area of 1.24% (Q1: 0.68, Q3: 2.38) and LCPI of 34.49 (Q1: 24.66, Q3: 51.76). The median ED Index was 246.00 (Q1: 203.00, Q3: 305.00) in rural areas and 150.00 (Q1: 127.25, Q3:173.50) in urban areas. Descriptive statistics stratified by urbanicity and income class are presented in Table 1 and Table S2, respectively. Fig. S1 shows the correlation matrix of exposure variables. The spatial distribution of mean NDVI across Tuscany municipalities is presented in Fig. 1.

Suggestive evidence of a borderline inverse association between NDVI and ischemic heart disease prevalence was found, with confidence intervals narrowly including 1: a 0.1 increase in NDVI resulted in a PR of 0.985 (95% CI: 0.958–1.013) in Model 1. Such weak association was consistent across models adjusting for spatial metrics as a co-exposure, with PRs of 0.98 (95% CI: 0.953–1.008) and 0.977 (95% CI: 0.95–1.004) in Model 2 and 3, respectively. We didn't find evidence of an association between NDVI and any other health outcome across all models (Table 2).

Further borderline inverse associations were identified for LCPI. In Model 2, an interquartile range (IQR) increase in LCPI was suggestively linked to a reduced prevalence of ischemic heart disease (PR 0.983, 95% CI: 0.963–1.004) and dementia (PR 0.970, 95% CI: 0.934–1.007).

For RMPS, we identified further borderline inverse associations in Model 2. An IQR increase corresponded to a lower prevalence of ischemic heart disease (PR 0.994, 95% CI: 0.979–1.009), heart failure (PR 0.989, 95% CI: 0.967–1.012), and diabetes (PR 0.995, 95% CI: 0.982–1.009), suggesting a minimal protective effect (Table 2).

Conversely, in Model 3, an IQR increase in ED Index was associated with a slightly higher prevalence of ischemic heart disease (PR 1.035, 95% CI: 1.009–1.061) (Table 2).

The models run on urban and rural municipalities separately suggest a generally more protective effect of NDVI on heart failure prevalence in rural municipalities, compared to urban ones, with confidence intervals for both urbanicity types including 1 (interaction term p-value = 0.148) (Fig. S2).

In the income-stratified analysis (Fig. S3), a generally stronger inverse association was observed in medium-income municipalities compared to low- and high-income ones, although interaction terms were non-significant. For diabetes, a suggestive gradient from low to high income was identified, with a stronger protective effect in low-income municipalities (interaction term p-value = 0.182).

In the analysis on the urban fabric variable as exposure, polycentric urban fabric was associated with higher prevalence of ischemic heart disease compared to sprawling municipalities (PR 1.041, 95% CI: 1.014–1.070) (Table 3). Also, across the remaining health outcomes, it consistently shows point PR estimates above 1.0, suggesting a general trend toward higher disease prevalence compared to sprawling municipalities. Compact monocentric urban fabric showed no associations with any of the examined health outcomes, as evidenced by confidence intervals that consistently included the null value. These results stay consistent when we further adjust for NDVI in the models.

A spatially constrained cluster analysis resulted in three clusters with distinct characteristics (Table 4):

- Cluster 1 (N = 95) represented moderate-density semi-structured municipalities with high NDVI (mean = 0.382), indicating good vegetation coverage, moderate built-up area (mean = 2.65 %) and moderate ED Index (mean = 193.94).
- Cluster 2 (N = 97) represented low-density fragmented municipalities with the highest NDVI (mean = 0.383), the lowest built-up area (mean = 1.42 %) and the highest ED Index (mean = 294.30).
- Cluster 3 (N = 81) represented high-density continuous municipalities with the lowest NDVI (mean = 0.348), the highest built-up area (mean = 13.88 %) and the lowest ED Index (mean = 142.79), showing compact development.

A correlation matrix of exposure variables and a map of municipalities, both stratified by cluster, are shown in figs. S4 and S5, respectively. Compared to low-density fragmented municipalities, moderate-density

Table 1
Descriptive statistics of health outcome and exposure variables, by urbanicity. Both cities and towns (categories 1 and 2 of the urbanicity classification) were considered as urban.

Variable	Overall, N = 273	Rural, N = 167	Urban, N = 106
Ischemic Heart Disease prevalence *(per 1000 inhabitants)*			
Median (Q1, Q3)	44.46 (40.05, 51.63)	47.38 (41.41, 54.25)	41.58 (38.77, 45.10)
Mean (SD)	46.97 (10.26)	49.59 (11.31)	42.86 (6.51)
Heart Failure prevalence *(per 1000 inhabitants)*			
Median (Q1, Q3)	24.25 (20.50, 29.21)	26.26 (21.19, 31.91)	21.93 (19.66, 25.56)
Mean (SD)	25.80 (7.41)	27.53 (8.17)	23.07 (4.92)
Diabetes prevalence *(per 1000 inhabitants)*			
Median (Q1, Q3)	73.54 (68.24, 80.59)	75.56 (69.84, 84.89)	70.58 (67.57, 75.72)
Mean (SD)	75.80 (11.74)	78.66 (13.47)	71.29 (6.06)
Dementia prevalence *(per 1000 inhabitants)*			
Median (Q1, Q3)	14.89 (12.71, 17.77)	15.88 (13.29, 19.15)	13.95 (12.10, 15.85)
Mean (SD)	15.73 (4.88)	16.87 (5.49)	13.92 (2.92)
Impervious surface *(%)*			
Median (Q1, Q3)	2.50 (0.94, 7.23)	1.24 (0.68, 2.38)	8.59 (5.33, 15.46)
Mean (SD)	5.54 (7.64)	1.70 (1.48)	11.60 (9.34)
Mean NDVI[1]			
Median (Q1, Q3)	0.38 (0.35, 0.40)	0.39 (0.36, 0.41)	0.36 (0.33, 0.38)
Mean (SD)	0.37 (0.04)	0.38 (0.04)	0.35 (0.04)
ED Index[2]			
Median (Q1, Q3)	200.00 (156.00, 261.00)	246.00 (203.00, 305.00)	150.00 (127.25, 173.50)
Mean (SD)	214.42 (77.77)	255.66 (68.26)	149.44 (36.53)
LCPI (%)[3]			
Median (Q1, Q3)	43.97 (28.42, 65.74)	34.49 (24.66, 51.76)	61.80 (48.11, 81.88)
Mean (SD)	48.44 (22.85)	40.11 (19.28)	61.56 (21.94)
RMPS[4]			
Median (Q1, Q3)	2.36 (1.56, 3.54)	1.86 (1.32, 2.76)	3.26 (2.27, 4.65)
Mean (SD)	2.73 (1.58)	2.21 (1.27)	3.55 (1.66)

[1] NDVI = Normalized Difference Vegetation Index.
[2] ED = Edge Density.
[3] LCPI = Largest Class Patch Index.
[4] RMPS = Residual Mean Patch Size.

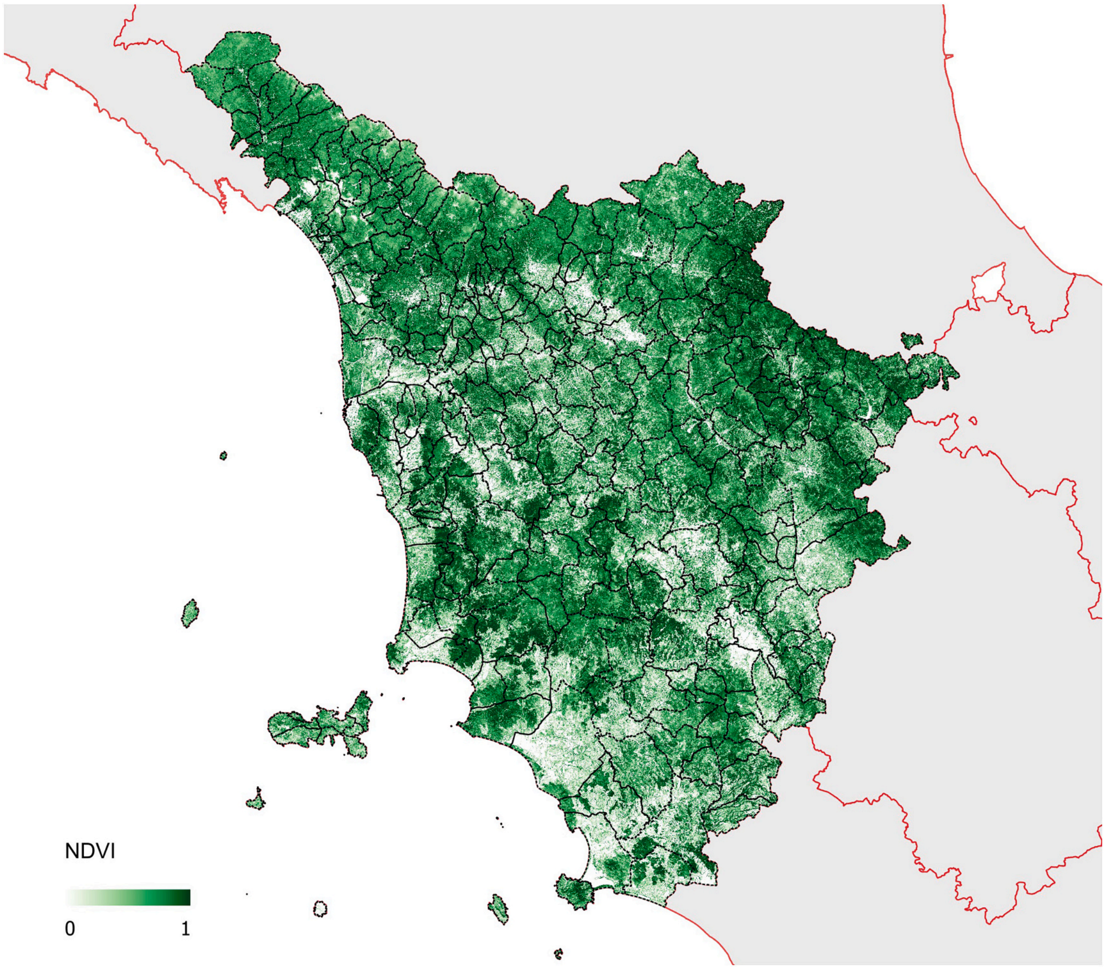

Fig. 1. Spatial distribution of mean NDVI across Tuscany, Italy in 2023.
NDVI = Normalized Difference Vegetation Index.

Table 2
PRs and 95% CIs of selected non-communicable diseases per increases of 0.1 NDVI, and increases of an IQR for LCPI, RMPS, and ED, in Tuscany.

		Model 1		Model 2		Model 3	
Outcome	Exposure	PR	95% CI	PR	95% CI	PR	95% CI
Ischemic heart disease	NDVI	0.985	0.958–1.013	0.980	0.953–1.009	0.977	0.950–1.004
	LCPI	–	–	0.983	0.963–1.004	–	–
	RMPS	–	–	0.994	0.979–1.009	–	–
	ED Index	–	–	–	–	1.035	1.009–1.061
Heart failure	NDVI	1.027	0.985–1.071	1.025	0.981–1.070	1.022	0.979–1.068
	LCPI	–	–	0.988	0.954–1.022	–	–
	RMPS	–	–	0.989	0.967–1.012	–	–
	ED Index	–	–	–	–	1.019	0.975–1.065
Diabetes	NDVI	1.000	0.978–1.023	0.999	0.977–1.022	0.999	0.976–1.022
	LCPI	–	–	0.995	0.978–1.012	–	–
	RMPS	–	–	0.995	0.982–1.009	–	–
	ED Index	–	–	–	–	1.004	0.982–1.026
Dementia	NDVI	1.026	0.979–1.075	1.016	0.969–1.064	1.017	0.969–1.067
	LCPI	–	–	0.97	0.934–1.007	–	–
	RMPS	–	–	0.994	0.965–1.023	–	–
	ED Index	–	–	–	–	1.033	0.989–1.079

NDVI = Normalized Difference Vegetation Index; ED = Edge Density; LCPI = Largest Class Patch Index; RMPS = Residual Mean Patch Size; IQR = Interquartile Range; PR = Prevalence Ratio; CI = Confidence Interval. IQR was 37.31 for LCPI, 1.98 for RMPS, and 105 for ED Index. Models were adjusted for age, sex, education, employment, foreigners, urbanicity, income, and spatial autocorrelation.

semi-structured municipalities showed lower prevalence of ischemic heart disease (PR = 0.959, 95% CI: 0.928–0.992) and diabetes (PR = 0.964, 95% CI: 0.941–0.989) (Fig. 2). For these outcomes, a borderline protective association was also found for dense urban areas. Heart failure and dementia prevalence showed no differences across clusters.

The spatially unconstrained cluster analysis identified two clusters. Cluster 1 represents more urbanized municipalities: with higher built-up area (mean = 11.79%), higher LCPI (mean = 65.85), i.e. more

Table 3
PRs and 95% CIs comparing urban fabric categories.

Disease	Urban Fabric Type vs Sprawling	Not Adjusted for NDVI	Adjusted for NDVI
Ischemic Heart Disease	Monocentric	1.015 (0.991–1.040)	1.013 (0.988–1.038)
	Polycentric	1.041 (1.014–1.070)	1.041 (1.013–1.070)
Heart Failure	Monocentric	1.009 (0.970–1.050)	1.017 (0.976–1.059)
	Polycentric	1.020 (0.971–1.073)	1.021 (0.972–1.072)
Diabetes	Monocentric	0.992 (0.971–1.012)	0.991 (0.970–1.012)
	Polycentric	1.018 (0.992–1.045)	1.018 (0.992–1.045)
Dementia	Monocentric	0.993 (0.953–1.035)	0.998 (0.958–1.041)
	Polycentric	1.025 (0.962–1.092)	1.026 (0.962–1.093)

NDVI = Normalized Difference Vegetation Index. Models were adjusted for age, sex, education, employment, foreigners, urbanicity, income and spatial autocorrelation.

Table 4
Municipalities characteristics by spatially constrained cluster.

Characteristic	Cluster 1 - Moderate-Density Semi-Structured Municipalities, N = 95	Cluster 2 - Low-Density Fragmented Municipalities, N = 97	Cluster 3 - High-Density Continuous Municipalities, N = 81
mean NDVI[1]			
Mean (SD)	0.382 (0.041)	0.383 (0.036)	0.348 (0.039)
Median (IQR)	0.387 (0.367, 0.408)	0.386 (0.362, 0.403)	0.351 (0.319, 0.380)
Impervious surface (%)			
Mean (SD)	2.65 (1.81)	1.42 (1.50)	13.88 (9.55)
Median (IQR)	2.32 (1.11, 3.62)	0.93 (0.54, 1.65)	9.97 (7.64, 18.52)
ED Index[2]			
Mean (SD)	193.94 (40.86)	294.30 (57.38)	142.79 (34.95)
Median (IQR)	190.00 (164.50, 220.50)	293.00 (250.00, 338.00)	147.00 (123.00, 166.00)
LCPI (%)[3]			
Mean (SD)	45.89 (18.80)	35.90 (16.85)	66.45 (22.20)
Median (IQR)	42.64 (31.09, 57.54)	30.82 (22.75, 43.74)	68.22 (52.18, 86.47)
RMPS[4]			
Mean (SD)	3.17 (1.42)	1.67 (0.62)	3.50 (1.85)
Median (IQR)	3.01 (2.24, 4.10)	1.53 (1.26, 2.07)	3.12 (2.00, 4.65)

[1] NDVI = Normalized Difference Vegetation Index.
[2] ED = Edge Density.
[3] LCPI = Largest Class Patch Index.
[4] RMPS = Residual Mean Patch Size.

continuous urban fabric, lower NDVI (mean = 0.343), i.e. less vegetation, lower ED Index (mean = 143.85) and higher RMPS (mean = 3.43), i.e. less fragmented. Cluster 2 represents municipalities with lower built-up area (mean = 1.87%), higher NDVI (mean = 0.389), i.e. more vegetation, higher ED Index (mean = 255.86) and lower RMPS, i.e. more fragmented development, and lower LCPI (mean = 38.22), i.e. less continuous urban areas (Table S3.). Municipalities in cluster 2 had a higher prevalence of heart failure and dementia, with PRs of 1.05 (95% CI 1.005–1.096) and 1.068 (95% CI 1.013–1.125), respectively, compared to those in cluster 1. Borderline positive associations were consistently found also for ischemic heart disease and diabetes (Table S4).

4. Discussion

4.1. Key findings

This study aimed to investigate the association between green areas, spatial metrics and the prevalence of chronic conditions gathering exposure, health, and covariate data at the municipality level in Tuscany, Italy. Key findings are the following:

- The study found suggestive inverse associations between NDVI and ischemic heart disease prevalence, though confidence intervals narrowly included the null. When incorporating landscape metrics, increased compactness was suggestively linked to lower ischemic heart disease and dementia prevalence, suggesting that urban fragmentation—defined as the spatial discontinuity of the built environment due to interspersed, poorly connected green patches— may contribute to cardiovascular risk.
- Analyses stratified by urbanicity revealed a slightly stronger protective effect of higher NDVI on heart failure in rural municipalities, while income-stratified models suggested a stronger protective effect on diabetes in low-income municipalities.
- Urban structure appears to be associated with disease prevalence: polycentric municipalities had a higher prevalence of ischemic heart disease compared to sprawling cities and a general trend toward worse health outcomes compared to sprawling areas, while monocentric cities showed no clear associations.
- In a spatially unconstrained cluster analysis, more fragmented and less urbanized municipalities appear to have a higher prevalence of heart failure and dementia, compared to more compact and urban ones. Borderline positive associations were consistently found also for ischemic heart disease and diabetes.
- Finally, the spatially constrained cluster analysis revealed that moderate-density semi-structured municipalities—with intermediate fragmentation and vegetation—were associated with lower prevalence of ischemic heart disease and diabetes compared to fragmented low-density areas. Interestingly, dense, compact areas also showed borderline protective effects for these outcomes, suggesting a non-linear relationship between urban form and health.

4.2. Comparisons and interpretations

Our findings provide suggestive evidence of a weak inverse association between NDVI and ischemic heart disease prevalence, though confidence intervals narrowly included 1. Greater exposure to green spaces may contribute to cardiovascular health through mechanisms such as stress reduction, increased opportunities for physical activity, facilitated social interactions and improved air quality (Liu et al., 2022). Our result aligns with a growing body of evidence supporting the cardiovascular benefits of green spaces. Liu et al. conducted a comprehensive meta-analysis of 8 cohort, cross-sectional and ecological studies, finding that residential greenness was associated with reduced ischemic heart disease mortality (OR 0.98–95% CI 0.96; 1.00) for each 0.1-unit increase in NDVI (Liu et al., 2022). Looking at ecological studies, Kasdagli et al. reported that higher NDVI was associated with reduced cardiovascular mortality in Greece, another Mediterranean setting with comparable landscape features to Tuscany (Kasdagli et al., 2021). However, no associations were identified between NDVI and other health outcomes in our study, suggesting that the relationship between urban green spaces and health may be influenced by additional contextual factors beyond vegetation coverage alone.

Our analysis of landscape metrics reinforces the importance of urban continuity for population health. The protective associations observed for both LCPI and RMPS, contrasted with the harmful associations of edge density, suggest that fragmented urban development may contribute to cardiovascular and cognitive disease burden. This pattern aligns with literature suggesting that continuous urban fabric facilitates active mobility, social connectivity, and efficient service delivery, while fragmented landscapes may create barriers to these health-promoting features (Avila-Palencia, Rodríguez, et al., 2022). Notably, these spatial configuration effects appeared independent of vegetation levels, further supporting the notion that how cities are organized matters as much as their greenness.

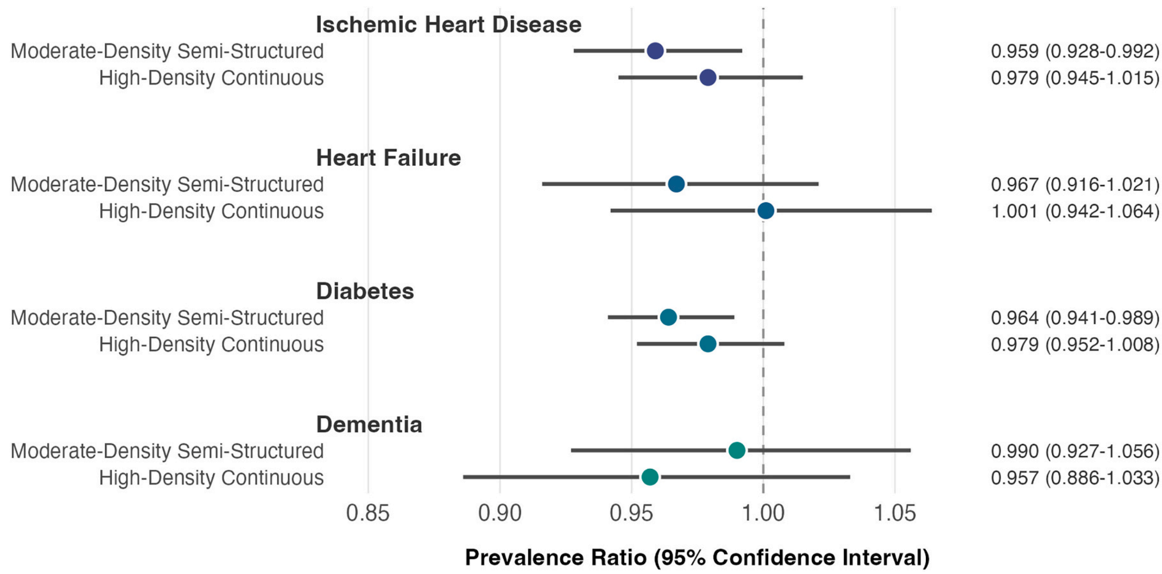

Fig. 2. PRs and 95% CIs comparing spatially constrained clusters vs. low-density, fragmented municipalities. Models were adjusted for age, sex, education, employment, foreigners, urbanicity, income and spatial autocorrelation.

In our study, stratification by urban and rural municipalities revealed a potentially stronger protective association between residential greenness (NDVI) and heart failure prevalence in rural areas compared to urban ones.

This pattern suggests that the health benefits of residential greenness may not be uniform across geographical contexts but may instead depend on environmental and urban characteristics that modify its impact. One possible explanation is that in urban areas, higher levels of air and noise pollution may attenuate or counterbalance the beneficial effects of greenness. In addition, urban environments often provide less accessible vegetation, which may limit opportunities for meaningful exposure and interaction with green spaces.

Most findings in the literature point to an absence of differential effects across urbanicity levels, with a smaller proportion reporting stronger greenspace effects in urban settings. Only 10.5% of studies showed stronger protective greenspace effects in rural areas, according to a recent systematic review (Browning et al., 2022). Although rural-stronger effects represent a minority position in the literature, our findings are consistent with several cohort studies on other cardiometabolic outcomes, where greenness showed more pronounced protective effects in rural or less urbanized settings. For instance, reduced risks of hypertension and diabetes have been observed in rural China (Huang et al., 2021; Yu et al., 2023) and a stronger association with lower blood pressure has been reported in townships compared to more urbanized U.S. areas (Poulsen et al., 2021).

Nevertheless, a cohort study involving older adults in East Anglia, UK (Dalton et al., 2016) did not find significant differences between urban and rural areas in terms of greenspace protective effect on diabetes.

Overall, our results highlight that urbanicity may act as an effect modifier in the relationship between residential greenness and cardiovascular health, underscoring the importance of considering geographical context when evaluating the health impact of environmental exposures.

The income-stratified analysis indicated that the inverse association between NDVI and health outcomes generally appeared slightly more pronounced in medium-income municipalities compared to low- and high-income areas, though product terms *p*-values were all higher than 0.05. This may reflect differences in green space distribution, accessibility, or utilization patterns among socio-economic groups. Notably, for diabetes, a suggestive gradient was identified, with a marginally stronger protective effect observed in low-income municipalities. This aligns with existing literature suggesting that urban green spaces may play a critical role in mitigating health disparities, particularly in disadvantaged populations where environmental stressors are more pronounced (Rigolon et al., 2021).

With regard to urban structure, we found that: (1) following a spatially unconstrained cluster analysis, municipalities characterized by more fragmented urban development, compared to more urbanized environments with a more compact urban fabric, exhibited a higher prevalence of heart failure and dementia; (2) the prevalence of ischemic heart disease and diabetes was lower in moderate-density semi-structured municipalities than in low-density fragmented municipalities, identified through a spatially constrained cluster analysis; (3) polycentric municipalities exhibited a higher prevalence of ischemic heart disease compared to sprawling ones. Taken together, these findings suggest that, rather than relying on a one-size-fits-all urban model, future urban planning should consider local landscape patterns, population distribution, and ecological context when aiming to optimize both environmental and health outcomes.

Our findings extend and nuance the existing literature. Previous studies have shown that less fragmented city shapes lead to health gains, including reductions in disability-adjusted life years (DALYs) related to cardiovascular disease (Stevenson et al., 2016) and that compact communities are associated with lower cardiovascular morbidity and mortality among women (Griffin et al., 2013). Our results reveal that the health effects of urban form are highly context-dependent and disease-specific. Consistently with our findings, Latin American cities with "scattered pixels" profiles, characterized by low fragmentation, high isolation and compact development, were more likely to achieve positive co-benefits in terms of environmental and health outcomes (Avila-Palencia, Sánchez, et al., 2022). These cities were generally small to medium-sized with relatively high population density. In contrast, "contiguous large inkblot" cities, which are highly fragmented, complex in shape, and densely populated (median ~ 3.7 million inhabitants), were least likely to be in the positive co-benefits category. Conflicting findings were reported as to chronic conditions prevalence: as urban forms shifted from scattered pixels to contiguous large inkblots, diabetes prevalence tended to rise while obesity prevalence fell, a pattern that resonates with the disease-specific associations we observed.

A possible explanation for these findings is that more continuous and less fragmented urban environments may support better health outcomes by fostering walkability, improving air quality, and strengthening social cohesion. Indeed, more compact city structures typically imply higher residential density (Griffin et al., 2013), which has been shown to be associated with greater active transportation (Sallis et al., 2016) and reduced car use, as distances between destinations tend to be shorter. This, in turn, leads to higher physical activity levels and lower stress levels (Legrain et al., 2015), all of which are important determinants of cardiometabolic diseases (Chandrabose et al., 2019) and dementia (Livingston et al., 2024). Lower air pollution may be an additional advantage stemming from lower private vehicle use, but according to a study on 919 European cities, including 92 Italian ones, air quality is worse in compact high-density cities (Iungman et al., 2024). However, this may not be the case for smaller municipalities, such as those that mostly make up the present study population. The impact of urban sprawl on air quality is likely the result of a balance between increased travel distances (and associated emissions) and greater exposure to vegetated areas that mitigate pollution (Gao et al., 2023). Lastly, it should be considered that rural areas can host intensive agriculture, which negatively affects health outcomes through harmful exposures such as pesticides (Shekhar et al., 2024).

Polycentric urban fabrics can be characterized by intermediate fragmentation combined with high population density, potentially concentrating risk factors such as air pollution, noise, and traffic-related stress across multiple urban centers. On the other hand, sprawling areas, despite being more fragmented, may benefit from greater green exposure, lower pollution, and reduced urban stress, which could partially offset the risks typically associated with lower accessibility. Lastly, in monocentric municipalities potential benefits and risks associated with this urban form may counterbalance each other: they offer significant health benefits due to accessibility, active mobility and social connectivity, but may pose environmental challenges related to pollution and urban stressors. A further original contribution of this study is the observation that adjusting for NDVI in our models did not substantially alter these associations, indicating that the effects of urban form on disease prevalence are not solely mediated by vegetation coverage. This finding reinforces the need for multidimensional characterization of urban environments beyond simple green space metrics and points to the importance of considering additional environmental and socio-economic factors, such as air quality, walkability, and social cohesion, in future research examining the relationship between urban structure and health.

Our study presents several strengths that enhance its scientific value. We employed cluster analysis, allowing us to simultaneously consider multiple variables and patterns in urban structure, while accounting for spatial dependence. We included urban structure metrics, such as the Largest Class Patch Index, which are rarely explored in the existing literature. This contributes to a deeper understanding of how spatial configuration influences public health. Our study leveraged updated, publicly available datasets, ensuring transparency, reproducibility, and alignment with the most recent epidemiological trends. We focused on a region with significant orographic variations (Tuscany), which provides a scientifically relevant case study due to its diverse urban and rural landscapes. This approach allows for a more nuanced understanding of the interaction between green spaces, urban structure, and health outcomes. Our study employed robust Poisson regression models, which yield valid confidence intervals even when the Poisson equidispersion assumption is violated. The research was conducted by a team from diverse backgrounds, including public health, epidemiology, and urban planning, ensuring transdisciplinarity and enhancing the study's comprehensiveness and interpretative depth.

Nevertheless, some limitations need to be addressed. First, this study is subject to ecological fallacy, as our analyses were based on aggregated data at the municipality level rather than on individual-level data. This means that we examined associations between environmental characteristics and health outcomes across groups of people, not individuals. Consequently, the observed associations cannot be assumed to apply directly to individuals residing in those municipalities. While a higher spatial resolution than the municipality level would have been preferable to better capture the complex relationships between the built environment and health—as well as to improve the statistical power of our analysis—we adopted this resolution as it represented the highest level of detail available for health outcomes. A significant limitation of our study concerns the use of prevalence measures as outcomes, which introduces several methodological challenges. Prevalence, being a function of both incidence and duration ($P \approx I \, x \, D$), reflects not only new disease occurrence but also survival, migration patterns, and healthcare quality. This composite nature makes causal interpretation particularly challenging in cross-sectional designs. For chronic conditions like diabetes and cardiovascular disease, areas with better healthcare access may paradoxically show higher prevalence due to improved survival, while areas with higher mortality may show lower prevalence despite potentially higher incidence. In our study, we observed higher prevalence of heart failure and dementia in fragmented rural municipalities. However, this could mean that the true burden is even greater than observed: if these areas have poorer healthcare access leading to shorter survival times, the prevalence would be suppressed relative to incidence. Thus, our findings of higher prevalence in fragmented rural areas might actually underestimate the true health disparities if survival is indeed compromised in these settings. Moreover, using prevalence prevents verification of the temporality criterion for causality, as we cannot determine whether environmental exposures preceded disease onset. This is particularly problematic for conditions with long latency periods, where current NDVI or urban structure may not reflect exposures at the time of disease initiation. While prevalence remains valuable for healthcare planning and is commonly used for chronic conditions like obesity where incidence data are scarce, these limitations should temper causal interpretations of our findings and suggest that the health inequalities we identified may be conservative estimates of the true disparities.

Moreover, despite adjustments for spatial correlation, variations in diagnostic coding practices across Italian Local Health Authorities (ASLs) may still have introduced some outcome misclassification.

Our study is limited in terms of generalizability, as it focuses on a single region within a European country. Although Tuscany includes municipalities that share characteristics with other European urban contexts, extending our findings to different geographical or socio-political settings remains challenging.

Additional methodological considerations exist. Since the CLC+ classification relies on annual Sentinel-2 imagery, impervious surfaces also include greenhouse-covered areas if these persist throughout the year. This can lead to very high imperviousness estimates in regions characterized by intensive agriculture. As with the imperviousness calculations, the Landscape metrics also have anomalies in areas with high greenhouse coverage throughout most of the year. These anomalies result from the misclassification of such surfaces as urbanized areas. We used NDVI, which may not fully capture the complexity of green spaces, overlooking important factors that influence health outcomes, such as the availability of recreational areas, green infrastructure (e.g., parks, gardens, wooded areas), and the presence of specific plant species that may have distinct health benefits. This limitation could restrict the ability to fully understand the health impacts of different types of green spaces. While NDVI effectively captures vegetation density from satellite imagery, it fails to measure important dimensions such as accessibility, visibility at eye-level, and quality characteristics of green spaces. A growing body of evidence suggests that health outcome findings related to greenspace are often dependent on which vegetation indices are used, indicating NDVI alone may not capture all relevant aspects influencing health. For instance, a study adopting a high spatial resolution approach based on census tracts, found that In Los Angeles, a one-interquartile increase in greenspace aggregation was linked to prevalence reductions in physical inactivity, diabetes, poor mental health, COPD, heart disease, and stroke (Wang & Tassinary, 2024). Future epidemiological research would benefit from multi-dimensional approaches integrating complementary metrics, including Enhanced Vegetation Index (EVI), park-based accessibility measures (Heo & Bell, 2023), street-view greenspace assessments (Larkin & Hystad, 2019), three-dimensional volumetric indicators (Spano et al., 2023), and composite metrics (Slawsky et al., 2022). Such comprehensive greenspace characterization could provide more nuanced insights into how different dimensions of urban green environments influence chronic disease outcomes, particularly in the unique context of Tuscany's medium-small cities. Additionally, considering spatiotemporal variability in greenspace metrics could further strengthen measurement precision and alignment with theoretical pathways linking greenspace to health (Yoo et al., 2024). We used annual average NDVI as exposure, which may mask important seasonal variations in greenspace exposure that could differentially affect health outcomes (Damasceno da Silva et al., 2024). We didn't adjust for air pollution and noise pollution, which are associated with an increased cardiovascular risk (Boogaard et al., 2022; X. Chen et al., 2023). However, these variables can be considered as mediators of the relationship between greenspace and health, and adjusting for them would have introduced over-adjustment bias, preventing estimation of the total effect of greenspace. An additional limitation is the absence of data on active mobility behaviors, such as walking and cycling rates: while such data are available for larger urban areas, they are generally lacking for smaller municipalities. We adjusted for age and sex by including the proportion of elderly and females as covariates in the models. This approach might lead to residual confounding, but the alternative approach of modeling standardized proportions leads to biased estimates, violating the logic of algorithms underlying multiple regressions (Rosenbaum & Rubin, 1984).

Future research should address several key limitations of the current ecological approach. Individual-level longitudinal studies incorporating multiple dimensions of green space exposure—beyond NDVI to include quality, accessibility, and usage patterns—would prevent ecological fallacy and strengthen causal inference. Mediation analyses quantifying the relative contributions of proposed pathways (air pollution reduction, physical activity promotion, stress reduction) could clarify mechanism-specific effects across different health outcomes. Assessment of effect modification by age, sex, and socioeconomic position, would reveal more nuanced environment-health relationships. Availability of health data with higher spatial resolution would benefit research initiatives and allow more detailed analyses. Lastly, integrating measures of social capital and mobility patterns would disentangle their role in the complex relationships between urban form, environmental exposures, and population health.

5. Conclusions

This study highlights the complex and multidimensional relationship between urban form and population health in Tuscany. By examining multiple chronic diseases across diverse urban configurations and using complementary classification approaches, our findings contribute to a more nuanced understanding of how cities' spatial organization and green spaces may influence health outcomes. Polycentric structures appear more at risk for ischemic heart disease, compared to sprawling areas; moderate-density semi-structured municipalities were associated with lower prevalence of ischemic heart disease and diabetes compared to fragmented low-density areas. The stability of estimates after NDVI adjustment suggests urban configuration affects health through mechanisms beyond just green space availability.

CRediT authorship contribution statement

Alessio Perilli: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Marta Rodeschini:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Data curation, Conceptualization. **Giorgia Gabrielli:** Writing – review & editing, Writing – original draft, Data curation. **Giulia Congedo:** Writing – review & editing, Investigation, Data curation. **Alessandro Filomeno:** Methodology, Formal analysis, Data curation. **Rita De Donno:** Writing – review & editing. **Giulio De Micco:** Writing – review & editing. **Mattia Di Russo:** Writing – review & editing, Conceptualization. **Gianluca Fevola:** Writing – review & editing. **Gaia Surya Lombardi:** Writing – review & editing, Conceptualization. **Marco Tononi:** Writing – review & editing, Methodology. **Doris Zjalic:** Writing – review & editing, Conceptualization. **Emanuele Garda:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Stefania Bruno:** Writing – review & editing, Supervision, Project administration, Conceptualization.

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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.cities.2026.107096.

Data availability

Data will be made available on request.

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