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Residing in urban areas with higher green space is associated with lower mortality risk: A census-based cohort study with ten years of follow-up

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ABSTRACT

Background: Epidemiological studies suggest that residing close to green space reduce mortality rates. We investigated the relationship between long-term exposure to residential green space and non-accidental and cardio-respiratory mortality.

Methods: We linked the Belgian 2001 census to population and mortality register follow-up data (2001–2011) among adults aged 30 years and older residing in the five largest urban areas in Belgium ($n = 2{,}185{,}170$ and mean follow-up time 9.4 years). Residential addresses were available at baseline. Exposure to green space was defined as 1) surrounding greenness (2006) [normalized difference vegetation index (NDVI) and modified soil-adjusted vegetation index (MSAVI2)] within buffers of 300 m, 500 m, and 1000 m; 2) surrounding green space (2006) [Urban Atlas (UA) and CORINE Land Cover (CLC)] within buffers of 300 m, 500 m, and 1000 m; and 3) perceived neighborhood green space (2001). Cox proportional hazards models with age as the underlying time scale were used to probe into cause-specific mortality (non-accidental, respiratory, COPD, cardiovascular, ischemic heart disease (IHD), and cerebrovascular). Models were adjusted for several sociodemographic variables (age, sex, marital status, country of birth, education level, employment status, and area mean income). We further adjusted our main models for annual mean (2010) values of ambient air pollution ($PM_{2.5}$, PM_{10}, NO_2 and BC, one at a time), and we additionally explored potential mediation with the aforementioned pollutants.

Results: Higher degrees of residential green space were associated with lower rates of non-accidental and respiratory mortality. In fully adjusted models, hazard ratios (HR) per interquartile range (IQR) increase in NDVI 500 m buffer (IQR: 0.24) and UA 500 m buffer (IQR: 0.31) were 0.97 (95%CI 0.96–0.98) and 0.99 (95%CI 0.98–0.99) for non-accidental mortality, and 0.95 (95%CI 0.93–0.98) and 0.97 (95%CI 0.96–0.99) for respiratory mortality. For perceived neighborhood green space, HRs were 0.93 (95%CI 0.92–0.94) and 0.94 (95%CI

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0.91–0.98) for non-accidental and respiratory mortality, respectively. The observed lower mortality risks associated with residential exposure to green space were largely independent from exposure to ambient air pollutants.

Conclusion: We observed evidence for lower mortality risk in associations with long-term residential exposure to green space in most but not all studied causes of death in a large representative cohort for the five largest urban areas in Belgium. These findings support the importance of the availability of residential green space in urban areas.

1. Introduction

As a consequence of the rapid urbanization worldwide, the amount of available green space in urban living environments is usually limited. In recent years, a growing body of literature on the association between residential green space and mortality has been made available (Villeneuve et al., 2012; Wilker et al., 2014; Tamosiunas et al., 2014; James et al., 2016; de Keijzer et al., 2017; Crouse et al., 2017; Vienneau et al., 2017; Wang et al., 2017; Nieuwenhuijsen et al., 2018; Silveira and Junger, 2018; Crouse et al., 2019; Orioli et al., 2019; Seo et al., 2019; Kim et al., 2019; Schinasi et al., 2019; Zijlema et al., 2019; Ji et al., 2019; Sun et al., 2020; Klompmaker et al., 2020), and has generally shown lower mortality rates with higher amounts of green space. Potential beneficial health effects of the presence of green space in the living environment have been suggested to act through various mechanisms, such as: mitigation effects through reduced exposure to air pollution, noise and excess heat; restorative effects by alleviating stress and restoration capacities by enhancing physical activity or stimulating social contacts (James et al., 2015; Markevych et al., 2017; Nieuwenhuijsen et al., 2017).

With regard to cause-specific mortality and long-term residential exposure to green space, evidence is still limited (Gascon et al., 2016; Rojas-Rueda et al., 2019). The majority of longitudinal studies investigating the aforementioned association with cause-specific mortality found stronger relations compared to all-cause mortality (Villeneuve et al., 2012; James et al., 2016; Crouse et al., 2017; Vienneau et al., 2017; Orioli et al., 2019). Overall, most longitudinal studies investigating cause-specific mortality observed the strongest associations for respiratory deaths followed by cardiovascular deaths (Villeneuve et al., 2012; James et al., 2016; Crouse et al., 2017; Vienneau et al., 2017), but this was not the case for all studies (Orioli et al., 2019; Klompmaker et al., 2020).

In Europe, only three studies have investigated the association between long-term residential exposure to green space and cause-specific mortality (Vienneau et al., 2017; Orioli et al., 2019; Klompmaker et al., 2020). Additionally, only a few studies used more than one green space metric to evaluate this association (Vienneau et al., 2017; Orioli et al., 2019; Klompmaker et al., 2020).

Therefore, we investigated in a prospective cohort study of more than 2 million adult residents of five urban areas in Belgium, the associations with long-term residential exposure to green space, as assessed by various green space indicators, with non-accidental and cardio-respiratory mortality.

2. Methods

2.1. Study population and design

We used data from the Belgian 2001 census and linked these individual data to individual mortality (and emigration) follow-up data (2001–2011; 10.25 years) from the official population and mortality register, made available by the Belgian Statistical Office (Statbel). We included all adults aged 30 years and older at baseline (October 1, 2001) and officially residing in one of the 5 largest urban areas in Belgium (Antwerp, Brussels, Charleroi, Ghent or Liège) at the time of the census. Urban areas in our study were defined by using the EU-OECD definition of (large) metropolitan sized Functional Urban Areas (Dijkstra et al., 2019), consisting of city and surrounding commuting zone and containing more than 250,000 inhabitants in each urban area. Antwerp and Ghent are in Flanders, the northern Dutch-speaking part of the country, whereas both Charleroi and Liège are in Wallonia, the French-speaking southern part of the country. Brussels, the centrally situated bilingual capital, is the largest urban area of the country.

2.2. Exposure assessment

Urban residential green space was defined based on two objective and one subjective green space metrics. Objective residential green space was characterized and quantified by both 1) surrounding greenness (i.e. an indicator for overall greenness), and 2) surrounding green space (i.e. an indicator including specific types of green). Both surrounding greenness and surrounding green space were assessed for different circular Euclidean buffers (300 m, 500 m and 1000 m). Buffer calculation for both indicators was achieved at the level of the centroid of each grid cell, using the focal function in R (R Core Team, 2019; RStudio Team, 2019; Hijmans, 2016). Subsequently, individuals' geocoded residential addresses at baseline were assigned to each corresponding grid cell (Klompmaker et al., 2020). Data for both objective green space indicators were collected for the year 2006, the midpoint of our study follow-up. Exposure assessment of the objective green space metrics was done using R (version 3.5.0) (R Core Team, 2019; RStudio Team, 2019) (packages: raster (Hijmans, 2016), gdalUtils (Greenberg and Mattiuzzi, 2015), rgdal (Bivand et al., 2017)). Lastly, the indicator for 3) subjective green space was constructed based on the household head's perceived presence of neighborhood green space.

2.3. Residential surrounding greenness

Residential surrounding greenness was defined by using two different remote sensing vegetation indices: the Normalized Difference Vegetation Index (NDVI) (Tucker, 1979) and the Modified Soil-adjusted Vegetation Index 2 (MSAVI2) (Huete, 1988; Qi et al., 1994a,b). For both vegetation indices, atmospherically corrected satellite images were derived from Landsat 5, available at 30 m spatial resolution (Gorelick et al., 2017). A selection of cloud-free images covering the entire study area was obtained for the months May-September for the year 2006. To reflect the study area at the peak of the growing season, we ran an algorithm to select the greenest pixels (i.e. maximal value), returning a composite mosaic for each vegetation index (Gorelick et al., 2017). Further details on the procedure of retrieving and manipulating the satellite data is documented in supplementary materials (S1).

Several prior studies have used NDVI as an indicator of greenness, which is derived from the difference of land surface reflectance, obtained by the ratio of visible (red) and near infrared (NIR) light bands (Tucker, 1979). Alternatively, we also used MSAVI2 which is a vegetation index that uses a soil brightness correction factor in addition to the red and NIR bands, which is of particular interest for study areas with a low degree of vegetation (e.g. urban areas, deserts, prairies) (Qi et al., 1994b). Both aforementioned vegetation indices have values ranging between -1 and $+1$, where higher positive values indicate increasing photosynthetically active vegetation. To avoid averaging out the presence of residential greenness, negative index values indicating water surfaces were set to zero prior to calculating different circular Euclidean buffers (Fuertes et al., 2016). Both vegetation indices were expressed as average index values for each available circular buffer.

2.4. Residential surrounding green space

We assessed residential surrounding green space for two different land cover datasets; Urban Atlas (UA) 2006 (EEA, 2019b) and CORINE Land Cover (CLC) 2006 (EEA, 2019a). From the 22 urban land use classes available in UA 2006, we identified and grouped four land use classes as green spaces in our study. The indicator of surrounding green space based on CLC was defined by grouping a selection of the 44 available land cover classes that referred to green spaces. More details on the land use classes used for both UA and CLC are described in the supplementary material (S2). The minimum mapping unit for the UA and the CLC were 0.25 ha (ha) and 25 ha, respectively. The indicators for residential surrounding green space were expressed as the proportion of green space available in a circular buffer around the residential address for both land use datasets.

2.5. Perceived neighborhood green space

The Belgian 2001 census (SEE01: (Vanneste et al., 2007)) contains a module on the provision of several neighborhood facilities. All heads of households were asked a battery of questions related to the neighborhood environment and included a question regarding the perceived provision of neighborhood green space, which we integrated as a subjective measure of green space. The following question was included: “What do you think of the neighborhood facilities? The green space” and was rated following a three-point Likert scale (“poorly equipped”, “normally equipped”, or “very well equipped”) (Vanneste et al., 2007). The different household scores on the presence of neighborhood green space were averaged at the level of the census tract to account for potential reverse causation bias, where individuals’ poor health status might affect neighborhood facility perception. Our study area consists of 5,068 census tracts with an average surface of 85.2 ha, which largely corresponds to the 500 m buffer size of the objective greenspace metrics.

2.6. Mortality outcomes

The studied mortality outcomes were identified through the WHO International Classification of Diseases, Tenth Revision codes (ICD-10) (WHO, 2004), and by selecting the primary underlying cause of death registered on the death certificate. We considered mortality of non-accidental (ICD-10: A00-R99), all cardiovascular (ICD-10: I10-I70) and all respiratory mortality causes (ICD-10: J00-J99). Additionally, we considered mortality subgroups for cardiovascular mortality [ischemic heart disease (IHD); ICD-10: I20-I25 and cerebrovascular; ICD-10: I60-I69] and for respiratory mortality [chronic obstructive pulmonary disease (COPD, excluding asthma); ICD-10: J40-J44, J47].

2.7. Covariate data

Various individual sociodemographic covariates were available through a questionnaire at baseline. Demographic characteristics included age, sex, marital status (single, married, separated/divorced or widowed), and country of birth (Belgium vs foreign). Education level (no/primary education, secondary education or tertiary education) and employment status (employed vs unemployed) were used as indicators for socioeconomic position (SEP) at individual level. In addition, as indicators for area level SEP, we included area mean net taxable income, unemployment rate and percentage of population with low (i.e. no/primary) education. These indicators were made available by Statbel for the year 2011 and was operationalized at the level of statistical sections (n = 1,434), i.e. geographical units with sizes lying between those of census tracts (n = 5,068) and municipalities LAU (n = 152). In addition, data on 2010 annual mean concentrations of several ambient air pollutants – particulate matter ($PM_{2.5}$ and PM_{10}), nitrogen dioxide (NO_2) and black carbon (BC) – at high resolution grids of 25 m × 25 m was made available by the Belgian Interregional Environment Agency (IRCEL-CELINE). Further details on the ambient air pollution data can be found in supplementary materials (S3).

2.8. Statistical analyses

Pairwise correlation coefficients were calculated between the different exposure metrics. The associations between each green space metric and mortality outcomes were assessed using Cox proportional hazards models with age as the underlying time scale. Individuals were right censored if they died due to a cause of death that was not under study, or if they were lost to follow-up because of emigration outside of the study area or before the end of the study period.

We fitted several nested survival models with increasing degrees of covariate adjustment for each green space metric separately. Our main model was adjusted for sex (strata term (Therneau, 2015)), marital status, country of birth, education level, employment status, and area mean income. Unobserved between-urban area heterogeneity was accounted for by including a shared frailty term, which allowed for different distributions of the underlying baseline hazard and accounted for the clustered nature of sociodemographic and environmental characteristics in each urban area.

Covariate selection was based on both prior similar research (Villeneuve et al., 2012; James et al., 2016; Crouse et al., 2017; Vienneau et al., 2017; Nieuwenhuijsen et al., 2018; Orioli et al., 2019; Klompmaker et al., 2020), and on the availability in our dataset. The proportional hazards assumption (Breslow, 1975) was tested for all covariates by graphically plotting the Kaplan-Meier curves. The assumption did not hold for sex, hence the use of a strata term to allow for differential baseline hazards.

We explored linearity of the exposure–response relationship by specifying natural spline terms with 2 degrees of freedom (Eisen et al., 2004) into our main model. We compared the goodness of fit of these models with the models specified with a continuous linear term using the linear likelihood-ratio test (LRT). We observed no substantial deviations from linearity based on the exposure–response curves and LRT p-values (Supplementary Figure S1). Therefore, we report our main results based on the continuous linear terms for the different residential green space metrics under study.

In additional analyses, we further adjusted our main models for several ambient air pollutants, i.e. particulate matter ($PM_{2.5}$ and PM_{10}), nitrogen dioxide (NO_2) and black carbon (BC), each included one at a time. In addition, we performed mediation analysis considering each of the aforementioned pollutants as separate mediators. We explored potential mediation by following the procedure described by Imai and colleagues (2010). In brief, we specified two models: an exposure-mediator-outcome model (survival regression), and an exposure-mediator model (linear regression), both fully adjusted for the covariates of our main model. By fitting both models, the average direct effect and average causal mediation effect can be estimated. The latter is often referred to as the indirect effect and obtained here by the difference method (Imai et al., 2010). Next, the proportion mediated is obtained by calculating the ratio between the direct and the total effect (i.e. direct + indirect) and is interpreted as the proportion of mortality reduction in the association with residential green space explained by ambient air pollution. We performed mediation analysis only when the observed association between outcome and green space metric in our main model was statistically significant. Proportions mediated were reported with their 95% Quasi-Bayesian confidence intervals (95%CI), obtained by 500 Monte Carlo simulations. The number of drawn simulations could not be increased to the default, recommended 1000 simulations (Tingley et al., 2014) because of computational power limits.

As sensitivity analyses, we reran our main models on a subset of individuals who: 1) did not move during the follow-up period (i.e. nonmovers), 2) reported a (very) good subjective general health status at baseline (i.e. healthy subpopulation), and 3) resided in city centers, thus excluding commuting zone inhabitants (i.e. city center residents). Additionally, we further adjusted our main models for alternative area level SEP indicators (unemployment rate and low education rate), both separately and combined (including mean income [main model], unemployment rate and low education rate).

We explored potential effect modification as several similar studies observed variations in the association with residential green space and mortality (Gascon et al., 2016; Vienneau et al., 2017). We included multiplicative interaction terms into our main models between the main green space metrics and age (<65 years or $\geq$ 65 years), sex, education level (no diploma/primary education, secondary education or tertiary education), and urban area (Brussels, Antwerp, Charleroi, Ghent or Liège). The goodness of fit of these models was tested by evaluating the statistical significance of the likelihood-ratio test (LRT), comparing the model with and without interaction term. Furthermore, we stratified our main models for the aforementioned potential effect modifiers.

Results are expressed as hazard ratios (HRs) with 95%CIs. We presented HRs of the objective green space metrics by one interquartile range (IQR) increase (the difference between the 75th and 25th percentile), considering their observed skewed distribution. All analyses were conducted with the statistical software R (version 3.5.0) (R Core Team, 2019; RStudio Team, 2019) using the splines, survival (Therneau, 2015), mediation (Tingley et al., 2014) and ggplot2 (Wickham, 2009) packages and dependencies.

3. Results

3.1. Study population and residential green space

The study population eligible for analysis consisted of 2,185,170 individuals. Exclusion criteria were missing geographic coordinates (3.9%) and missing covariate information (12.3%). The total person-years at risk amounted to 20,512,560 (mean follow-up: 9.4 years). The characteristics of the studied cohort at baseline (Belgian 2001 census) are described in Table 1. Around 53% of the study population were women. More than half were cohabiting/married (64.4%). The majority of the study population was born in Belgium (82.1%) and obtained a secondary education degree or higher (76.9%). Around 40% of our study population resided in Brussels, the Belgian capital. The total number of non-accidental deaths was 298,693, with 32.9% being cardiovascular and 11.7% respiratory mortality (Table 1).

Detailed descriptions and pairwise correlations for the different environmental exposures are presented in Supplementary Table S1-S2. Variations across different buffer sizes were smaller for residential surrounding greenness than for residential surrounding green space (Supplementary Table S1). Correlations between different buffer sizes were stronger for residential surrounding greenness (0.92–0.99) compared to residential surrounding green space (0.74–0.94) (Supplementary Table S2). Correlations between residential surrounding greenness and residential surrounding green space metrics ranged from (0.65–0.90). Objective residential green space metrics were weakly to moderately correlated with perceived neighborhood green space (0.28–0.50). The different objective residential green space metrics were moderately to strongly negatively correlated with air pollution. The correlations between perceived neighborhood green space and the different pollutants were weak.

3.2. Association between residential green space and mortality

We observed statistically significant inverse (i.e. HR below unity) associations for overall (non-accidental) mortality and respiratory mortality with all three indicators of residential green space under study (Fig. 1 and Supplementary Table S3 for all green space metrics and buffer sizes). In general, the associations were strongest with perceived residential neighborhood green space compared to residential surrounding greenness and residential surrounding green space. Also, attenuation after incremental adjustment for individual and area level sociodemographic covariates was most pronounced for perceived residential neighborhood green space. In fully adjusted models, the overall (non-accidental) mortality risk per IQR increase was lower for NDVI 500 m [2.80% (95%CI 1.98%-3.62%) (IQR: 0.24)] than for UA 500 m [1.14% (95%CI 0.54%-1.74%) (IQR: 0.31)]. Similarly, respiratory mortality risk per IQR increase was lower for NDVI 500 m [4.72% (95% CI 2.33%-7.05%)] than for UA 500 m [2.65% (95%CI 0.88%-4.39%)]. Observed associations with perceived neighborhood green space were stronger for cardiovascular mortality than for respiratory mortality, while the opposite is true for residential surrounding greenness and residential surrounding green space. After adjusting for area mean income in our final model (M3), we no longer observed significant

Table 1
Characteristics of the studied cohort at baseline (Belgian 2001 census).

Variable	*Description*
N total (greater than30 years): n	2,185,170
Age: median (IQR)	51.14 (24.85)
Sex: n (%)	
Men	1,036,656 (47.4)
Women	1,148,514 (52.6)
Marital status: n (%)	
Single	312,426 (14.3)
Married	1,408,004 (64.4)
Separated/divorced	240,864 (11.0)
Widowed	223,876 (10.2)
Country of birth: n (%)	
Belgium	1,794,488 (82.1)
Foreign	390,682 (17.9)
Education level: n (%)	
No/primary education	503,405 (23.0)
Secondary education	1,089,255 (49.8)
Tertiary education	592,510 (27.1)
Employment status: n (%)	
Employed	1,074,864 (49.2)
Unemployed	1,110,306 (50.8)
Area mean income: median (IQR)	28568.28 (10142.56)
Area unemployment rate: median (IQR)	0.09 (0.10)
Area low education rate: median (IQR)	0.15 (0.08)
Urban area: population n (%)	
Brussels	906,370 (41.5)
Antwerp	504,276 (23.1)
Charleroi	207,973 (9.5)
Ghent	230,867 (10.6)
Liège	335,684 (15.4)
Nonmovers: n (%)	1,474,617 (67.5)
Healthy subpopulation: n (%)	1,430,822 (65.5)
City center residents: n (%)	1,077,872 (49.3)
N mortality[a]: n (%)	
Non-accidental (ICD-10[b]: A00- R99)	298,693 (13.7)
All respiratory (ICD-10[b]: J00-J99)	34,797 (1.6)
COPD (ICD-10[b]: J40-J44, J47)	14,368 (0.7)
All cardiovascular (ICD-10[b]: I10-I70)	98,190 (4.5)
Ischemic heart disease (IHD) (ICD-10[b]: I20-I25)	32,694 (1.5)
Cerebrovascular (ICD-10[b]: I60-I69)	23,003 (1.1)
Surrounding greenness (NDVI) 500 m buffer: median (IQR)	0.59 (0.24)
Surrounding green space (Urban Atlas) 500 m buffer: median (IQR)	0.19 (0.31)
Perceived neighborhood green space: median (IQR)	2.07 (0.54)
Ambient air pollution: median (IQR)	
$PM_{2.5}$ ($\mu g/m^3$)	17.54 (3.44)
PM_{10} ($\mu g/m^3$)	24.97 (3.87)
NO_2 ($\mu g/m^3$)	29.69 (11.26)
BC ($\mu g/m^3$)	1.87 (0.85)

Source: Belgian 2001 census linked to population and mortality register (2001–2011) and linked to exposure data.

[a] Mortality follow-up October 1, 2001-December 31, 2011.

[b] ICD-10: WHO International Classification of Diseases, Tenth Revision codes.

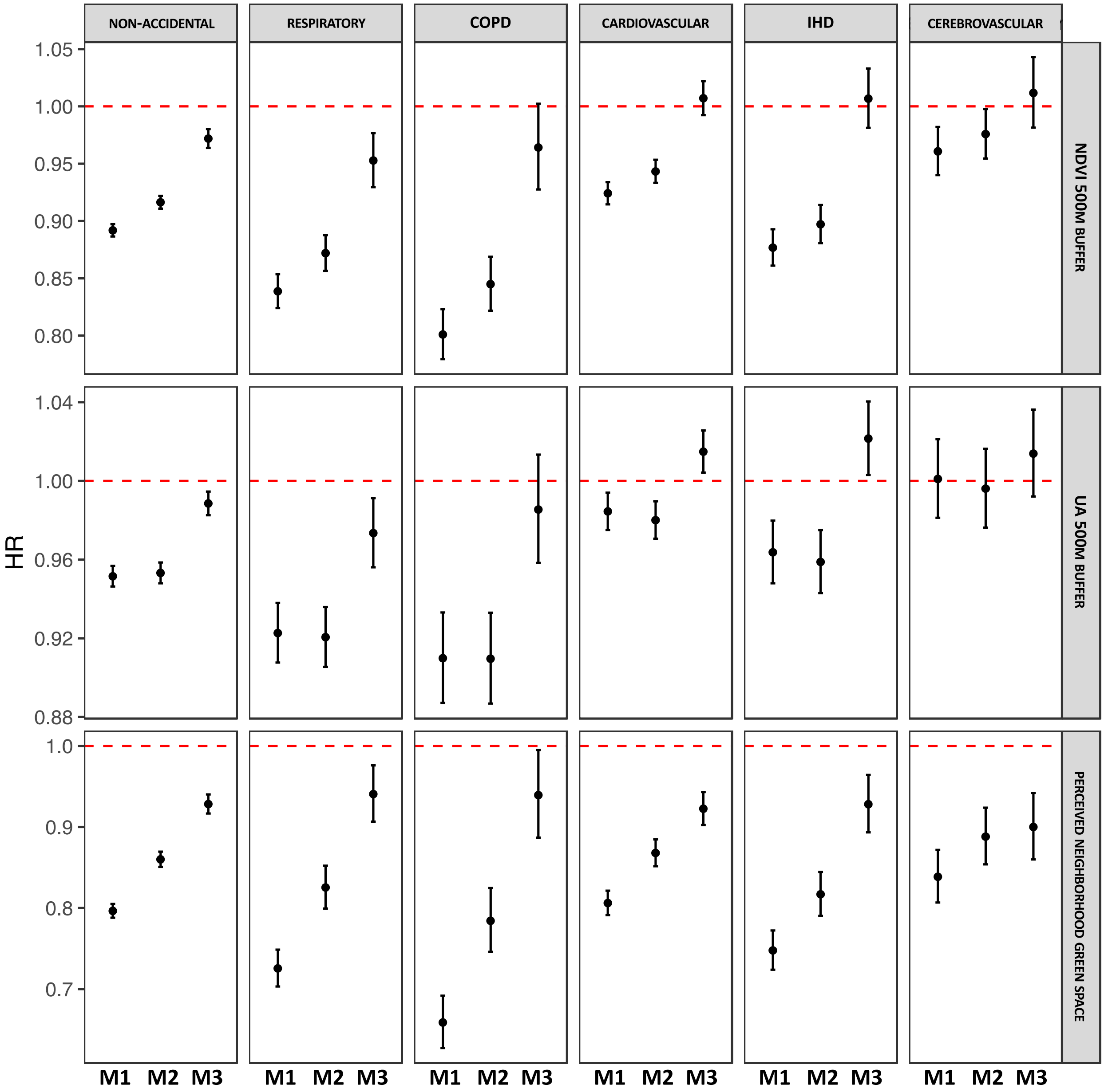

Fig. 1. Hazard ratios (HR) and 95% confidence intervals (95% CI) with increasing degree of adjustment for the association between mortality outcomes with different green space metrics (NDVI 500 m buffer[a], UA 500 m buffer[a] and perceived neighborhood green space). Note: **M1**: stratified by sex and accounted for between-area variability by including a shared frailty term; **M2**: M1 + adjusted for individual sociodemographic covariates (marital status, country of birth, education level and employment status); **M3**: M2 + area mean income. [a] reported HRs are expressed by one interquartile increase (IQR) for NDVI (IQR: 0.24) and UA (IQR: 0.31). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

associations between residential surrounding greenness for cardiovascular, IHD, cerebrovascular and COPD causes of death. Similarly, associations with residential surrounding green space in M3 lost statistical significance for cerebrovascular and COPD mortality, while for cardiovascular and IHD mortality associations remained statistically significant but changed direction (Fig. 1 and Supplementary Table S3). Adjusted HRs were similar when using alternative residential green space metrics, i.e. residential surrounding greenness (MSAVI2) and residential surrounding green space (CLC) (Supplementary Table S3). No notable differences were observed when comparing associations using different buffer sizes (Supplementary Table S3).

After further adjustment of our main models (M3) for different air pollutants ($PM_{2.5}$, PM_{10}, NO_2 and BC, one at a time), HRs remained unchanged for the majority of mortality outcomes and green space metrics (Table 2). Only for respiratory mortality, associations with residential surrounding greenness (HR: 0.98, 95%CI 0.95–1.01; HR: 0.97, 95%CI 0.94–1.00) and with residential surrounding green space (HR: 0.99, 95%CI 0.97–1.01; HR: 0.99, 95%CI 0.97–1.01) lost significance after adjustment for $PM_{2.5}$ and NO_2, respectively (Table 2). Likewise, for cardiovascular mortality in relation to residential surrounding green space, associations were no longer significant after adjustment for $PM_{2.5}$ and NO_2.

Mediation analyses were carried out only for overall (non-accidental) mortality and respiratory mortality since associations with residential green space in our main model were consistently statistically significant for these two outcomes only (Supplementary Table S4). Assuming that underlying statistical assumptions to conduct mediation analysis (VanderWeele, 2015) were valid, we found that approximately 18–60% of the association between residential green space and respiratory mortality is potentially partially mediated by $PM_{2.5}$. Further, for

Table 2
Adjusted hazard ratio (HR) and 95% confidence intervals (95% CI) of the association between mortality outcomes with different green space metrics (NDVI 500 m buffer[a], UA 500 m buffer[a] and perceived neighborhood green space) after adjustment for ambient air pollution ($PM_{2.5}$, PM_{10}, NO_2 and BC).

	Mortality outcome **(n = 2185170)**								
	Non-accidental			**Respiratory**			**COPD**		
	NDVI 500 m HR (95% CI)	**UA 500 m HR (95% CI)**	**Perceived neighborhood green space HR (95% CI)**	**NDVI 500 m HR (95% CI)**	**UA 500 m HR (95% CI)**	**Perceived neighborhood green space HR (95% CI)**	**NDVI 500 m HR (95% CI)**	**UA 500 m HR (95% CI)**	**Perceived neighborhood green space HR (95% CI)**
Main model[b]	**0.97 (0.96–0.98)**	**0.99 (0.98–0.99)**	**0.93 (0.92–0.94)**	**0.95 (0.93–0.98)**	**0.97 (0.96–0.99)**	**0.94 (0.91–0.98)**	0.96 (0.93–1.00)	0.99 (0.96–1.01)	**0.94 (0.89–0.99)**
Main model[b] + $PM_{2.5}$	**0.97 (0.96–0.98)**	**0.99 (0.98–0.99)**	**0.93 (0.92–0.94)**	0.98 (0.95–1.01)	0.99 (0.97–1.01)	**0.95 (0.91–0.98)**	0.99 (0.94–1.03)	1.00 (0.97–1.03)	0.94 (0.89–1.00)
Main model[b] + PM_{10}	**0.97 (0.96–0.98)**	**0.99 (0.98–0.99)**	**0.93 (0.92–0.94)**	**0.96 (0.93–0.99)**	**0.98 (0.96–0.99)**	**0.95 (0.91–0.98)**	0.97 (0.92–1.01)	0.99 (0.96–1.02)	**0.94 (0.89–0.99)**
Main model[b] + NO_2	**0.97 (0.96–0.98)**	**0.99 (0.98–0.99)**	**0.93 (0.92–0.94)**	0.97 (0.94–1.00)	0.99 (0.97–1.01)	**0.95 (0.91–0.98)**	0.97 (0.92–1.02)	0.99 (0.96–1.03)	**0.94 (0.89–0.99)**
Main model[b] + BC	**0.97 (0.96–0.98)**	**0.99 (0.98–0.99)**	**0.93 (0.92–0.94)**	**0.96 (0.93–0.99)**	**0.98 (0.96–0.99)**	**0.94 (0.91–0.98)**	0.96 (0.92–1.01)	0.99 (0.96–1.02)	**0.94 (0.89–0.99)**
	Cardiovascular			**Ischemic heart disease**			**Cerebrovascular**		
	NDVI 500 m HR (95% CI)	**UA 500 m HR (95% CI)**	**Perceived neighborhood green space HR (95% CI)**	**NDVI 500 m HR (95% CI)**	**UA 500 m HR (95% CI)**	**Perceived neighborhood green space HR (95% CI)**	**NDVI 500 m HR (95% CI)**	**UA 500 m HR (95% CI)**	**Perceived neighborhood green space HR (95% CI)**
Main model[b]	1.01 (0.99–1.02)	**1.01 (1.00–1.03)**	**0.92 (0.90–0.94)**	1.01 (0.98–1.03)	**1.02 (1.00–1.04)**	**0.93 (0.89–0.96)**	1.01 (0.98–1.04)	1.01 (0.99–1.04)	**0.90 (0.86–0.94)**
Main model[b] + $PM_{2.5}$	0.99 (0.97–1.01)	1.01 (1.00–1.02)	**0.92 (0.90–0.94)**	1.02 (0.98–1.05)	**1.03 (1.01–1.05)**	**0.93 (0.89–0.96)**	0.99 (0.95–1.04)	1.00 (0.98–1.03)	**0.90 (0.86–0.94)**
Main model[b] + PM_{10}	0.99 (0.98–1.02)	**1.01 (1.00–1.02)**	**0.92 (0.90–0.94)**	1.01 (0.97–1.04)	**1.02 (1.00–1.04)**	**0.93 (0.89–0.96)**	0.99 (0.96–1.04)	1.01 (0.99–1.03)	**0.89 (0.85–0.93)**
Main model[b] + NO_2	0.99 (0.97–1.01)	1.01 (1.00–1.02)	**0.92 (0.90–0.94)**	1.00 (0.97–1.03)	**1.02 (1.00–1.04)**	**0.93 (0.89–0.96)**	0.99 (0.96–1.04)	1.01 (0.98–1.03)	**0.90 (0.86–0.94)**
Main model[b] + BC	0.99 (0.98–1.01)	**1.01 (1.00–1.02)**	**0.92 (0.90–0.94)**	1.00 (0.98–1.03)	**1.02 (1.00–1.04)**	**0.93 (0.89–0.96)**	1.01 (0.97–1.04)	1.01 (0.99–1.04)	**0.90 (0.86–0.94)**

[a] Reported HRs are expressed by one interquartile increase (IQR) for NDVI (IQR: 0.24) and UA (IQR: 0.31).

[b] Stratified by sex, accounted for between-area variability by including a shared frailty term and adjusted for individual sociodemographic covariates (marital status, country of birth, education level and employment status) and area level SEP (mean income).

the association between residential surrounding greenness and respiratory mortality, the observed proportion mediated possibly related to a reduction in NO_2 concentrations was 0.43 (95%CI 0.08–1.42). There was very weak evidence of potential mediation in the association between residential green space and overall (non-accidental) mortality. Only NO_2 seemed to mediate 2% (95%CI 1%-5%) of the association with perceived neighborhood green space.

Sensitivity analyses did not change our main findings substantially (Supplementary Table S5). In a subset of nonmovers, inverse associations were stronger for all residential green space metrics. Further, relationships between residential surrounding greenness and respiratory mortality were slightly attenuated and lost statistical significance in the subset of “healthy population” and in city center residents. In city center residents the associations of residential surrounding green space with either non-accidental or respiratory mortality also had wider 95%CIs that included unity. Alternative regression models with further adjustment for different area level SEP indicators (separately and combined) were generally consistent with our main results, however we observed that for cardiovascular causes of death, direct associations (i.e. HR above unity) lost statistical significance or became inversely statistically significant when adjusting for alternative SEP indicators.

3.3. *Effect modification by age, sex, education level and urban area*

In Fig. 2 we present the associations between cause-specific mortality and residential green space (NDVI 500 m buffer, UA 500 m buffer, and perceived neighborhood green space) stratified by age, sex, education level, and urban area. Results for all mortality outcomes are presented in Supplementary Table S6.

We observed indications for effect modification by age with greater inverse associations in younger age (<65 years) for both residential surrounding greenness and residential surrounding green space for all investigated causes of mortality (LRT p-values: 0.01). Furthermore, direct associations were observed in older age (≥65 years) between all cardiovascular mortality and both residential surrounding greenness (HR: 1.04, 95%CI 1.02–1.06) and residential surrounding green space (HR: 1.03, 95%CI 1.02–1.05). No effect modification by age was observed in the association between non-accidental mortality and perceived neighborhood green space, although the interaction term was significant (LRT p-value: 0.01). With regards to other mortality outcomes and perceived neighborhood green space, we observed stronger inverse associations in younger individuals for all cardiovascular and IHD mortality.

Sex-stratified analyses suggested lower mortality risks in men for

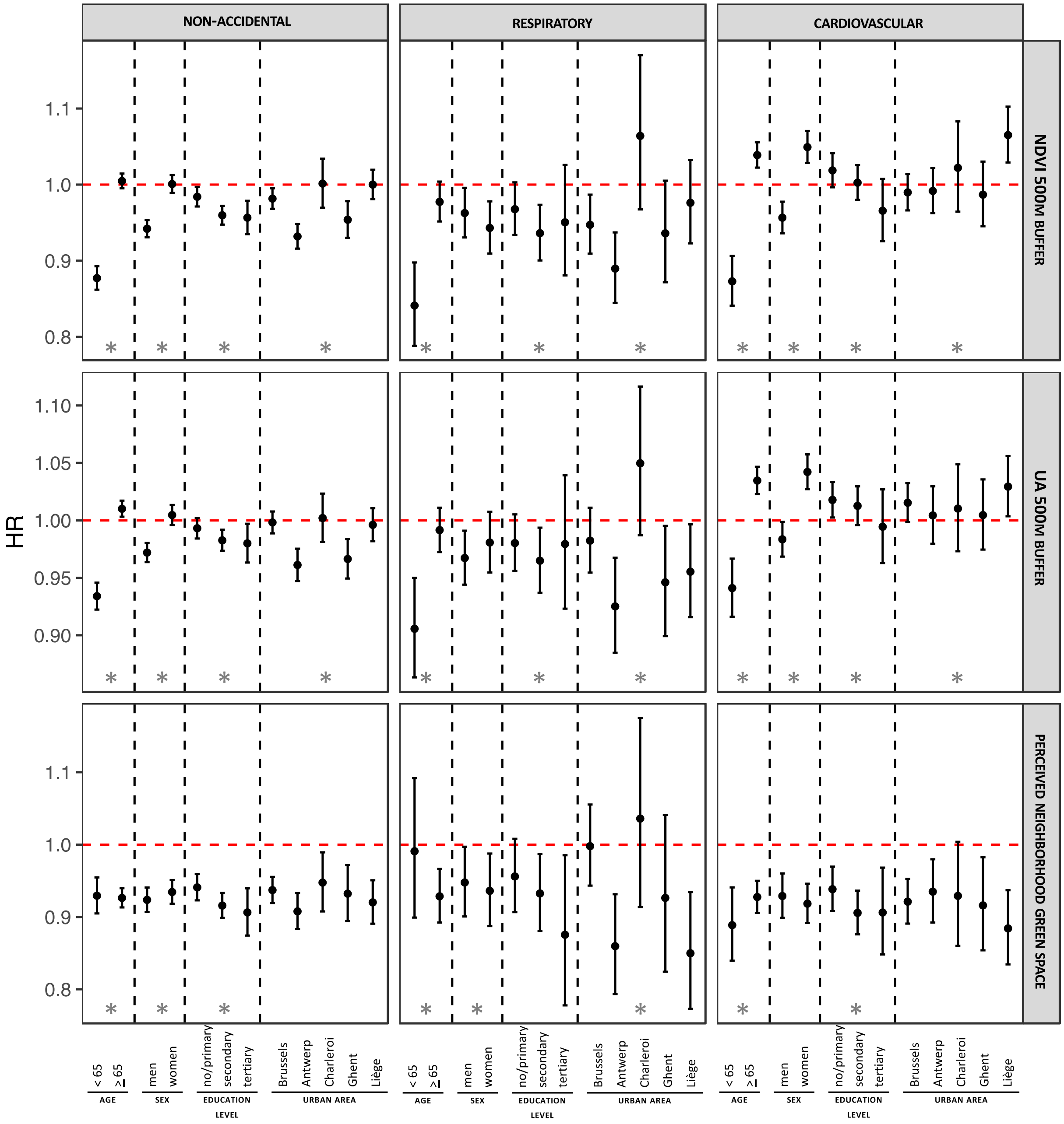

Fig. 2. Adjusted hazard ratios (HR) and 95% confidence intervals (95% CI) for the association between mortality outcomes and different green space metrics (NDVI 500 m buffer, UA 500 m buffer and perceived neighborhood green space), stratified by potential effect modifiers (age, sex, education level and urban area). Note: Fully adjusted models with age as the underlying timescale, accounted for between-area variability by including a shared frailty term and adjusted for individual sociodemographic covariates (sex [strata], marital status, country of birth, education level and employment status) and area mean income. Reported HRs are expressed by one interquartile increase (IQR) for NDVI (IQR: 0.24) and UA (IQR: 0.31). HRs are displayed with their 95%CIs represented as error bars. The asterisks represent the LRT p-values (<0.05) of comparing the main model with and without interaction term. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

non-accidental and all cardiovascular mortality, and lower mortality risks in women for COPD mortality for both residential surrounding greenness and residential surrounding green space. We found direct associations among women for all cardiovascular mortality with both objective indicators of residential green space. Sex-stratified analyses revealed only small differences between men and women with regard to perceived neighborhood green space.

Observed patterns for effect modification by education level were mostly suggestive of stronger inverse associations for individuals with secondary or higher education, although patterns were not always clear nor statistically significant for all mortality causes and across all three residential green space metrics under study.

Stratified analysis by urban area showed heterogeneous patterns between the different areas. Observed LRT p-values ranged between 0.01 and 0.22 (Supplementary Table S6). Generally, associations with non-accidental and respiratory mortality were indicative of significant inverse associations in the urban areas of Antwerp, Ghent and, to a lesser extent, in Brussels. In contrast, although not statistically significant, associations were mainly suggestive to be direct, i.e. counterintuitively positive, for the urban area of Charleroi for all mortality outcomes under study.

4. Discussion

We found lower mortality risk associated with residential surrounding greenness and residential surrounding green space for both overall (non-accidental) mortality and respiratory mortality. No mortality associations with residential surrounding greenness were observed for the various cardiovascular causes under study. We observed higher mortality risk associated with residential green space (500 m and 1000 m buffers) for both cardiovascular and IHD mortality. Furthermore, we observed beneficial associations with perceived neighborhood green space for all mortality causes under study. The majority of our findings were robust after adjustments of our main models for different air pollutants. The validity of our findings is supported by the internal consistency observed between the analyses using different methods to quantify exposure to residential green space.

Although environmental factors are assumed to explain only a relatively small share in the burden of noncommunicable disease compared to other well-known risk factors (such as smoking, diet, and exercise), our observed associations are important given that these are mostly preventable. Additionally, we consider our findings biologically plausible as several studies provide cumulative evidence of associations between residential green space and longer telomeres at birth, in children, in adults, and in elderly (Martens and Nawrot, 2018). Telomeres are important biomarkers of ageing as they are “memories” of both chronic inflammation and oxidative stress, and telomere length has been shown to be inversely related with the risk of noncommunicable disease.

4.1. Interpretation of results in the context of available evidence

The majority of similar cohort studies that evaluated the association between residential green space and mortality used a single measure of residential surrounding greenness (i.e. based on remote sensing vegetation indices) (Villeneuve et al., 2012; James et al., 2016; Crouse et al., 2017; Vienneau et al., 2017; Nieuwenhuijsen et al., 2018; Orioli et al., 2019; Klompmaker et al., 2020). Only a few other studies have also evaluated the relationship with mortality using other green space metrics such as residential surrounding green space (i.e. based on land cover data) (Vienneau et al., 2017; Nieuwenhuijsen et al., 2018; Klompmaker et al., 2020) or perceived neighborhood green space (Takano et al., 2002). In general, our and similar cohort studies (Vienneau et al., 2017; Klompmaker et al., 2020) observed very comparable results between residential surrounding greenness and residential surrounding green space in the association with mortality. However, direct comparison of our findings across different studies should be viewed with caution and is rather challenging due to heterogeneity in contextual and methodological sources.

Our main findings regarding the relations of overall (non-accidental) mortality and respiratory mortality with residential surrounding greenness are consistent with results of previous cohort studies (Villeneuve et al., 2012; James et al., 2016; Crouse et al., 2017; Vienneau et al., 2017; Nieuwenhuijsen et al., 2018; Orioli et al., 2019), although reported estimates were stronger in the majority of these studies. In contrast, a recent study in the Netherlands found no association with residential surrounding greenness for both non-accidental and respiratory mortality (Klompmaker et al., 2020). Similarly, an Italian study did not observe an association for respiratory mortality in the city of Rome (HR: 1.01, 95%CI 0.99–1.04) (Orioli et al., 2019). We did not observe associations between residential surrounding greenness and cardiovascular mortality. This finding is in line with two other studies (James et al., 2016; Klompmaker et al., 2020), although the majority of other similar longitudinal studies did find beneficial associations between cardiovascular mortality and residential surrounding greenness (Villeneuve et al., 2012; Crouse et al., 2017; Vienneau et al., 2017; Orioli et al., 2019). In addition, we found no associations between either IHD or cerebrovascular mortality and residential surrounding greenness. Evidence regarding IHD and cerebrovascular mortality in relation to residential surrounding greenness is mixed. In Canada, Crouse et al. (2017) found protective associations for IHD and cerebrovascular mortality in 30 census metropolitan areas, while another Canadian study conducted by Villeneuve et al. (2012) in 10 urban areas in the province of Ontario, observed a beneficial relationship with IHD mortality but not with cerebrovascular mortality. Similarly, two American studies (Wilker et al., 2014; James et al., 2016) also did not observe an association with cerebrovascular mortality. These findings differ from two European studies by Vienneau et al. (2017) and Orioli et al. (2019) that did observe beneficial effects of residential surrounding greenness for cerebrovascular mortality but not for IHD mortality.

For residential surrounding green space in relation to non-accidental and respiratory mortality we observed similar but weaker estimates compared to the study of Vienneau et al. (2017). In contrast to the aforementioned study, we observed statistically significant direct associations for cardiovascular and IHD mortality in relation to residential surrounding green space in our main model. A potential explanation for this counterintuitive observation might lie in the complex interplay between green space and area level SEP indicators (Markevych et al., 2017) which has been observed in our sensitivity analyses (Supplementary Table S5). Area level SEP could be related to the quality (e.g. size, safety, infrastructure) of the available surrounding green space, which might be an important feature of available green space, especially with regard to cardiovascular causes of mortality where physical inactivity is an important risk factor.

To our knowledge, the study of elderly individuals in Tokyo of Takano et al. (2002) is the only other longitudinal study that investigated the association between residential green space and mortality using a self-reported green space measure. In line with our study, that study showed higher survival among those reporting having plenty of parks and tree lined streets near the residence, however, findings need to be interpreted with caution as these might have been influenced by older age health status.

In our study, associations were strongest with perceived neighborhood green space compared to both objective measures of residential surrounding greenness and green space. At the same time, our metric for perceived neighborhood green space seemed to be most sensitive for confounder adjustment. While perceived measures are generally more subject to potential bias, efforts to reduce this were carried out by aggregating our subjective indicator at the smallest available neighborhood level. The observed differential pattern where associations were stronger for cardiovascular relative to respiratory mortality with regard to subjective green space, and vice versa for objective green space, might be explained by the influence of a psychological component such as stress, which is identified as an important risk factor contributing to the aetiology of cardiovascular disease (WHO, 2013). The indicator of perceived neighborhood green space might partly reflect quality characteristics of green space, such as safety, walkability, biodiversity etc., and is therefore a potentially important – and appropriate – green space metric to investigate the association with mortality, as has been stated by Nieuwenhuijsen et al. (2017).

Several cohort studies took into account air pollution either by further adjusting for air pollution as a confounder (Villeneuve et al., 2012; Wilker et al., 2014; Vienneau et al., 2017) or by performing mediation analysis (James et al., 2016; Vienneau et al., 2017; Orioli et al., 2019). Our findings of only modest pollution effects are in line with the majority of these studies, which reported little or no differences in their estimates. Only one study reported strong mediating effects by air pollution (Orioli et al., 2019). In addition, we observed negative proportions potentially mediated by air pollution in the relationship between non-accidental mortality and residential surrounding greenness (Supplementary Table S4). We detected opposite signs between direct and indirect (i.e. mediation) effects (results not shown), which were likely caused by multicollinearity between exposure and mediator given their high negative correlations (−0.68, −0.77) (Supplementary Table S2). We, therefore, suspect inconsistent mediation and considered the interpretation of these negative proportions not valid. Differential findings of our mediation analyses between non-accidental and respiratory mortality might have been influenced partly by (very small) differences in exposures (in both green space metrics and ambient air pollutants) between individuals dying from non-accidental or respiratory mortality and their respective 'control' groups in the regression models.

In general, existing reviews report that evidence regarding effect modification by age and sex in the association between exposure to residential green space and health is still inconclusive (James et al., 2015; Markevych et al., 2017; Nieuwenhuijsen et al., 2017). We observed stronger beneficial associations in younger individuals using both objective green space indicators, which is in line with two Canadian (Villeneuve et al., 2012; Crouse et al., 2017), and two European studies (Vienneau et al., 2017; Orioli et al., 2019). We generally found stronger associations for men compared to women, which is consistent with the study of Crouse et al. (2017), but different from the studies of Vienneau et al. (2017) and Orioli et al. (2019) that observed stronger beneficial associations in women. We speculate that differential levels of physical activity mainly driven by variations in daily time use and activity patterns during the life course might partly explain these differences, although this could not be assessed with our existing dataset.

We found indications for effect modification by education level, suggesting stronger inverse associations in individuals with higher levels of education, which has also been reported by the majority of previous similar longitudinal studies (Villeneuve et al., 2012; Crouse et al., 2017; Vienneau et al., 2017; Orioli et al., 2019). In our study, we observed higher prevalences of residential exposure to green space and lower levels of ambient air pollutants among higher educated compared to lower educated individuals. People with higher education generally have a better health status and higher survival rate compared to people in less affluent groups (Wilkinson and Marmot, 2003). Different mechanisms have been put forward to explain this social gradient in health, such as worse health-related behaviors among individuals with a lower SEP (e.g. lower levels of physical activity, poor diet, more tobacco and alcohol consumption), or lack of sufficient resources (e.g. health care access, housing conditions, social contact). The aforementioned mechanisms could also reflect the availability, quality, access and use of residential green space and potentially explain the observed heterogeneous patterns by education level. Although residential green space appeared to be mainly beneficial among the higher educated, we may presume that it would also be of benefit to the lower educated, if other, more potent risk factors affecting health were alleviated.

With regards to between-area variability, our stratified results reflect a well-documented geographic pattern in mortality differences in Belgium. Several previous studies have mapped out a marked north–south divide in the country, with generally increasing mortality rates towards the south of the country (Van Hemelrijck et al., 2016; Trabelsi et al., 2019). Although we were able to adjust for some relevant key confounders, we acknowledge that important unobserved confounding may still have been present. Aside from historical context, potential explanations for these between-area differences have been put forward, such as variations in diagnostic and therapeutic practices, cultural habits, exposure to environmental factors, etc. (Van Hemelrijck et al., 2016; Trabelsi et al., 2019). Future research should shed further light upon the complex interplay of these potential pathways in area-specific settings.

4.2. *Strengths and limitations*

A key strength of our study is the large, representative sample size (n = 2,185,170) in combination with the long mortality follow-up period available. The aforementioned provided substantial statistical power to assess the association between residential green space and different mortality outcomes. Additionally, the exposure assessment was done at the level of the residential address and was based on data sources with high spatial resolution. The implementation of various green space metrics, both objective and subjective, allowed us to consider different features of urban green space. Last, we were able to explore both confounding and mediation by several ambient air pollutants (i.e. $PM_{2.5}$, PM_{10}, NO_2 and BC). These are important environmental risk factors that are prominent in urban areas and potentially influence the relation between residential green space and the various mortality outcomes under study.

This study has a number of important limitations. No information on individual health-related behaviors was available such as physical activity, and tobacco and alcohol consumption, which is one of the main limitations since these are important risk factors for cardiorespiratory disease. Indirect adjustment for these risk factors could not be conducted for our study due to incompatibility of data, as is often the case with administrative cohort studies. Similar studies that were able to perform additional adjustment, mainly for smoking status (James et al., 2016; Villeneuve et al., 2012; Crouse et al., 2017; Orioli et al., 2019; Klompmaker et al., 2020), alcohol consumption (Klompmaker et al., 2020), BMI and physical activity (James et al., 2016; Crouse et al., 2017; Klompmaker et al., 2020), concluded that findings were robust and did not report substantial changes in the associations. Overall, additional adjustment only slightly attenuated the results, although these must be interpreted with caution because of heterogeneity in adjustment techniques, study design and exposure assessment. Therefore, we acknowledge that our inability to assess the influence of these key indicators leads to uncertainty regarding the direction to which our estimates are potentially biased. Another limitation of our study is that we only had time-fixed exposure measures available, thus potentially not fully representing the entire follow-up period. We assumed that although the amount of available green space may vary across time, its relative spatial distribution remains relatively stable, although we were unable to evaluate potential changes in exposure with our current dataset for which measures were only available for one year. Furthermore, individual residential addresses were only available at one time point (i.e. census 2001), and exact information on residential history could not be obtained. However, we could identify a subset of nonmovers during the follow-up period of our study and this was included into sensitivity analyses. In addition, we did not have information on green space exposure in locations other than the residence. Consequently, potential exposure misclassification could arise by not taking into account individual spatiotemporal patterns through which actual personal exposure to the outdoor environment could differ and, hence, influence our estimates (Dons et al., 2011; James et al., 2015). Furthermore, mortality associations could only be evaluated with measures of the presence of residential green space, since additional metrics on quality, access and use of green space were not available. Nevertheless, the latter aspects were possibly captured by our index of "subjectively perceived greenness" and this did not invalidate the findings obtained with the objective parameters.

5. Conclusion

Long-term exposure to residential green space was associated with the risks of lower overall (non-accidental) mortality and of respiratory mortality risk among more than 2 million adults residing in the five largest urban areas in Belgium. Evidence for cardiovascular causes of mortality was mixed and varied by green space metric, where both lower and higher mortality risks were observed. Our findings highlight the need and importance for policymakers from both public health and urban planning domains to consider the integration of more residential green space into the urban living environment, with special attention to the incorporate of features that promote physical activity.

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Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.106365.

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