Environmental Research 270 (2025) 120938

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Long-term exposure to air pollution and greenness in association with respiratory emergency room visits and hospitalizations: The Life-GAP project

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ARTICLE INFO

Keywords:
Air pollution
Emergency room visits
Green space
Hay fever
Hospital admissions
Longitudinal study

ABSTRACT

Background: Air pollution has been linked to respiratory diseases, while the effects of greenness remain inconclusive.
Objective: We investigated the associations between exposure to particulate matter ($PM_{2.5}$ and PM_{10}), black carbon (BC), nitrogen dioxide (NO_2), ozone (O_3), and greenness (normalized difference vegetation index, NDVI) with respiratory emergency room visits and hospitalizations across seven Northern European centers in the European Community Respiratory Health Survey (ECRHS) study.
Methods: We used modified mixed-effects Poisson regression to analyze associations of exposure in 1990, 2000 and mean exposure 1990–2000 with respiratory outcomes recorded duing ECRHS phases II and III. We assessed interactions of air pollution and greenness, and of atopic status (defined by nasal allergies and hay fever status) and greenness, on these outcomes.
Results: The analysis included 1675 participants, resulting in 119 emergency visits and 48 hospitalizations. Increased $PM_{2.5}$ by 5 μg/m^3 was associated with higher relative risk (RR) of emergency visits (1990: RR 1.16, 95% CI: 1.00–1.35; 2000: RR 1.24, 95% CI: 0.98–1.57; 1990–2000: RR 1.17, 95% CI: 0.97–1.41) and hospitalizations (1990: RR 1.42, 95% CI: 1.00–2.01; 2000: RR 2.20, 95% CI: 1.43–3.38; 1990–2000: RR 1.44, 95% CI: 1.04–2.00). Similar trends were observed for PM_{10}, BC, and NO_2, with only PM_{10} showing significant

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https://doi.org/10.1016/j.envres.2025.120938
Received 21 October 2024; Received in revised form 6 January 2025; Accepted 22 January 2025
Available online 23 January 2025
0013-9351/

associations with hospitalizations across all periods. No associations were found for O_3. Greenness exposure was linked to more emergency visits in 2000 but to fewer hospitalizations in 1990. Significant interactions were observed between greenness and atopic status for emergency visits, and between NDVI with O_3 and BC for some time windows.

Conclusion: Long-term exposure to particulate matter was associated with increased emergency room visits and hospitalizations. Significant associations were observed for BC and NO_2 with hospitalizations. No link was found with O_3. Greenness indicated a lower risk of hospitalizations, but increased risks for emergency visits for those with atopic status.

1. Introduction

The global burden of respiratory diseases continues to pose a significant public health challenge, with air pollution identified as a major risk factor (Momtazmanesh et al., 2023). Air pollution comprises various pollutants such as particulate matter (PM), nitrogen dioxide (NO_2) and ozone (O_3), each with distinct sources and health effects (WHO, 2021). Epidemiological studies have consistently demonstrated the adverse effects of both short-term and long-term exposure to air pollutants on respiratory health, including reduced lung function, the onset of respiratory diseases, and acute exacerbations of chronic conditions such as asthma and chronic obstructive pulmonary disease (COPD) (Bălă et al., 2021; Kim et al., 2018; Rice et al., 2013). In addition, air pollution is linked to a marked increase in the utilization of healthcare services. The immediate impacts, particularly during peaks in air pollution, frequently result in emergency room visits and a rise in respiratory mortality (Meng et al., 2021; Yee et al., 2021; Zhang et al., 2020). However, while the short-term effects are well-documented due to their direct and observable clinical impacts, studies exploring the long-term effects on emergency room visits, especially in the adult population, are comparatively sparse. Epidemiological evidence indicates that long-term exposure to air pollution may influence hospital admissions for various conditions, though findings are inconsistent and vary across different regions and studies (Danesh Yazdi et al., 2021; Halonen et al., 2016; Panunzi et al., 2023; Salimi et al., 2018a)

The role of greenness—defined as degree of vegetation over an area shrubs—has attracted increasing interest in the field of public health research. Greenness can be measured using various metrics such as normalized difference vegetation index (NDVI), tree canopy cover, landcover/land-use maps, and percentage of green space (Vilcins et al., 2024). Generally, greenness is associated with a range of health benefits, including improved air quality, reduced heat exposure, and increased levels of physical activity (Markevych et al., 2017). However, a higher availability of green spaces also entails a higher exposure to pollen and other allergens, which can exacerbate respiratory conditions such as asthma and allergic rhinitis. The complex interplay between air pollution and greenness, particularly in the context of long-term exposure and its effects on respiratory emergency room visits and hospitalizations, remains unclear.

This study hypothesized that long-term exposure to air pollution is associated with an increased risk for respiratory emergency room visits and hospitalizations, while exposure to greenness has a protective effect, reducing these healthcare utilizations. Using data from the Northern European centers in the European Community Respiratory Health Survey (ECRHS), we aimed to investigate the associations between long-term exposure to air pollution and greenness with respiratory emergency room visits and hospitalizations.

2. Methods

2.1. Study design and population

The ECRHS (https://www.ecrhs.org/) is a large, multi-center cohort study that aims to understand the variations in respiratory health and allergies across different countries (Burney et al., 1994; Janson et al., 2001). Initially, in its first phase (1990–1994), adults born 1945-73 were randomly selected from 56 centers across 25 countries. All selected individuals were asked to fill in a postal questionnaire on smoking, respiratory diseases, and symptoms (ECRHS I stage 1). A 20% random subset of the participants were invited to also attend a more extensive on-site examination with lung function tests and clinical interviews (ECRHS I stage 2). Moreover, individuals who reported experiencing respiratory symptoms, asthma attacks, or were using asthma medication in ECRHS I stage 1 ("symptomatic sample") were also invited for the ECRHS I stage 2 clinical assessment (Burney et al., 1994). The participants from ECRHS I stage 2 were then followed up in 1999–2002 (ECRHS II) and in 2011–2014 (ECRHS III) (Fig. 1).

In this study, we focus on participants enrolled in seven Northern European centers in the ECRHS, where data on exposure to air pollution and greenness are available from the Respiratory Health in Northern Europe (RHINE) study. RHINE (https://rhine.w.uib.no/) is a postal follow-up study of the ECRHS I stage 1 participants from seven centers: Reykjavik (Iceland); Bergen (Norway); Aarhus (Denmark); Umea, Uppsala, and Gothenburg (Sweden); and Tartu (Estonia) (Fig. 1). Except for Tartu, information about addresses was obtained through register linkage for the years 1990, 2000, and 2010. In the Tartu center, addresses were self-reported through the questionnaire.

The study outcome is the cumulative incidence of respiratory emergency room visits and hospitalizations between ECRHS II and III. Therefore, we considered participants in ECRHS II as our baseline population and followed them until ECRHS III. Exposure assessment included baseline exposure in ECRHS II (2000), retrospective exposure in 1990, and annual mean exposure during 1990–2000. This longitudinal analysis includes 1675 participants with complete data on exposures, covariates, and outcomes. Fig. 2 shows the participant selection process.

2.2. Exposure periods

We geocoded the residential addresses of participants from the National Population Registries in each study center to assess retrospective exposure for ECRHS I (addresses retrieved in 1990) and to establish baseline exposure for ECRHS II (addresses retrieved in 2000). Outcomes were retrieved from the ECRHS III follow-up study. To calculate annual mean exposures for the period between ECRHS I and II (1990–2000), we assigned exposure levels for each individual year from 1990 to 2000 to calculate an 11-year average exposure, taking into account moving history from self-reported answer to the question "Year of moving into current home?" Details of the exposure assignment are described elsewhere (Xu et al., 2023).

2.3. Air pollution exposure assessment

Except for Tartu, the air pollution assessment was based on a combination of the Danish Eulerian Hemispheric Model (DEHM) (Brandt et al., 2012) and the Urban Background Model (UBM) (Brandt et al., 2003), going to a spatial resolution of 1 km × 1 km. This study focused on a range of pollutants, including $PM_{2.5}$ and PM_{10} (with diameter $\leq$2.5 μm (μm) and $\leq$10 μm, respectively), black carbon (BC), NO_2, and ground-level O_3. The derivation of model outputs for this assessment was based on the comprehensive modeling provided by the Nordic-WelfAir project (Frohn et al., 2022; Paunu et al., 2021, 2024). The DEHM/UBM model's performance was evaluated during the Nordic-WelfAir project. This thorough evaluation confirmed the model's generally robust performance, albeit with some variations observed across different pollutants and among the countries studied (Frohn et al., 2022). Specifically, the correlation coefficients between model results and measurements for $PM_{2.5}$ were 0.43 in Denmark, 0.56 in Norway, and 0.96 in Sweden. For NO_2, the coefficients were 0.83 in Denmark, 0.72 in Norway, and 0.76 in Sweden. For O_3, the coefficients recorded were 0.70 in Denmark, 0.60 in Norway, and 0.73 in Sweden (Frohn et al., 2022). These variations reflect differences in the quality of emission inventories, meteorological inputs, and country-specific environmental conditions, such as the use of road salt in Denmark, which affected model performance for $PM_{2.5}$ during specific winters (Frohn et al., 2022).

In Tartu, data regarding BC and O_3 were not available. Annual mean concentrations of $PM_{2.5}$, PM_{10} and NO_2 in Tartu were estimated using the Eulerian air quality dispersion model. This model operates within the Airviro Air Quality Management System and features a spatial resolution of 1 km × 1 km. Airviro is a web-based platform extensively used for air quality data management. It integrates emissions data from various sources, including point (e.g., industrial facilities), road, and area sources, stored in the Emission Database (EDB). Meteorological inputs, such as wind speed, direction, temperature, and atmospheric stability, along with emission data from EDB, are incorporated into a Gaussian dispersion model to simulate pollutant dispersion and transformation (AirViro. SMHI Airviro User's Reference, 2011).

2.4. *Greenness exposure assessment*

Greenness exposure was assessed using the NDVI, derived from the cloud-free satellite images captured by the Landsat 4–5 Thematic Mapper (TM). NDVI values range from −1 to 1, with higher positive values indicating denser vegetation. NDVI values below zero, typically representing water bodies, were recoded to zero to focus on vegetated areas. For this study, satellite images captured during the most vegetation-rich months close to the time of each ECRHS survey were used. The analysis included data corresponding to the ECRHS I and ECRHS II phases for each center. Details of the Landsat 4–5 TM satellite images used for NDVI calculations are provided in Supplementary Table S1. Residential greenness was defined as the mean NDVI value, calculated following World Health Organization (WHO) recommendations (WHO, 2016), within 300-m circular buffer zones around each participant's home address.

2.5. *Outcome definition*

Data on respiratory emergency room visits and hospitalizations were obtained from the ECRHS III clinical questionnaire and referred to the time elapsed between ECRHS II and III. Self-reported respiratory emergency room visits were defined by a positive response to the question, "Since the last survey, have you visited a hospital casualty department or emergency room (for any reason, apart from accidents and injuries)?" coupled with an affirmative answer to the follow-up question, "Was this due at least once to breathing problems?" Self-reported respiratory hospitalizations were defined by a positive response to "Since the last survey, have you spent a night in hospital (for any reason, apart from accidents and injures)?" followed by an affirmative answer to "Was this due at least once to breathing problems?" For each outcome, we used a binary classification: no respiratory emergency room visits versus one or more visits, and no hospitalizations versus one or more hospitalizations.

2.6. *Covariates*

Covariates were assessed at ECRHS II and selected based on a review of existing literature (Danesh Yazdi et al., 2022; Klompmaker et al., 2022). These covariates include age in years, sex, body mass index (BMI, measured in kg/m^2), education level as a proxy for socioeconomic status (categorized as high or low, with "low" defined as having completed full-time education before age 19 years, indicating these individuals likely did not pursue education beyond secondary school), smoking status (never smoker, former smoker, or current smoker), and sample source (random or symptomatic sample).

2.7. *Statistical analysis*

Data analyses were performed using Stata statistical software (version 18.0, Stata Corporation, College Station, Texas, USA). Descriptive statistics were used to analyze the general characteristics of participants. To compare characteristics across groups, we employed the Mann-Whitney *U* test for continuous variables and the Chi-square test for categorical variables. Spearman correlation coefficients (ρ) were used to estimate the correlation between air pollutants and greenness variables measured in 1990, 2000 and mean exposure in 1990–2000 across different study centers. We used mixed-effects Poisson regression with robust standard errors, calculated using the sandwich estimation

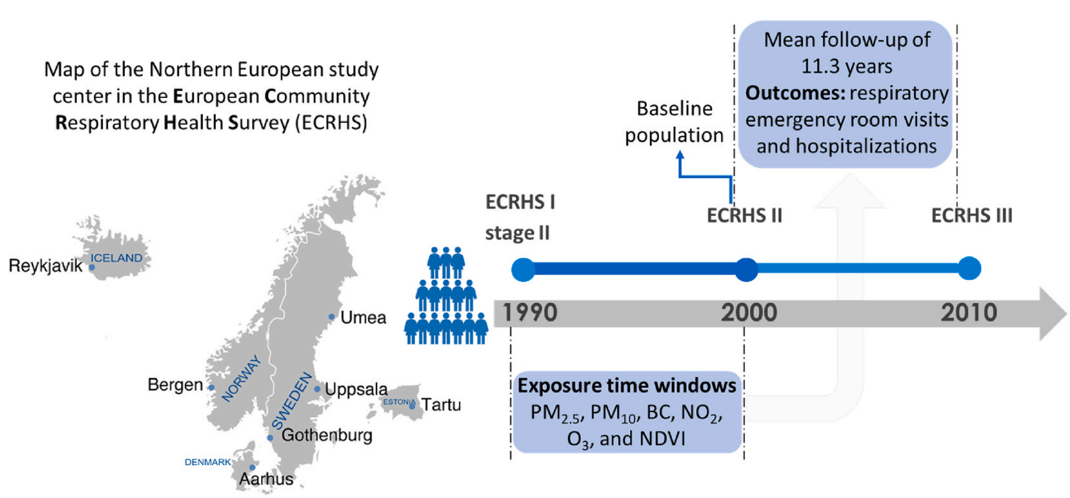

Fig. 1. Overview of study design and location.
Abbreviation: $PM_{2.5}$ = particulate matter with an aerodynamic diameter less than 2.5 μm (μm); PM_{10} = particulate matter with an aerodynamic diameter less than 10 μm (μm); BC = black carbon; NO_2 = nitrogen dioxide; O_3 = ozone; NDVI = normalized difference vegetation index.

method, to examine the association between air pollution and greenness exposure in the years 1990, 2000 and the mean exposure during 1990–2000, with the cumulative incidence of respiratory emergency room visit and hospitalizations between ECRHS II and ECRHS III. The robust standard errors were applied based on the modified Poisson regression approach proposed by Zou (2004), ensuring consistent and reliable estimation of relative risks for binary outcomes. Details of the specific Stata command used are provided in the **Supplementary Materials**. Associations were estimated using progressively adjusted models: Model 1, a single-exposure model, adjusted for age at baseline, sex, and sample source (random or symptomatic), with study center included as a random effect to account for regional heterogeneity across centers. Model 2, our main analysis, expanded upon Model 1 by further adjusting for education level, BMI, and smoking status at baseline. In addition, we explored the interaction between air pollution and NDVI on respiratory emergency room visits and hospitalizations by including the interaction term (individual air pollutant × NDVI tertiles) within the same exposure time windows in Model 2. Estimates of air pollution associations across different NDVI tertiles were derived using linear combinations of regression coefficients.

Several sensitivity analyses were conducted to test the robustness of our findings. First, we used a two-exposure model that included mutual adjustments for individual air pollutants and the NDVI within the same exposure windows, alongside the covariates from Model 2. Second, given that the Tartu center used a different air pollution assessment model, we performed an additional analysis excluding participants from Tartu to evaluate the potential influence of this variation on our results. Third, to further assess the potential impact of selection bias, we conducted a sensitivity analysis by excluding all symptomatic individuals. Moreover, considering the potential for greenness to introduce pollen and other aeroallergens that may affect respiratory health, we specifically analyzed the interaction between NDVI, assessed at various time windows, and atopic status—defined in the ECRHS II questionnaire as "Do you have any nasal allergies including hay fever?"—in association with respiratory emergency room visits and hospitalizations. Estimates of the associations between greenness and these respiratory outcomes by atopic status were derived using linear combinations of regression coefficients.

To facilitate a direct comparison of effect sizes across different exposure time points, exposure increments were standardized as follows: 5 μg/m^3 for $PM_{2.5}$, 10 μg/m^3 for PM_{10}, NO_2, and O_3, 0.4 μg/m^3 for BC, and 0.1 unit for NDVI. These increments were chosen based on previous studies and align with the typical range of variations observed in the literature (Liu et al., 2021; Strak et al., 2021; Xu et al., 2023, 2024). Associations were reported as relative risks (RRs) with 95% confidence intervals per standardized increments, representing the ratio of cumulative incidence proportions over the constant follow-up period between ECRHS II and ECRHS III for all participants.

3. Results

The analysis included a total of 1675 participants, of whom 1425 came from the random sample and 250 from the symptomatic sample. The subjects excluded from the analyses tended to be younger, less educated, and more likely to be current smokers at baseline compared to those included (p-values <0.05) (Supplementary Table S2). Supplementary Table S3 shows the center-specific sample source. The average age of participants was 41.7 years at baseline (Table 1). Females represented 54% of the study population. Over 60% of the participants had attained a higher education level and about half were never smokers (Table 1).

Annual mean air pollution levels from 1990 to 2000 were 8.39 μg/m^3 for $PM_{2.5}$, 15.27 μg/m^3 for PM_{10}, 0.40 μg/m^3 for BC, 14.05 μg/m^3 for NO_2 and 56.27 μg/m^3 for O_3 (Table 1). The levels of $PM_{2.5}$, PM_{10}, BC, and NO_2 in 1990 were, on average, higher than those recorded in 2000. Individuals hospitalized for respiratory conditions exhibited higher levels of PM_{10} in both 1990 ($p = 0.033$) and 2000 ($p = 0.038$) compared to those not hospitalized. Greenness exposure levels were higher in 2000 compared to 1990, and the average NDVI value during 1990–2000 was 0.31. Except for O_3, correlations among air pollutants were predominantly positive and notably strong within each study period (Supplementary Fig. S1). For example, correlation coefficients for the mean exposure period from 1990 to 2000 ranged from 0.69 (between PM_{10} and BC) to 0.93 (between $PM_{2.5}$ and BC). Conversely, O_3 showed moderate to high negative correlations with the other pollutants across all exposure time points. NDVI displayed varied correlations with pollutants across different exposure periods. Specifically, NDVI was inversely correlated with PM, BC, and NO_2, but positively correlated with O_3 during the 1990 and mean 1990–2000 periods. For the 2000 exposure period, NDVI exhibited very weak correlations with air pollutants, with correlation coefficients ranging from −0.16 (between NDVI and NO_2) to 0.07 (between NDVI and BC). Supplementary Figures S2 to Figure S8 present the center-specific correlation coefficients, and show notable variations in the correlations across

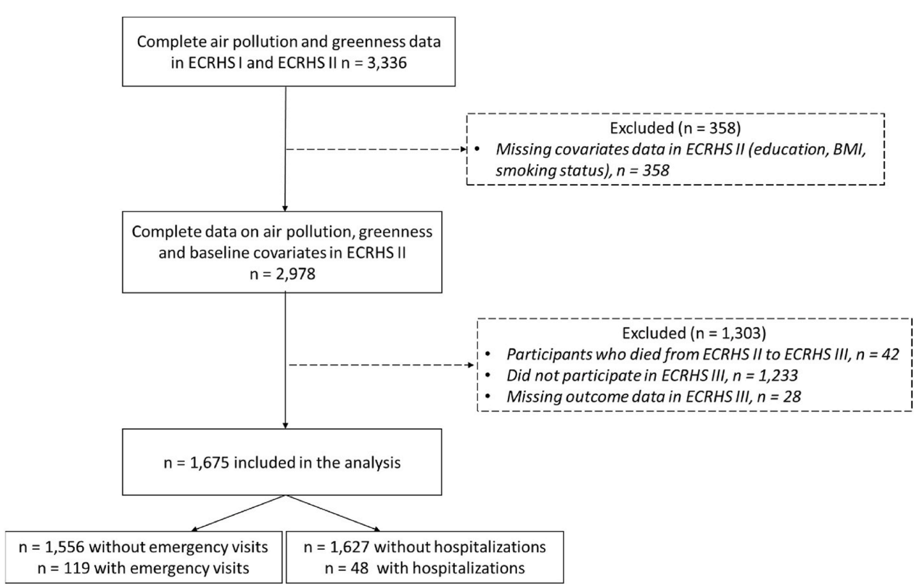

Fig. 2. Flowchart of the study population.

Table 1
Baseline characteristics of participants (ECRHS II), and exposure levels to air pollution and greenness across different time windows.

Characteristic		Total (n = 1675)	Without emergency room visits (n = 1556)	Emergency room visit (n = 119)	*p* value[a]	Without hospitalizations (n = 1627)	Hospitalizations (n = 48)	*p* value[a]
Age (years), mean ± SD		41.7 ± 7.1	41.7 ± 7.1	41.8 ± 7.1	0.925	41.7 ± 7.1	42.1 ± 7.4	0.650
Female, n (%)		907 (54.1)	830 (53.3)	77 (64.7)	0.016	877 (53.9)	30 (62.5)	0.239
Body mass index (kg/m^2), mean ± SD		24.9 ± 4.0	24.8 ± 3.9	25.4 ± 4.5	0.150	24.8 ± 3.9	26.0 ± 5.4	0.242
Education, n (%)								0.231
Low		590 (35.2)	547 (35.2)	43 (36.1)	0.829	577 (35.5)	13 (27.1)	
High		1085 (64.8)	1009 (64.9)	76 (63.9)		1050 (64.5)	35 (72.9)	
Smoking status, n (%)								
Never		813 (48.5)	758 (48.7)	55 (46.2)	0.682	785 (48.3)	28 (58.3)	0.379
Former		453 (27.0)	422 (27.1)	31 (26.1)		443 (27.3)	10 (20.8)	
Current		409 (24.4)	376 (24.2)	33 (27.7)		399 (24.5)	10 (20.8)	
Exposure in 1990	$PM_{2.5}$, μg/m^3, mean ± SD	9.13 ± 4.51	9.09 ± 4.46	9.64 ± 5.02	0.568	9.09 ± 4.50	10.34 ± 4.74	0.059
	PM_{10}, μg/m^3, mean ± SD	16.35 ± 7.39	16.28 ± 7.29	17.19 ± 8.52	0.774	16.28 ± 7.37	18.63 ± 7.65	0.033
	BC[b], μg/m^3, mean ± SD	0.41 ± 0.26	0.41 ± 0.26	0.43 ± 0.26	0.595	0.41 ± 0.26	0.48 ± 0.27	0.082
	NO_2, μg/m^3, mean ± SD	14.63 ± 8.05	14.56 ± 7.97	15.62 ± 9.00	0.376	14.57 ± 8.03	16.72 ± 8.31	0.078
	O_3[b], μg/m^3, mean ± SD	55.82 ± 6.54	55.86 ± 6.51	55.32 ± 6.94	0.510	55.84 ± 6.53	55.04 ± 6.90	0.541
	NDVI, mean ± SD	0.30 ± 0.14	0.30 ± 0.14	0.31 ± 0.14	0.507	0.30 ± 0.14	0.26 ± 0.17	0.353
Exposure in 2000	$PM_{2.5}$, μg/m^3, mean ± SD	6.80 ± 2.80	6.79 ± 2.78	6.91 ± 2.98	0.790	6.77 ± 2.78	7.77 ± 3.20	0.047
	PM_{10}, μg/m^3, mean ± SD	13.05 ± 4.63	13.06 ± 4.59	12.94 ± 5.18	0.640	13.00 ± 4.61	14.71 ± 5.15	0.038
	BC[b], μg/m^3, mean ± SD	0.38 ± 0.24	0.38 ± 0.25	0.38 ± 0.23	0.719	0.38 ± 0.22	0.42 ± 0.24	0.207
	NO_2, μg/m^3, mean ± SD	13.23 ± 7.49	13.22 ± 7.47	13.35 ± 7.76	0.961	13.20 ± 7.51	14.05 ± 6.84	0.336
	O_3[b], μg/m^3, mean ± SD	56.84 ± 6.83	56.84 ± 6.87	56.84 ± 6.37	0.754	56.83 ± 6.82	57.28 ± 7.12	0.611
	NDVI, mean ± SD	0.33 ± 0.14	0.33 ± 0.14	0.35 ± 0.13	0.084	0.33 ± 0.14	0.31 ± 0.15	0.655
Mean exposure in 1990–2000	$PM_{2.5}$, μg/m^3, mean ± SD	8.39 ± 3.89	8.36 ± 3.85	8.75 ± 4.27	0.547	8.36 ± 3.88	9.36 ± 3.97	0.085
	PM_{10}, μg/m^3, mean ± SD	15.27 ± 6.30	15.23 ± 6.22	15.78 ± 7.26	0.852	15.22 ± 6.29	17.13 ± 6.42	0.034
	BC[b], μg/m^3, mean ± SD	0.40 ± 0.25	0.40 ± 0.25	0.41 ± 0.24	0.728	0.40 ± 0.25	0.45 ± 0.24	0.170
	NO_2, μg/m^3, mean ± SD	14.05 ± 7.46	14.00 ± 7.40	14.68 ± 8.12	0.524	14.01 ± 7.47	15.38 ± 6.77	0.150
	O_3[b], μg/m^3, mean ± SD	56.27 ± 6.25	56.29 ± 6.25	56.05 ± 6.21	0.682	56.27 ± 6.25	56.24 ± 6.07	0.987
	NDVI, mean ± SD	0.31 ± 0.13	0.31 ± 0.13	0.33 ± 0.12	0.085	0.31 ± 0.13	0.28 ± 0.14	0.312

Abbreviation: $PM_{2.5}$ = particulate matter with an aerodynamic diameter less than 2.5 μm (μm); PM_{10} = particulate matter with an aerodynamic diameter less than 10 μm (μm); BC = black carbon; NO_2 = nitrogen dioxide; O_3 = ozone; NDVI = normalized difference vegetation index.

[a] Mann-Whitney *U* test for continuous variables and Chi-squared test for categorical variables.

[b] Data on BC and O_3 were unavailable at the Tartu center. A total of 1535 participants had data available for BC and O_3. Among these participants, 1419 did not have respiratory emergency room visits, while 116 had such visits. Additionally, 1489 participants did not experience respiratory hospitalizations, whereas 46 participants were hospitalized for respiratory conditions.

Table 2
Relative risk (95% CI) of respiratory emergency room visits and hospitalizations associated with air pollution and greenness exposure across various time windows (n = 1675) in Model 1.

Exposure	Increments	Exposure in 1990		Exposure in 2000		Mean exposure in 1990–2000	
		Respiratory emergency room visit	Respiratory hospitalizations	Respiratory emergency room visit	Respiratory hospitalizations	Respiratory emergency room visit	Respiratory hospitalizations
$PM_{2.5}$	5 $\mu g/m^3$	1.15 (1.00–1.34)	1.38 (0.97–1.96)	1.21 (0.96–1.53)	2.04 (1.29–3.24)	1.16 (0.97–1.39)	1.39 (1.00–1.94)
PM_{10}	10 $\mu g/m^3$	1.23 (1.07–1.41)	1.51 (0.98–2.33)	1.14 (0.78–1.67)	2.55 (1.63–4.01)	1.23 (0.94–1.62)	1.58 (1.06–2.37)
BC[a]	0.4 $\mu g/m^3$	1.13 (0.90–1.42)	1.49 (1.04–2.14)	1.07 (0.80–1.45)	1.30 (0.89–1.89)	1.11 (0.84–1.45)	1.38 (0.96–1.97)
NO_2	10 $\mu g/m^3$	1.20 (0.95–1.52)	1.39 (1.02–1.87)	1.02 (0.72–1.45)	1.11 (0.58–2.14)	1.17 (0.90–1.52)	1.28 (0.89–1.84)
O_3[a]	10 $\mu g/m^3$	0.94 (0.68–1.29)	0.84 (0.54–1.30)	1.03 (0.72–1.46)	1.36 (0.78–2.37)	0.99 (0.69–1.41)	1.08 (0.67–1.74)
NDVI	0.1 unit	1.00 (0.85–1.19)	0.80 (0.64–0.99)	1.14 (1.03–1.26)	0.91 (0.74–1.13)	1.13 (0.98–1.30)	0.84 (0.69–1.01)

Abbreviation: $PM_{2.5}$ = particulate matter with an aerodynamic diameter less than 2.5 μm (μm); PM_{10} = particulate matter with an aerodynamic diameter less than 10 μm (μm); BC = black carbon; NO_2 = nitrogen dioxide; O_3 = ozone; NDVI = normalized difference vegetation index.
Model 1 adjusted for sex, age, and sample source, with study center included as a random effect.
[a] Data on BC and O_3 were unavailable at the Tartu center. A total of 1535 participants had data available for BC and O_3. Among these participants, 1419 did not have respiratory emergency room visits, while 116 had such visits. Additionally, 1489 participants did not experience respiratory hospitalizations, whereas 46 participants were hospitalized for respiratory conditions.

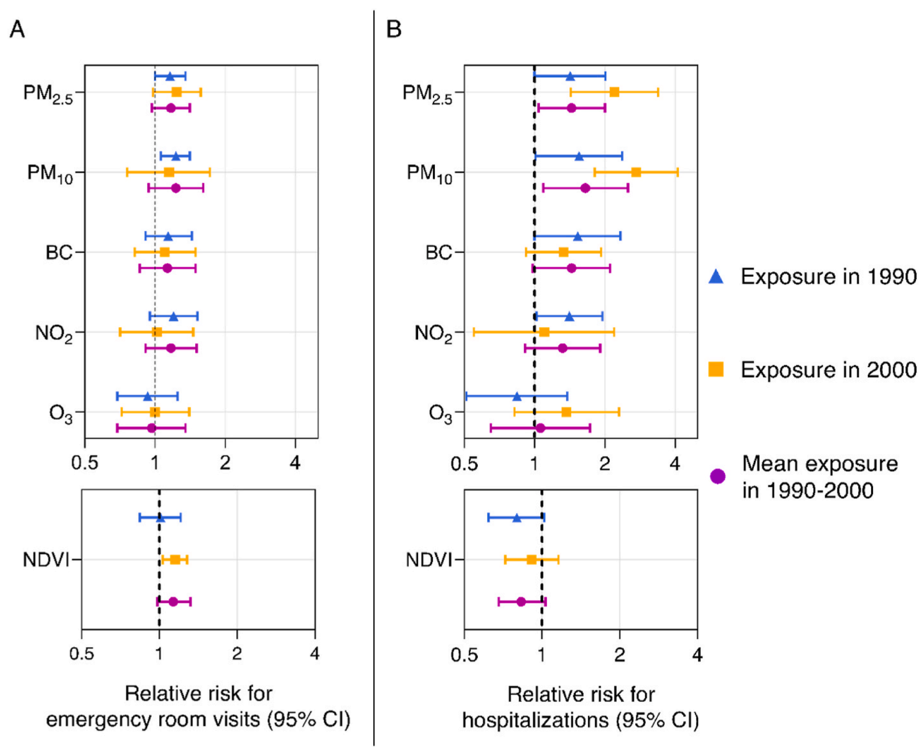

Fig. 3. Relative risk and 95% confidence intervals (CI) for the associations between air pollution and greenness with the risk of respiratory emergency room visits (Panel A) and hospitalizations (Panel B) across various exposure time windows in Model 2.
Abbreviation: $PM_{2.5}$ = particulate matter with an aerodynamic diameter less than 2.5 μm (μm); PM_{10} = particulate matter with an aerodynamic diameter less than 10 μm (μm); BC = black carbon; NO_2 = nitrogen dioxide; O_3 = ozone; NDVI = normalized difference vegetation index. Model 2 adjusted for sex, age, sample source, education, body mass index, and smoking status, with study center included as a random effect.
The increment of the exposure is as follows: 5 $\mu g/m^3$ for $PM_{2.5}$, 10 $\mu g/m^3$ for PM_{10}, NO_2 and O_3, 0.4 $\mu g/m^3$ for BC, and 0.1 unit for NDVI. The axis is on a log-2 scale.

different study centers.

Between the ECRHS II and III, 119 participants reported respiratory emergency room visits (cumulative incidence of 7.1%), and 48 reported respiratory hospitalizations (cumulative incidence of 2.9%), over a mean follow-up of 11.3 years. Center-specific cumulative incidences are presented in Supplementary Table S4: Gothenburg had the highest cumulative incidence of respiratory emergency room visits at 11.1%, while Tartu had the lowest at 2.1%. Aarhus recorded the highest cumulative incidence of respiratory hospitalizations at 5.7%, and Umea had the lowest at 1.2%.

Table 2 presents the associations of air pollutants and greenness exposure with respiratory emergency room visits and hospitalizations using the single-exposure Model 1, while Fig. 3 illustrates these associations for Model 2. A slight difference in the estimates was observed after adjusting for individual characteristics between the two models. Overall, our findings indicate a relatively consistent association between long-term exposure to $PM_{2.5}$ and PM_{10} and higher cumulative incidence of respiratory emergency room visits and hospitalizations. Notably, the risk for hospitalizations was consistently higher than for emergency room visits within the same exposure windows (Fig. 3, panel A *vs.* B). Specifically, in 1990, each 5 $\mu g/m^3$ increase in $PM_{2.5}$ was linked to a 42% higher risk of hospitalizations (RR = 1.42, 95% CI: 1.00–2.01), compared to a 16% increase for emergency room visits (RR = 1.16, 95% CI: 1.00–1.35). In 2000, each 5 $\mu g/m^3$ increase in $PM_{2.5}$ was associated

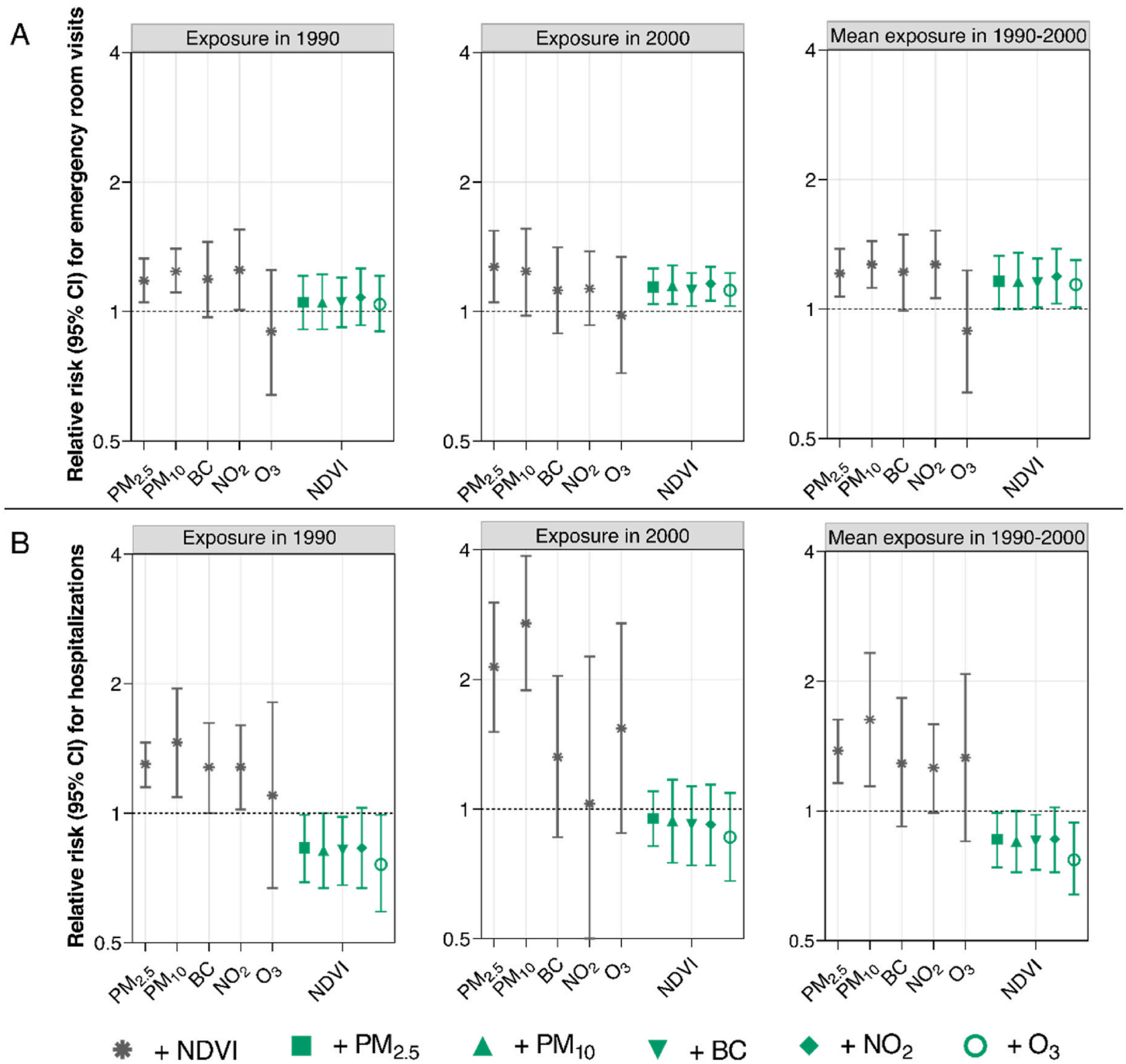

Fig. 4. Relative risk and 95% confidence intervals (CI)) for the associations of air pollution and greenness with respiratory emergency room visits and hospitalizations in a **two-exposure model** across different exposure time windows.
Abbreviation: $PM_{2.5}$ = particulate matter with an aerodynamic diameter less than 2.5 μm (μm); PM_{10} = particulate matter with an aerodynamic diameter less than 10 μm (μm); BC = black carbon; NO_2 = nitrogen dioxide; O_3 = ozone; NDVI = normalized difference vegetation index. Two-exposure models included each pollutant + NDVI within the same exposure time windows and were adjusted for sex, age, sample source, education, body mass index, and smoking status, with the study center included as a random effect.
The increment of the exposure is as follows: 5 μg/m3 for $PM_{2.5}$, 10 μg/m^3 for PM_{10}, NO_2 and O_3, 0.4 μg/m^3 for BC, and 0.1 unit for NDVI.

Table 3
P-values for interaction between NDVI across exposure windows (1990, 2000, and mean 1990–2000) and atopic status; relative risks (95% CI) for respiratory emergency room visits and hospitalizations associated with NDVI exposure, analyzed by atopic status at baseline, derived from linear combinations of regression estimators.

Interaction	Exposure time windows	RR (95% CI) for emergency room visits		P value for interaction	RR (95% CI) for hospitalizations		P value for interaction
		Non-atopic (n = 1178)	Atopic (n = 497)		Non-atopic (n = 1178)	Atopic (n = 497)	
NDVI × atopic status	1990	0.87 (0.76–0.99)	1.26 (0.94–1.68)	0.014	0.79 (0.63–0.99)	0.82 (0.43–1.54)	0.923
NDVI × atopic status	2000	1.07 (0.97–1.18)	1.28 (1.18–1.39)	<0.001	0.96 (0.75–1.25)	0.79 (0.54–1.14)	0.202
NDVI × atopic status	1990–2010	0.99 (0.90–1.10)	1.39 (1.11–1.73)	0.013	0.88 (0.70–1.10)	0.73 (0.47–1.13)	0.415

Abbreviation: NDVI = normalized difference vegetation index.
Model adjusted for sex, age, sample source, education, body mass index, and smoking status, with study center included as a random effect.

with a 120% higher risk of hospitalizations (RR = 2.20, 95% CI: 1.43–3.38), and each 10 μg/m^3 increase in PM_{10} with a 172% increased risk (RR = 2.72, 95% CI: 1.81–4.10). The mean exposure from 1990 to 2000 also showed increased risks for hospitalizations for both $PM_{2.5}$ (RR = 1.44, 95% CI: 1.04–2.00) and PM_{10} (RR = 1.65, 95% CI: 1.09–2.51). However, the associations of PM_{10} with emergency room visits did not reach statistical significance during the same periods. Exposure to BC and NO_2 was associated with higher risk of both emergency room visits and hospitalizations, but only the 1990 associations for hospitalizations were statistically significant (Fig. 3). O_3 showed no consistent associations with either outcome across all periods. NDVI demonstrated divergent associations; it was associated with an increased risk of emergency room visits in 2000, with each 0.1 unit increase in NDVI associated with a 15% higher risk (RR = 1.15, 95% CI: 1.03–1.28) (Fig. 3). Conversely, it showed a protective effect against hospitalizations in 1990 (RR = 0.80, 95% CI: 0.62–1.02), a trend that was initially significant in Model 1 (RR = 0.80, 95% CI: 0.64–0.99) (Table 2) and remained consistent across the exposure periods although it diminished after adjusting for covariates. Detailed statistical results of Model 2 are presented in Supplementary Table S5.

In the two-exposure models, the direction of associations remained consistent with the main analysis for both outcomes. The magnitudes of association of $PM_{2.5}$, PM_{10}, BC and NO_2 on respiratory emergency room visits showed slight upward shifts after adjusting for NDVI within the same exposure time windows (Fig. 4). In contrast, for respiratory hospitalizations, the associations of $PM_{2.5}$, PM_{10}, BC, and NO_2 were reduced when adjusted for NDVI. Detailed statistical results of the two-exposure model are presented in Supplementary Table S6. Significant interactions were observed between NDVI and BC for emergency room visits (1990 and 2000) and hospitalizations (2000 and mean 1990–2000), as well as between NDVI and O_3 for emergency room visits during the mean 1990–2000 period (Supplementary Tables S7 and S8). For emergency room visits, BC exposure showed higher RRs with increasing NDVI tertiles, while O_3 exposure showed lower RRs with higher NDVI tertiles. For hospitalizations, BC demonstrated mixed patterns across these exposure periods.

After excluding Tartu center in the sensitivity analysis, the direction and magnitude of associations were similar to those observed in the main analysis (Supplementary Table S9). Similarly, the sensitivity analysis excluding symptomatic individuals further supported the robustness of the main findings (Supplementary Table S10). Notably, among the random sample participants, the associations exhibited a generally consistent direction with the main analysis, while the effect estimates were higher in this subset compared to the overall study population. Of the participants, 497 participants (29.7%) indicated they had an atopic status, while 1178 participants (70.3%) reported no atopic status. We found significant interactions between NDVI and atopic status on respiratory emergency room visits across three exposure time windows (p-values <0.05) (Table 3). Higher NDVI was associated with a higher risk for emergency room visits among those with atopic status at baseline. Each 0.1 unit increase in NDVI was linked to a 26% higher risk of emergency room visits in 1990 exposure (RR = 1.26, 95% CI: 0.94–1.68), a 28% higher risk in the 2000 exposure (RR = 1.28, 95% CI: 1.18–1.39), and a 39% higher risk in the mean 1990–2000 exposure (RR = 1.39, 95% CI: 1.11–1.73) (Table 3). The direction of associations among the atopic group was consistent with the main analysis, but even higher compared to the overall study population. In contrast, NDVI showed a protective association with emergency room visits in the 1990 exposure period among those without atopic status (RR = 0.87, 95% CI: 0.76–0.99) (Table 3). No significant interaction was found between NDVI and atopic status on hospitalizations in any period (Table 3).

4. Discussion

In this study conducted across the Northern European centers of the ECRHS, we observed that higher ambient levels of $PM_{2.5}$, PM_{10}, BC, and NO_2 were associated with an increased risk of respiratory hospitalizations. $PM_{2.5}$ and PM_{10} were also notably associated with a higher risk of respiratory emergency room visits. No clear associations were found between O_3 and either respiratory emergency room visits or hospitalizations. Interestingly, while greenness appeared to reduce the risk of respiratory hospitalizations, it was positively associated with emergency room visits, particularly among individuals with atopic status.

The outcomes of our investigation—respiratory emergency room visits and hospitalizations—represent significant health events that underscore the public health implications of air pollution. In this study, we separated respiratory emergency room visits from hospitalizations to reflect their distinct healthcare functions. Emergency departments, more accessible than general hospitals, handle urgent but generally less severe conditions, providing immediate care, particularly outside of regular general practitioner hours. In contrast, hospitals manage more severe health crises requiring specialized and prolonged care. Interestingly, we observed higher risk estimates for respiratory hospitalizations compared to emergency room visits. This difference likely reflects the severity of conditions requiring hospitalizations, which often result from chronic or exacerbated states of respiratory diseases. Additionally, the smaller number of hospitalizations (48 cases) as compared to emergency room visits (119 cases) may have affected the precision of our estimates. This means that our point association estimates for hospitalizations might be more susceptible to random fluctuations, which might have resulted in overestimating the true effect. Therefore, while our findings suggest a significant association between air pollutants and respiratory hospitalizations, these results should be interpreted with caution due to the potential for statistical variability. Moreover, the “toxicant-induced loss of tolerance” (TILT) model (Miller, 1997) provides a theoretical framework to understand these findings, suggesting that prolonged exposure to pollutants leads to cumulative health impacts and decreased physiological resilience. This reduction in resilience increases the vulnerability of individuals to air pollutants, leading to their susceptibility to levels of air pollution that would normally not affect them. This increased susceptibility is particularly important, resulting in severe health outcomes that require hospital-level care rather than short-term emergency treatment.

This study highlights the complex relationship between air pollution, greenness and respiratory emergency room visits and hospitalizations across three distinct time windows. Significant associations between $PM_{2.5}$ and PM_{10} with both respiratory emergency room visits and hospitalizations were observed during the 1990 exposure period, but the risk for hospitalizations was also increased for the other time points. BC and NO_2 were significantly associated with hospitalizations in 1990. Thus, overall, our results indicate that the 1990 exposure seemed to be of particular importance. This period is critical as it approximates long-term exposure spanning at least one decade back in time from the outcomes, suggesting that elevated pollution levels may have prolonged effects on respiratory health. This finding parallels our previous research on the association between air pollution, greenness, and all-cause mortality across similar exposure windows, where we observed that particulate matter exposure in 1990 was associated with increased all-cause mortality (Xu et al., 2023). In our study, exposure in 2000 resulted in higher association estimates for hospitalization, while 1990 exposure had higher estimates on the emergency room visits, compared to other periods. Hospitalizations may be more closely linked to acute effects of air pollution, consequently with the exposure window closer to the outcome period being more important. Also, changes in the composition and toxicity of pollutants over time might have contributed differently to these outcomes, suggesting different health impacts linked to the nature of the pollutants at each time. The mean exposure during 1990–2000, incorporating residential histories, were likely better at capturing variations in concentration over time. Nonethelss, they resulted in lower association estimates compared to the baseline or remote exposures. This could be because these exposures, while considering residential changes and both spatial and temporal variations, may dilute the apparent immediate impact of air pollution observed in closer temporal proximity to health outcomes.

Long-term exposure to air pollutants exacerbates respiratory conditions by causing persistent inflammation, triggering immune responses, and releasing pro-inflammatory cytokines, which lead to lung inflammation and fibrosis—precursors to severe respiratory issues (Jones et al., 2017; Kelly and Fussell, 2011). Oxidative stress from pollutants also generates reactive oxygen species that damage lung cells, worsening chronic diseases like asthma and COPD and often leading to acute medical episodes requiring hospital care (Kelly and Fussell, 2011). Comparing our findings with previous studies is challenging due to variations in study populations, geographic locations, designs, exposure assessments, and definitions of outcomes. There have been few studies examining the long-term effects of air pollution on respiratory emergency room visits, as most existing research in the adult population has focused on the short-term effects of air pollution on respiratory emergency room visits, often using daily measurements of both exposure and emergency room visits (Rodopoulou et al., 2015; Stieb et al., 2009; Yadav et al., 2023). A recent Italian study, however, has shed light on the long-term effects, revealing that long-term air pollution exposure was associated with more frequent emergency room admissions in children and adolescents (Panunzi et al., 2023). In line with these findings, our study contributes to this gap by demonstrating that long-term exposure to particulate matter also increases the cumulative incidence of emergency room visits for respiratory conditions in the adult population. This longitudinal perspective shows that the effects of air pollution go beyond immediate effects, leading to longer-term health declines. However, given that our study does not account for short-term exposure variations, our findings should be interpreted with caution.

Compared to respiratory emergency room visits, the effects of long-term exposure to air pollution on respiratory hospitalizations have been more frequently explored. Except for O_3, our results generally align well with previous findings on the positive association between long-term exposure to air pollution and hospitalizations for various respiratory conditions. This includes asthma hospitalizations (Andersen et al., 2012), low respiratory tract infection hospitalizations (Gandini et al., 2018), as well as COPD, pneumonia, and lung cancer hospitalizations (Danesh Yazdi et al., 2019, 2022; Gandini et al., 2018; Tsai and Yang, 2014). However, other research yields varying outcomes. A study from London suggested that the relationship between long-term exposure to traffic pollution and hospital admissions for cardio-respiratory diseases is complex and influenced by the presence of other risk factors (Halonen et al., 2016). Similarly, an Australian study did not find consistent associations between NO_2 and $PM_{2.5}$ with hospitalizations for all respiratory diseases, pneumonia and COPD (Salimi et al., 2018b).

We did not find consistent patterns in the association between O_3 and respiratory emergency room visits and hospitalizations across the three time windows examined. Few studies have investigated the long-term effects of O_3 on these respiratory outcomes. A recent study by Danesh Yazdi et al. (2022) reported a positive association between O_3 exposure and respiratory hospitalizations. This variability in the observed effects of O_3 may be influenced by its negative correlation with other pollutants, fluctuations in environmental temperatures, and distinct seasonal variations in its levels. O_3 is typically higher during summer months due to the photochemical reactions facilitated by increased sunlight and warmer temperatures. Conversely, the peak in respiratory emergency room visits and hospitalizations often occurs during winter, a period marked by exacerbations of chronic lung diseases due to colder weather (Mourtzoukou and Falagas, 2007). This seasonal misalignment might mask the effects of O_3 observed in our study, complicating our understanding of its impact on respiratory health.

Our study presents the complex role of greenness on respiratory emergency room visits and hospitalizations. We observed a protective trend with increased NDVI on respiratory hospitalizations, supporting theories that greenness enhances health through mechanisms such as improved air quality, increased physical activity, and psychological benefits (Markevych et al., 2017). However, our findings contrast with those reported by Klompmaker et al. (2022), who found that greenness, measured by NDVI, was positively associated with respiratory disease hospitalizations (HR: 1.02, 95% CI: 1.00–1.03) among U.S. Medicare beneficiaries in urban settings.

Our study identified higher NDVI levels as associated with an increased risk of respiratory emergency room visits, particularly among populations with atopic status. This suggests that increased NDVI may elevate the risk of emergency room visits due to allergen-producing components in greener areas, exacerbating respiratory symptoms in susceptible individuals. The inclusion of atopic status in our analysis offers crucial insights into how individual susceptibilities to allergens, potentially exacerbated by greenness, modify the health outcomes of environmental exposures. Notably, our findings reveal significant interactions between NDVI and atopic status affecting emergency room visits but not hospitalizations, underscoring the nuanced roles of greenness in respiratory health. This differentiation aligns with our goal to comprehensively assess the environmental impacts on health. Furthermore, this finding contrasts with a Belgian study where greater tree coverage was linked to fewer emergency room visits (Vranken et al., 2023). Such discrepancies underline the variability in how different metrics of greenness, like NDVI and tree coverage, may influence health outcomes. These results, combined with insights from a Dutch national health survey by Klompmaker et al. (2018), which showed varying associations of green space with being overweight based on different green space definitions, emphasize the need for careful consideration of the specific measures of greenness most appropriate for particular health outcomes. Recognizing that environmental factors such as pollution and greenness may affect atopic status highlights the complex interplay with individual health profiles. This complexity calls for further research to explore these dynamics, considering seasonal variations and short-term exposures.

Greenness contains diverse components—from pollutant-absorbing trees to allergen-producing shrubs and grasses—that can influence respiratory health in contrasting ways. While certain plants may exacerbate allergy symptoms, the overall biodiversity within these environments can also play a crucial role in enhancing immune responses, this is supported by the "biodiversity hypothesis". This hypothesis suggests that contact with natural environments can improve immune regulation and potentially reduce the prevalence of allergic and autoimmune diseases (Haahtela, 2019; Haahtela et al., 2013).

Greenness is often recognized for its potential to reduce air pollution (Setälä et al., 2013). In our two-exposure model, we observed that the associations between air pollution and respiratory hospitalizations were attenuated after adjusting for NDVI, whereas the associations with respiratory emergency room visits slightly increased. Our analysis also showed complex interactions between air pollution and NDVI, particularly in the highest NDVI tertiles, where synergistic effects increased the risk of respiratory emergency room visits, and hospitalizations risks associated with BC exposure. Conversely, the interaction between NDVI and O_3 showed that the lowest risk of O_3 was observed in the highest NDVI tertile. Some green areas can accumulate pollution due to their design and location. Moreover, the observed dynamic correlations of NDVI with various pollutants across different exposure periods and study centers underline the complex nature of their correlations. This emphasizes the importance of considering temporal changes, geographical location, and the composition of greenness in these areas, which significantly affect the respiratory outcome associated with greenness. Our findings, along with the inconsistent results highlighted in recent reviews (Johannessen et al., 2023), call for a broader research scope to fully understand the complex effects of greenness on respiratory health.

Our study has several strengths. The longitudinal design tracks the same participants over two decades, offering insights into the effects of long-term environmental exposure on these two severe respiratory health outcomes. We assigned exposure to participants using geocoding from the population registry, based on their exact residential addresses, which ensured an accurate assessment of home-based exposure. Additionally, our application of advanced atmospheric dispersion and transport modeling techniques enabled us to evaluate historical exposure to air pollution. This retrospective approach was instrumental in thoroughly examining how air pollution impacts respiratory emergency room visits and hospitalizations over different time periods of exposure.

Our study has several important limitations. Firstly, a significant loss to follow-up occurred during the second follow-up, introducing the potential for selection bias, which might have affected the representativeness of the study sample. Another concern is recall bias, as the study outcomes are based on self-reported data collected during the second follow-up, where participants were asked if they had experienced the events since the last survey. However, given the severity of the reported conditions, it is less likely that recall bias would substantially influence the accuracy of the outcome reporting. Furthermore, residential self-selection could influence causal inference, as individuals who choose to live in greener areas might differ systematically from those who do not, potentially affecting the observed associations. Residual confounding is also a potential limitation. Previous studies have adjusted for a comprehensive range of covariates including income, occupation, area-levels socioeconomic status, and environmental factors such as temperature and season (Andersen et al., 2012; Danesh Yazdi et al., 2022; Gandini et al., 2018; Klompmaker et al., 2022). However, we were not able to adjust for these factors in our analysis, which might potentially affect the results. Notably, the seasonal effects of respiratory diseases and the seasonal variations in air pollution and greenness exposure are well-documented. Our inability to include these factors in the analysis might have led to underestimation or overestimation of the true effects, and we were not able to take short-term exposures into account. Moreover, the presence of zero counts of symptomatic samples in centers like Bergen and Aarhus limited our ability to adjust for country, potentially affecting the control of unmeasured confounders that vary across countries (Basagaña et al., 2018). Additionally, our assessment only accounted for residential exposure and did not capture the full exposure picture including for example occupational exposure, which could lead to exposure misclassification. Given that the determination of exposure was made independently of the outcome, any resulting misclassification is likely to be nondifferential, potentially biasing the results toward the null.

5. Conclusions

Long-term exposure to $PM_{2.5}$ and PM_{10} was associated with increased respiratory emergency room visits and hospitalizations, with these associations remaining relatively consistent across the exposure periods in 1990, 2000, and the mean exposure from 1990 to 2000. BC and NO_2 were associated with an increased risk of respiratory hospitalizations when considering the 1990 exposure. Contrarily, we observed no significant association between O_3 and respiratory outcomes across all investigated periods. Interestingly, greenness exhibited a protective trend against respiratory hospitalizations but was associated with increased emergency room visits, especially among individuals with atopic status, a subsample including pollen-sensitised individuals. These findings highlight the importance of long-term environmental exposures, even for outcomes commonly thought of as acutely triggered. Our study supports the need to integrate air pollution control measures into public health considerations into urban planning strategies, particularly to address the long-term effects on different population groups.

CRediT authorship contribution statement

Shanshan Xu: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Alessandro Marcon:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Randi Jacobsen Bertelsen:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Bryndis Benediktsdottir:** Writing – review & editing. **Jørgen Brandt:** Writing – review & editing, Investigation. **Lise Marie Frohn:** Writing – review & editing, Investigation. **Camilla Geels:** Writing – review & editing, Investigation. **Thorarinn Gislason:** Writing – review & editing. **Joachim Heinrich:** Writing – review & editing. **Mathias Holm:** Writing – review & editing. **Christer Janson:** Writing – review & editing. **Iana Markevych:** Writing – review & editing. **Lars Modig:** Writing – review & editing. **Hans Orru:** Writing – review & editing. **Vivi Schlünssen:** Writing – review & editing. **Torben Sigsgaard:** Writing – review & editing. **Ane Johannessen:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization.

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.

Acknowledgement

This work was funded by a grant from the Research Council of Norway (No. 300765). Iana Markevych is partially supported by the "Strategic research and innovation program for the development of Medical University—Plovdiv" No BG-RRP-2.004-0007-C01, Establishment of a network of research higher schools, National plan for recovery and resilience, financed by the European Union—NextGenerationEU. Nordforsk under the Nordic Programme on Health and Welfare (Project #75007: NordicWelfAir).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2025.120938.

Data availability

The data presented in this paper are not readily available due to potential privacy violations, but can be obtained with justifiable request and with the consent of the national ethics committee.

References

AirViro. SMHI Airviro User's Reference, 2011. Working with the Dispersion Module. How to Simulate the Dispersion of Pollutants. Swedish Meteorological and Hydrological Institute.

Andersen, Z.J., Bønnelykke, K., Hvidberg, M., Jensen, S.S., Ketzel, M., Loft, S., Sørensen, M., Tjønneland, A., Overvad, K., Raaschou-Nielsen, O., 2012. Long-term exposure to air pollution and asthma hospitalisations in older adults: a cohort study. Thorax 67, 6–11.

Bălă, G.-P., Râjnoveanu, R.-M., Tudorache, E., Motișan, R., Oancea, C., 2021. Air pollution exposure—the (in) visible risk factor for respiratory diseases. Environ. Sci. Pollut. Control Ser. 28, 19615–19628.

Basagaña, X., Pedersen, M., Barrera-Gómez, J., Gehring, U., Giorgis-Allemand, L., Hoek, G., Stafoggia, M., Nieuwenhuijsen, M.J., Brunekreef, B., Slama, R., 2018. Analysis of multicentre epidemiological studies: contrasting fixed or random effects modelling and meta-analysis. Int. J. Epidemiol. 47, 1343–1354.

Brandt, J., Christensen, J.H., Frohn, L.M., Berkowicz, R., 2003. Air pollution forecasting from regional to urban street scale—implementation and validation for two cities in Denmark. Phys. Chem. Earth, Parts A/B/C 28, 335–344.

Brandt, J., Silver, J.D., Frohn, L.M., Geels, C., Gross, A., Hansen, A.B., Hansen, K.M., Hedegaard, G.B., Skjøth, C.A., Villadsen, H., Zare, A., Christensen, J.H., 2012. An integrated model study for Europe and North America using the Danish Eulerian Hemispheric Model with focus on intercontinental transport of air pollution. Atmos. Environ. 53, 156–176.

Burney, P.G., Luczynska, C., Chinn, S., Jarvis, D., 1994. The European community respiratory health survey. Eur. Respir. J. 7, 954–960.

Danesh Yazdi, M., Wang, Y., Di, Q., Wei, Y., Requia, W.J., Shi, L., Sabath, M.B., Dominici, F., Coull, B.A., Evans, J.S., Koutrakis, P., Schwartz, J.D., 2021. Long-term

association of air pollution and hospital admissions among medicare participants using a doubly robust additive model. Circulation 143, 1584–1596.
Danesh Yazdi, M., Wang, Y., Di, Q., Zanobetti, A., Schwartz, J., 2019. Long-term exposure to PM(2.5) and ozone and hospital admissions of Medicare participants in the Southeast USA. Environ. Int. 130, 104879.
Danesh Yazdi, M., Wei, Y., Di, Q., Requia, W.J., Shi, L., Sabath, M.B., Dominici, F., Schwartz, J., 2022. The effect of long-term exposure to air pollution and seasonal temperature on hospital admissions with cardiovascular and respiratory disease in the United States: a difference-in-differences analysis. Sci. Total Environ. 843, 156855.
Frohn, L.M., Geels, C., Andersen, C., Andersson, C., Bennet, C., Christensen, J.H., Im, U., Karvosenoja, N., Kindler, P.A., Kukkonen, J., Lopez-Aparicio, S., Nielsen, O.-K., Palamarchuk, Y., Paunu, V.-V., Plejdrup, M.S., Segersson, D., Sofiev, M., Brandt, J., 2022. Evaluation of multidecadal high-resolution atmospheric chemistry-transport modelling for exposure assessments in the continental Nordic countries. Atmos. Environ. 290, 119334.
Gandini, M., Scarinzi, C., Bande, S., Berti, G., Carnà, P., Ciancarella, L., Costa, G., Demaria, M., Ghigo, S., Piersanti, A., Rowinski, M., Spadea, T., Stroscia, M., Cadum, E., 2018. Long term effect of air pollution on incident hospital admissions: results from the Italian Longitudinal Study within LIFE MED HISS project. Environ. Int. 121, 1087–1097.
Halonen, J.I., Blangiardo, M., Toledano, M.B., Fecht, D., Gulliver, J., Anderson, H.R., Beevers, S.D., Dajnak, D., Kelly, F.J., Tonne, C., 2016. Long-term exposure to traffic pollution and hospital admissions in London. Environ. Pollut. 208, 48–57.
Haahtela, T., 2019. A biodiversity hypothesis. Allergy 74, 1445–1456.
Haahtela, T., Holgate, S., Pawankar, R., Akdis, C.A., Benjaponpitak, S., Caraballo, L., Demain, J., Portnoy, J., von Hertzen, L., 2013. The biodiversity hypothesis and allergic disease: world allergy organization position statement. World Allergy Organ J 6 (3).
Janson, C., Anto, J., Burney, P., Chinn, S., de Marco, R., Heinrich, J., Jarvis, D., Kuenzli, N., Leynaert, B., Luczynska, C., Neukirch, F., Svanes, C., Sunyer, J., Wjst, M., 2001. The European community respiratory health survey: what are the main results so far? European community respiratory health survey II. Eur. Respir. J. 18, 598–611.
Johannessen, A., Xu, S., Abbah, A.P., Janson, C., 2023. Greenness exposure: beneficial but multidimensional. Breathe 19.
Jones, B., Donovan, C., Liu, G., Gomez, H.M., Chimankar, V., Harrison, C.L., Wiegman, C. H., Adcock, I.M., Knight, D.A., Hirota, J.A., 2017. Animal models of COPD: W hat do they tell us? Respirology 22, 21–32.
Kelly, F.J., Fussell, J.C., 2011. Air pollution and airway disease. Clin. Exp. Allergy 41, 1059–1071.
Kim, D., Chen, Z., Zhou, L.-F., Huang, S.-X., 2018. Air pollutants and early origins of respiratory diseases. Chronic Diseases and Translational Medicine 4, 75–94.
Klompmaker, J.O., Hoek, G., Bloemsma, L.D., Gehring, U., Strak, M., Wijga, A.H., van den Brink, C., Brunekreef, B., Lebret, E., Janssen, N.A.H., 2018. Green space definition affects associations of green space with overweight and physical activity. Environ. Res. 160, 531–540.
Klompmaker, J.O., Laden, F., Browning, M.H.E.M., Dominici, F., Ogletree, S.S., Rigolon, A., Hart, J.E., James, P., 2022. Associations of parks, greenness, and blue space with cardiovascular and respiratory disease hospitalization in the US Medicare cohort. Environ. Pollut. 312, 120046.
Liu, S., Jørgensen, J.T., Ljungman, P., Pershagen, G., Bellander, T., Leander, K., Magnusson, P.K., Rizzuto, D., Hvidtfeldt, U.A., Raaschou-Nielsen, O., 2021. Long-term exposure to low-level air pollution and incidence of chronic obstructive pulmonary disease: the ELAPSE project. Environ. Int. 146, 106267.
Markevych, I., Schoierer, J., Hartig, T., Chudnovsky, A., Hystad, P., Dzhambov, A.M., de Vries, S., Triguero-Mas, M., Brauer, M., Nieuwenhuijsen, M.J., Lupp, G., Richardson, E.A., Astell-Burt, T., Dimitrova, D., Feng, X., Sadeh, M., Standl, M., Heinrich, J., Fuertes, E., 2017. Exploring pathways linking greenspace to health: theoretical and methodological guidance. Environ. Res. 158, 301–317.
Meng, X., Liu, C., Chen, R., Sera, F., Vicedo-Cabrera, A.M., Milojevic, A., Guo, Y., Tong, S., Coelho, M.d.S.Z.S., Saldiva, P.H.N., Lavigne, E., Correa, P.M., Ortega, N.V., Osorio, S., Garcia, Kyselý, J., Urban, A., Orru, H., Maasikmets, M., Jaakkola, J.J.K., Ryti, N., Huber, V., Schneider, A., Katsouyanni, K., Analitis, A., Hashizume, M., Honda, Y., Ng, C.F.S., Nunes, B., Teixeira, J.P., Holobaca, I.H., Fratianni, S., Kim, H., Tobias, A., Íñiguez, C., Forsberg, B., Åström, C., Ragettli, M.S., Guo, Y.-L.L., Pan, S.-C., Li, S., Bell, M.L., Zanobetti, A., Schwartz, J., Wu, T., Gasparrini, A., Kan, H., 2021. Short term associations of ambient nitrogen dioxide with daily total, cardiovascular, and respiratory mortality: multilocation analysis in 398 cities. BMJ 372, n534.
Miller, C.S., 1997. Toxicant-induced loss of tolerance–an emerging theory of disease? Environ. Health Perspect. 105 (Suppl. 2), 445–453.
Momtazmanesh, S., Moghaddam, S.S., Ghamari, S.-H., GBD 2019 Chronic Respiratory Diseases Collaborators, 2023. Global burden of chronic respiratory diseases and risk factors, 1990–2019: an update from the Global Burden of Disease Study 2019. eClinicalMedicine 59, 101936.
Mourtzoukou, E.G., Falagas, M.E., 2007. Exposure to cold and respiratory tract infections. Int J Tuberc Lung Dis 11, 938–943.
Panunzi, S., Marchetti, P., Stafoggia, M., Badaloni, C., Caranci, N., de Hoogh, K., Giorgi Rossi, P., Guarda, L., Locatelli, F., Ottone, M., Silocchi, C., Ricci, P., Marcon, A., 2023. Residential exposure to air pollution and adverse respiratory and allergic outcomes in children and adolescents living in a chipboard industrial area of Northern Italy. Sci. Total Environ. 864, 161070.
Paunu, V.-V., Karvosenoja, N., Segersson, D., López-Aparicio, S., Nielsen, O.-K., Plejdrup, M.S., Thorsteinsson, T., Niemi, J.V., Vo, D.T., Denier van der Gon, H.A.C., Brandt, J., Geels, C., 2021. Spatial distribution of residential wood combustion emissions in the Nordic countries: how well national inventories represent local emissions? Atmos. Environ. 264, 118712.
Paunu, V.-V., Karvosenoja, N., Segersson, D., López-Aparicio, S., Nielsen, O.-K., Schmidt Plejdrup, M., Thorsteinsson, T., Vo, D.T., Kuenen, J., Denier van der Gon, H., 2024. Air pollution emission inventory using national high-resolution spatial parameters for the Nordic countries and analysis of PM 2.5 spatial distribution for road transport and machinery and off-road sectors. Earth Syst. Sci. Data 16, 1453–1474.
Rice, M.B., Ljungman, P.L., Wilker, E.H., Gold, D.R., Schwartz, J.D., Koutrakis, P., Washko, G.R., O'Connor, G.T., Mittleman, M.A., 2013. Short-term exposure to air pollution and lung function in the Framingham Heart Study. Am. J. Respir. Crit. Care Med. 188, 1351–1357.
Rodopoulou, S., Samoli, E., Chalbot, M.-C.G., Kavouras, I.G., 2015. Air pollution and cardiovascular and respiratory emergency visits in Central Arkansas: a time-series analysis. Sci. Total Environ. 536, 872–879.
Salimi, F., Morgan, G., Rolfe, M., Samoli, E., Cowie, C.T., Hanigan, I., Knibbs, L., Cope, M., Johnston, F.H., Guo, Y., Marks, G.B., Heyworth, J., Jalaludin, B., 2018a. Long-term exposure to low concentrations of air pollutants and hospitalisation for respiratory diseases: a prospective cohort study in Australia. Environ. Int. 121, 415–420.
Salimi, F., Morgan, G., Rolfe, M., Samoli, E., Cowie, C.T., Hanigan, I., Knibbs, L., Cope, M., Johnston, F.H., Guo, Y., Marks, G.B., Heyworth, J., Jalaludin, B., 2018b. Long-term exposure to low concentrations of air pollutants and hospitalisation for respiratory diseases: a prospective cohort study in Australia. Environ. Int. 121, 415–420.
Setälä, H., Viippola, V., Rantalainen, A.-L., Pennanen, A., Yli-Pelkonen, V., 2013. Does urban vegetation mitigate air pollution in northern conditions? Environ. Pollut. 183, 104–112.
Stieb, D.M., Szyszkowicz, M., Rowe, B.H., Leech, J.A., 2009. Air pollution and emergency department visits for cardiac and respiratory conditions: a multi-city time-series analysis. Environ. Health 8, 25.
Strak, M., Weinmayr, G., Rodopoulou, S., Chen, J., de Hoogh, K., Andersen, Z.J., Atkinson, R., Bauwelinck, M., Bekkevold, T., Bellander, T., Boutron-Ruault, M.-C., Brandt, J., Cesaroni, G., Concin, H., Fecht, D., Forastiere, F., Gulliver, J., Hertel, O., Hoffmann, B., Hvidtfeldt, U.A., Janssen, N.A.H., Jöckel, K.-H., Jørgensen, J.T., Ketzel, M., Klompmaker, J.O., Lager, A., Leander, K., Liu, S., Ljungman, P., Magnusson, P.K.E., Mehta, A.J., Nagel, G., Oftedal, B., Pershagen, G., Peters, A., Raaschou-Nielsen, O., Renzi, M., Rizzuto, D., van der Schouw, Y.T., Schramm, S., Severi, G., Sigsgaard, T., Sørensen, M., Stafoggia, M., Tjønneland, A., Verschuren, W. M.M., Vienneau, D., Wolf, K., Katsouyanni, K., Brunekreef, B., Hoek, G., Samoli, E., 2021. Long term exposure to low level air pollution and mortality in eight European cohorts within the ELAPSE project: pooled analysis. BMJ 374, n1904.
Tsai, S.S., Yang, C.Y., 2014. Fine particulate air pollution and hospital admissions for pneumonia in a subtropical city: taipei, Taiwan. J. Toxicol. Environ. Health 77, 192–201.
Vilcins, D., Sly, P.D., Scarth, P., Mavoa, S., 2024. Green space in health research: an overview of common indicators of greenness. Rev. Environ. Health 39, 221–231.
WHO, 2016. Urban green spaces and health. World Health Organization. Regional Office for Europe.
WHO, 2021. World Health Organization (WHO) Global Air Quality Guidelines: Particulate Matter (PM2.5 and PM10), Ozone, Nitrogen Dioxide, Sulfur Dioxide and Carbon Monoxide. World Health Organization, Geneva eđeds.
Xu, S., Marcon, A., Bertelsen, R.J., Benediktsdottir, B., Brandt, J., Engemann, K., Frohn, L.M., Geels, C., Gislason, T., Heinrich, J., Holm, M., Janson, C., Markevych, I., Modig, L., Orru, H., Schlünssen, V., Sigsgaard, T., Johannessen, A., 2023. Long-term exposure to low-level air pollution and greenness and mortality in Northern Europe. The Life-GAP project. Environ. Int. 181, 108257.
Xu, S., Marcon, A., Bertelsen, R.J., Benediktsdottir, B., Brandt, J., Frohn, L.M., Geels, C., Gislason, T., Heinrich, J., Holm, M., Janson, C., Markevych, I., Modig, L., Orru, H., Schlünssen, V., Sigsgaard, T., Johannessen, A., 2024. Associations of long-term exposure to air pollution and greenness with incidence of chronic obstructive pulmonary disease in Northern Europe: the Life-GAP project. Environ. Res. 257, 119240.
Yadav, R., Nagori, A., Madan, K., Lodha, R., Kabra, S.K., 2023. Short-term exposure to air pollution and emergency room visits for acute respiratory symptoms among adults. Int J Tuberc Lung Dis 27, 761–765.
Yee, J., Cho, Y.A., Yoo, H.J., Yun, H., Gwak, H.S., 2021. Short-term exposure to air pollution and hospital admission for pneumonia: a systematic review and meta-analysis. Environ. Health 20, 6.
Zhang, Y., Ding, Z., Xiang, Q., Wang, W., Huang, L., Mao, F., 2020. Short-term effects of ambient PM1 and PM2.5 air pollution on hospital admission for respiratory diseases: case-crossover evidence from Shenzhen, China. Int. J. Hyg Environ. Health 224, 113418.
Zou, G., 2004. A modified Poisson regression approach to prospective studies with binary data. Am. J. Epidemiol. 159, 702–706.