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Sex-specific associations of environmental exposures with prevalent diabetes and obesity – Results from the KORA Fit study

Fiona Niedermayer [a,b,*], Kathrin Wolf [b], Siqi Zhang [b,h], Marco Dallavalle [a,b], Nikolaos Nikolaou [b], Lars Schwettmann [c,d], Peter Selsam [e], Barbara Hoffmann [f], Alexandra Schneider [b], Annette Peters [a,b,g]

[a] Chair of Epidemiology, IBE, Faculty of Medicine, LMU Munich, Munich, Germany
[b] Institute of Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany
[c] Institute of Health Economics and Health Care Management, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany
[d] Department of Health Services Research, School of Medicine and Health Sciences, Carl von Ossietzky Universität Oldenburg, Oldenburg, Germany
[e] Department Monitoring and Exploration Technologies, Helmholtz Centre for Environmental Research GmbH—UFZ, Leipzig, Germany
[f] Institute of Occupational, Social and Environmental Medicine, Centre for Health and Society, Medical Faculty, Heinrich-Heine University Düsseldorf, Düsseldorf, Germany
[g] German Center for Diabetes Research (DZD), München-Neuherberg, Neuherberg, Germany
[h] Department of Environmental Health Sciences, Yale School of Public Health, New Haven, United States

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ABSTRACT

Promising evidence suggests a link between environmental factors, particularly air pollution, and diabetes and obesity. However, it is still unclear whether men and women are equally susceptible to environmental exposures. Therefore, we aimed to assess sex-specific long-term effects of environmental exposures on metabolic diseases.

We analyzed cross-sectional data from 3,034 participants (53.7% female, aged 53-74 years) from the KORA Fit study (2018/19), a German population-based cohort. Environmental exposures, including annual averages of air pollutants [nitrogen oxides (NO_2, NO_x), ozone, particulate matter of different diameters (PM_{10}, PM_{coarse}, $PM_{2.5}$), $PM_{2.5}$abs, particle number concentration], air temperature and surrounding greenness, were assessed at participants' residences. We evaluated sex-specific associations of environmental exposures with prevalent diabetes, obesity, body-mass-index (BMI) and waist circumference using logistic or linear regression models with an interaction term for sex, adjusted for age, lifestyle factors and education. Further effect modification, in particular by urbanization, was assessed in sex-stratified analyses.

Higher annual averages of air pollution, air temperature and greenness at residence were associated with diabetes prevalence in men (NO_2: Odds Ratio (OR) per interquartile range increase in exposure: 1.49 [95% confidence interval (CI): 1.13, 1.95], air temperature: OR: 1.48 [95%-CI: 1.15, 1.90]; greenness: OR: 0.78 [95%-CI: 0.59, 1.01]) but not in women.

Conversely, higher levels of air pollution, temperature and lack of greenness were associated with lower obesity prevalence and BMI in women. After including an interaction term for urbanization, only higher greenness was associated with higher BMI in rural women, whereas higher air pollution was associated with higher BMI in urban men.

To conclude, we observed sex-specific associations of environmental exposures with metabolic diseases. An additional interaction between environmental exposures and urbanization on obesity suggests a higher susceptibility to air pollution among urban men, and higher susceptibility to greenness among rural women, which needs corroboration in future studies.

1. Introduction

In the last decade, the number of people suffering from metabolic

* Corresponding author. Ingolstädter Landstr. 1, 85764 Neuherberg, Germany.
E-mail address: fiona.niedermayer@helmholtz-munich.de (F. Niedermayer).

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diseases such as diabetes mellitus or obesity has increased worldwide (IDF (International Diabetes Federation), 2021; WHO, 2022). To reverse this trend, prevention is urgently needed, not only because metabolic diseases represent a major global health burden on their own, they are also linked to secondary diseases and constitute risk factors for other diseases (Kivimaki et al., 2022). The risk of metabolic diseases accumulates over a lifetime, resulting in prevalence of metabolic diseases being highest in middle-aged and older adults (WHO, 2022; Diseases and Injuries, 2020). Although it is known that metabolic diseases develop through a complex interplay of biological, social, behavioral and environmental factors (Bluher, 2019), current prevention strategies mainly focus on changing individual behaviors, such as dietary and physical activity habits, without addressing the context in which these changes are supposed to occur (WHO, 2022). However, single interventions alone may not provide effective prevention of these complex diseases on their own (WHO, 2022). To understand the extent to which the environment acts as an obesogenic factor, the positive and negative effects of environmental factors on metabolic diseases need to be further elucidated.

Abbreviations

BMI	Body-Mass-Index
CI	Confidence Interval
DAG	Directed acyclic graph
IQR	Interquartile range
KORA	Cooperative Health Research of Augsburg
NDVI	Normalized difference vegetation index
NO	Nitrogen (di)oxide
OR	Odds ratio
PM	Particulate matter
PNC	Particle number concentration
WC	Waist circumference

There is increasing evidence that air pollutants play a role in the development of metabolic diseases (He et al., 2017; An et al., 2018). With regard to diabetes, a recent meta-analysis revealed a 25 % higher risk with a 10 μg/m^3 increase in particulate matter less than 2.5 μm in diameter ($PM_{2.5}$) (He et al., 2017). However, to date, only few studies have addressed the effects of air pollution on obesity (An et al., 2018; De la Fuente et al., 2020). A study in mice suggested that short-term exposure adversely affects adipose tissue through inflammatory processes, whereas long-term exposure induced leptin resistance, leading to higher risk of adiposity (Campolim et al., 2020). A systematic review of human studies by An et al. (2018) observed that 29 (44 %) of the long-term associations between air pollution and obesity were positive, but an equal number of associations showed no association and even 8 (12%) associations were negative. In conclusion, previous studies have focused on assessing the effects of air pollution, mainly particulate matter, on diabetes and obesity, while other air pollutants have so far rarely been studied. In addition, associations regarding obesity were often conflicting, which requires further investigation.

Moreover, only a limited number of studies have focused on the effects of ambient air temperature (Valdes et al., 2014, 2019; Yang et al., 2015). These studies found that increased annual averages of air temperature were associated with higher prevalence of obesity and diabetes and higher levels of glucose metabolism markers (Valdes et al., 2014, 2019). Conversely, higher levels of surrounding greenness can lead to increased physical activity levels (De la Fuente et al., 2020; Fong et al., 2018) and therefore directly mitigate an important risk factor for metabolic diseases. Other potential pathways include improved mental health and well-being due to surrounding greenness (Fong et al., 2018), which may simultaneously have a positive impact on metabolic health. Indeed, a systematic review of greenness confirmed a protective effect of living near green spaces on diabetes, but the association between greenness and obesity was inconclusive (De la Fuente et al., 2020).

Along with the lack of evidence mentioned above, potential sex-specific associations with metabolic diseases are missing or have been inconsistent (Wang et al., 2014; Weinmayr et al., 2015). Nevertheless, research on respiratory outcomes has often shown sex-specific susceptibility to environmental exposures (Clougherty, 2010). Moreover, there are notable sex differences in metabolic health, such as women's reduced tendency to accumulate abdominal fat or a delayed onset of metabolic diseases compared with men (Chang et al., 2018; Kautzky-Willer et al., 2023). In addition to potential sex-specific effects, previous studies have shown that health behaviors and obesity prevalence may differ according to urbanization (NCD Risk Factor Collaboration, 2019; Cohen et al., 2018). However, most of the previous studies were conducted in urban areas and therefore, could not account for different urbanization levels in their study region. Consequently, evidence of associations at different levels of urbanization is lacking.

The present study aimed to evaluate the long-term effects of multiple environmental exposures, including several air pollutants, ambient air temperature and surrounding greenness on prevalent diabetes and obesity in cross-sectional data from a population-based cohort in Augsburg, Germany. We specifically examined sex-specific associations in these middle-aged to older adults, who have often been underrepresented in studies but are at highest risk for metabolic diseases (Schienkiewitz et al., 2022). We further explored these effects by investigating potential differences between urban and rural areas.

2. Methods

2.1. Study population

We used cross-sectional data from the KORA ("Cooperative Health Research in the Region Augsburg") FIT study, a population-based cohort from the city of Augsburg, Southern Germany, and its two adjacent mainly rural counties (Holle et al., 2005). Briefly, the KORA Fit study is a follow-up examination of participants from the four original cohorts S1 (baseline assessment: 1984–1985), S2 (1989–1990), S3 (1994–1995) and S4 (1999–2001) (Rooney et al., 2022). In 2018 and 2019, 3047 participants aged 53–74 years underwent comprehensive standardized physical examination and in-person interviews with a specific focus on cardiometabolic health. All KORA studies adhered to the Declaration of Helsinki. Each participant gave written informed consent and ethical approval was granted by the Ethics Committee of the Bavarian Medical Association and the Bavarian commissioner for data protection and privacy.

2.2. Outcome assessment

Outcomes were prevalent diabetes mellitus and obesity status, as well as continuous body mass index (BMI) and waist circumference (WC) as assessed by standardized anthropometric measurements. Seca's measuring systems (Seca GmbH & Co, KG, Hamburg) were used to measure height and weight, whereupon BMI was calculated as weight in kg divided by squared height in meters (kg/m^2). WC was determined by using an inelastic tape at the level midway between the lower rib margin and the iliac crest (Rospleszcz et al., 2019). Participants were classified as having diabetes mellitus if they reported a physician-based diagnosis of diabetes mellitus diagnosis or intake of glucose-lowering medication during the interview. The latter was verified by checking the medication brought along on the day of the examination. Prevalent obesity was defined by BMI $\geq$30 kg/m^2 and by sex-specific WC cut-offs (men: $\geq$94 cm; women: $\geq$80 cm) (WHO, 2008). In the following paragraphs, unless otherwise noted, the term obesity refers to obesity defined by BMI.

2.3. Exposure assessment

We analyzed the long-term exposure to several environmental factors, including air pollution, air temperature and surrounding greenness, which were linked to participants' geocoded residential addresses.

Air pollution was modeled based on measurements from 20 monitoring stations located within the KORA study area in 2014 and 2015. Land-use regression models were separately developed for each air pollutant and applied to a 50 m × 50 m grid to estimate individual residential annual mean concentrations. Air pollutants included nitrogen oxides (NO_2 and NO_x), ozone (O_3), particulate matter diameter <10 μm in diameter (PM_{10}), 10–2.5 μm (PM_{coarse}), <2.5 μm ($PM_{2.5}$), soot ($PM_{2.5}$abs) and particle number concentration (PNC). $PM_{2.5}$abs can be used as proxy for black carbon, also known as soot, and can be simply measured by the reflectance in the $PM_{2.5}$ filters (Cyrys et al., 2003). More information on the air pollution measurements and predictors used in the modeling has been described elsewhere (Wolf et al., 2017).

Daily mean air temperature was available on a 1 km × 1 km gridded dataset across Germany, derived from a multi-stage regression-based approach. A more detailed description on the air temperature modeling is published elsewhere (Nikolaou et al., 2023). Briefly, several data from multiple sources, including weather station observations and a variety of remote sensing spatiotemporal predictors were incorporated in a modeling procedure which consisted of two linear mixed models and a thin plate spline interpolation technique. The models achieved high accuracy ($R^2 \geq 0.95$) and low errors (Root Mean Square Error (RMSE) ≤ 1.54°C) while validation with a dense and independent monitoring network in Augsburg -the region of the KORA study-confirmed the good performance ($R^2 = 0.99$, RMSE = 1.07°C) (Nikolaou et al., 2023). For the present analysis, we used the annual mean air temperature data from 2018 to match the examination year of most of the participants (69% examined in year 2018). In order to compare exposure effects reflecting more extreme air temperature levels, we additionally analyzed mean air temperature levels of winter and summer by calculating the mean of daily air temperature levels from December to February and from June to August, respectively.

For surrounding greenness, the median normalized difference vegetation index (NDVI) in a Euclidean distance of 300 m, 500 m and 1000 m buffer around participants' residences was available. Briefly, NDVI was extracted and calculated from cloud-free satellite images taken between April and October (Dandolo et al., 2022). Mean values of two different satellites (Landsat 8 and Sentinel-2) were used, which provided images with a resolution of 30 m and 10 m, respectively. Pixels with negative values were excluded prior to assignment (Markevych et al., 2014). Detailed description of the NDVI calculation is given elsewhere (Dandolo et al., 2022; Kabisch et al., 2019). For the present analysis, we used NDVI data from the year 2018, which reflected the main examination year of the KORA Fit sample, and selected the 500 m buffer, which represents a reachable distance within 5–10 min on foot (Smith et al., 2017).

2.4. Study area and degree of urbanization

We used publicly available data on the degree of urbanization in 2020 provided by the EUROSTAT, the statistical office of the European Union (https://ec.europa.eu/eurostat). A basic description of the categorization of municipalities is given elsewhere (European Union, 2018). Briefly, grid cells were defined as high-, moderate- and low-density clusters based on the population density per km (WHO, 2022) and the total number of inhabitants. Municipalities (local administrative units) were then classified as urban, suburban/towns or rural areas based on the proportion of grid cell categories. The KORA study area consists of 77 local administrative units, of which 22 % were classified as urban, 20 % as suburban and 58 % as rural (Supplementary Figure S1).

2.5. Covariate assessment

Participants were asked about sociodemographic characteristics and lifestyle factors in standardized face-to-face interviews. Alcohol consumption was assessed as grams per day derived from participants self-reported consumption of beer, wine and spirits on weekday and weekend. Subjects were classified as never-smokers, ex-smokers or smokers based on their self-reported smoking behavior. Participants' physical activity level was determined by the reported duration of leisure time spent on sport activities. They were classified as active if they spent at least 1 h per week in sports activities during summer and winter, otherwise they were classified as inactive (Conzade et al., 2019). Educational level served as proxy for the individual socioeconomic status. Participants reported their highest level of education attainment, which was categorized based on the International Standard Classification of Education (ISCED) (OECD, 2015). Finally, education was grouped into three categories: low (ISCED levels 0–2), medium (ISCED levels 3–4), and high (ISCED levels 5–8). As an indicator of neighborhood socioeconomic status, the percentage of low-income households (<1250 euro) within a 5 km * 5 km area provided by a private company (WiGeoGIS) for the year 2018 was used.

2.6. Statistical analysis

We performed all analyses with the statistical software R 4.1.2 (R Core Team, 2021). Statistical significance was indicated by two-sided p-values <0.05. Our approach is described in detail in the following sections.

2.6.1. Descriptive

Continuous variables of baseline characteristics and exposure levels are presented as mean and standard deviation (SD), categorical variables are presented as absolute numbers and percentages. For strata differences, we applied two-sample t-tests (or Wilcoxon rank-sum test in case of non-normal distribution) for continuous variables, and Chi (WHO, 2022) test of independence for categorical variables. We performed Spearman's rank correlation to assess correlations between environmental exposures.

2.6.2. Analysis of associations

To estimate sex-specific effects of each environmental exposure on prevalent diabetes and obesity, we applied multivariable logistic regression models with a multiplicative interaction term between exposure and sex. For the continuous obesity measures BMI and WC, we applied multivariable linear regression models including an interaction between exposure and sex. Odds ratios and absolute changes derived from regression models are given for an interquartile range (IQR) increase in environmental exposure with 95% confidence intervals (95% CI). For all linear models, the residuals were normally distributed (data not shown). All models were adjusted for confounders, which we selected a priori using a combined approach of previous studies and knowledge and drawing directed acyclic graphs (DAGs). DAGs help to visualize the interdependence of outcome, exposure, and covariates and help to identify potential bias introduced by confounders and colliders. We used the web-version of the program "DAGitty" (http://www.dagitty.net/), which proposed three minimally sufficient adjustment sets that included only necessary variables to block all backdoor paths (open confounding paths from outcome to exposure), thereby reducing the risk of overadjustment (Pearce and Lawlor, 2016). Our main confounder set consisted of age, lifestyle factors (physical activity, alcohol consumption, smoking), and individual socioeconomic status reflected by educational level (Fig. 1). The other two proposed confounder sets were used in sensitivity analyses.

2.6.3. Effect modification

We split our data by sex to further test for multiple, secondary effect

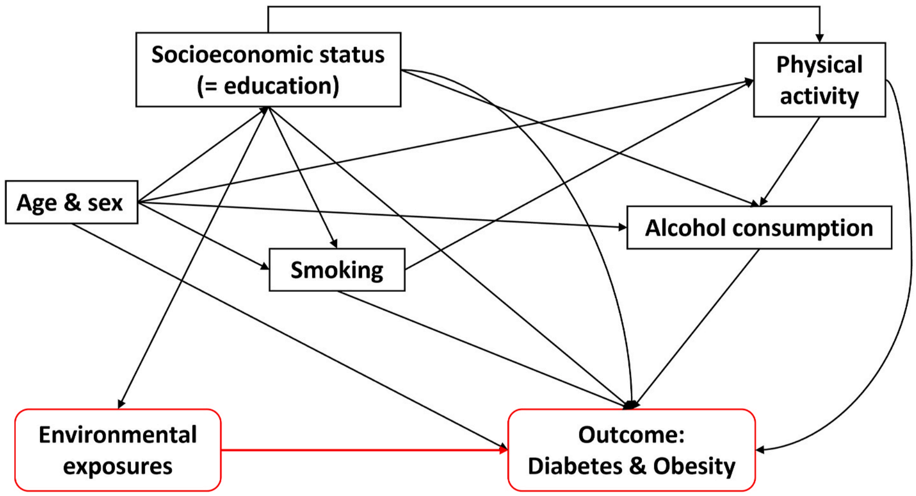

Fig. 1. Directed acyclic graphs presenting hypothesized relationship between exposures, main confounders and the outcomes diabetes and obesity.

modifications found in previous studies by including a multiplicative interaction term with the exposure variable in sex-stratified analyses. We used the following binary effect modifiers: urbanization (urban vs. towns and rural areas), age (≥65 years vs.< 65 years), smoking (never vs. ex- and current smokers), physical activity (yes vs. no), education (low-medium vs. high), and obesity (yes vs. no, only for the outcome diabetes). We only tested for binary effect modifiers in our sex-stratified sample to in order to have enough power in the subgroups. Therefore, for urbanization, we subsumed suburban and rural areas, and for smoking, we subsumed ex-smokers and current smokers together.

2.6.4. Exploratory analysis

We determined the exposure-response function between each outcome and environmental exposure visually by plotting the results of generalized additive models with thin plate splines of exposures fitted to our main model. Based on the results of the single-exposure analysis for obesity, we further evaluated potential confounding and interaction of air pollution and greenness on obesity. Therefore, we applied a two-exposure linear and generalized additive model. Because this exploratory analysis was a consequence of the single-exposure models, we describe the methods in more detail in the Results section for a better understanding of the reasoning.

2.6.5. Sensitivity analysis

We conducted several sensitivity analyses to check the robustness of our findings: (1) we applied linear and logistic regression models with the other two proposed confounder sets and a third set combining all variables of the different sets (see Supplementary Figure S2). Confounder set 2 included marital status instead of physical activity, which can alternatively be used to block one present backdoor path; confounder set 3 included only neighborhood and socioeconomic status blocking all present backdoor paths. (2) We excluded participants who had moved in the last 10 years to reduce potential misclassification of exposure levels. (3) We adjusted for dietary factors instead of education using the "alternative healthy eating index" (described in detail elsewhere (Wawro et al., 2020)) which was only available in a subsample of 702 participants. (4) We excluded physical activity from the adjustment model of our primary analysis to exclude the possibility that physical activity may act as potential intermediate factor in the association of environmental exposures with metabolic disease.

3. Results

3.1. Study population

Our final analytic sample comprised 3034 participants after excluding 13 individuals with missing information on either exposures, outcomes, or covariates (Supplementary Figure S3). Of these, 53.7 % were female (Table 1). The mean age at examination was 63 years and 49.5 % lived in urban and 50.5 % in rural areas at the time of examination. BMI, WC, lifestyle factors, and education level, were significantly different between men and women. Men had on average a higher BMI, WC, and education level, were less physically active and were more often ex-smokers compared to women (Table 1). Men had a higher prevalence of diabetes and obesity based on BMI, whereas women had a higher obesity prevalence defined by WC (diabetes: 9.1 % vs. 7.1 %, obesity (BMI): 31.0 % vs. 29.1 %, obesity (WC): 69.2 % vs. 71.7 %, non-significant).

When we additionally stratified participant characteristics by urbanization, we observed sex and urbanization differences in outcome variables (Supplementary Table S1). For example, the proportion of diabetes was highest in urban men (11.2%) but lowest in urban women (6.9%). BMI-based obesity prevalence was highest in rural women (31.4%) and lowest in urban women (26.8%), whereas it was similar in urban and rural men. In contrast, the distribution of BMI values for men and women did not show a clear urban-rural difference (Supplementary Figure S4).

3.2. Environmental exposures

The annual mean concentrations of NO_2 (13.6 μg/m^3), $PM_{2.5}$ (11.6 μg/m^3), and PM_{10} (16.3 μg/m^3) did not exceed the EU limit values (Table 2). Air pollutants were strongly correlated with each other (range: r = 0.55–0.92), except for ozone. Air temperature variables were moderately to strongly correlated with air pollutants (range: r = 0.39–0.76), except for ozone. Greenness was negatively correlated with air pollutants (range: r = −0.84 to −0.73) and temperature (range: r = −0.64 to −0.53) and weakly positively correlated with ozone (r = 0.09). Exposure concentrations differed significantly between urban and rural areas, with higher levels of air pollutants and temperature and lower levels of greenness in urban areas (Supplementary Figure S5 and Table S2). No sex differences in exposure were found except for $PM_{2.5}$abs (Supplementary Table S2).

Table 1
Characteristics of the study participants.

	Total (n = 3034)	Men (n = 1404)	Women (n = 1630)	p-value
Age [years]	63.2 ± 5.5	63.0 ± 5.6	63.4 ± 5.5	0.046
Degree of urbanization				
Urban	1502 (49.5%)	677 (48.2%)	825 (50.6%)	0.201
Rural	1532 (50.5%)	727 (51.8%)	805 (49.4%)	
Lifestyle factors				
Alcohol [g/day]	14.8 ± 19.5	22.1 ± 23.3	8.5 ± 12.3	<0.001
Smoking status				<0.001
Never	1343 (44.3%)	538 (38.3%)	805 (49.4%)	
Ex-smoker	1258 (41.5%)	670 (47.7%)	588 (36.1%)	
Current Smoker	433 (14.3%)	196 (14.0%)	237 (14.5%)	
Physically active	2182 (71.9%)	977 (69.6%)	1205 (73.9%)	0.009
Individual socioeconomic status				
Education				<0.001
low	93 (3.1%)	19 (1.3%)	74 (4.5%)	
medium	2200 (72.5%)	964 (68.7%)	1236 (75.8%)	
high	742 (24.4%)	421 (30.0%)	320 (19.6%)	
Neighborhood socioeconomic status				
Household with low income [%]	25.0 ± 20.1	24.4 ± 19.8	25.5 ± 20.3	0.236
Marital status				
Married	2369 (78.1%)	1194 (85.0%)	1175 (72.1%)	<0.001
Outcome				
Diabetes mellitus	244 (8.0%)	128 (9.1%)	116 (7.1%)	0.051
Obesity				
defined by BMI	909 (30.0%)	435 (31.0%)	474 (29.1%)	0.271
defined by waist circumference	2141 (71.0%)	972 (69.2%)	1169 (71.7%)	0.145
BMI [kg/m^2]	28.2 ± 5.3	28.6 ± 4.6	27.8 ± 5.9	<0.001
Waist circumference [cm]	94.6 ± 14.3	100.7 ± 8.2	89.3 ± 13.8	<0.001

Legend: Continuous variables are given as arithmetic mean and standard deviation. Categorical variables are given as counts and percentages. Differences between sex were quantified by two-sample *t*-test (if not normally distributed: Wilcoxon test) and Chi^2 test, respectively. BMI-based obesity was defined by BMI ≥30 kg/m^2; WC-based obesity was defined by WC ≥ 94 cm for men and ≥80 cm for women.

3.3. Association of environmental exposures with diabetes – interaction sex

In single-exposure models, the associations of NO_2, PM_{10}, $PM_{2.5}$abs and air temperature with diabetes prevalence showed significant interactions with sex (Table 3). In men, we found positive associations between prevalent diabetes and an IQR increase in air pollutants and air temperature (e.g., NO_2: OR: 1.49 [95% CI: 1.13, 1.95], mean temperature: OR: 1.48 [95% CI: 1.15, 1.90], Table 3), and a borderline significant negative association between diabetes and greenness (OR: 0.78, [95% CI: 0.59, 1.01]). Only ozone was not associated with diabetes prevalence in men. In women, we did not observe any association between environmental exposures and prevalent diabetes (Table 3).

The exposure-response functions did not show any clear deviations from linearity (Supplementary Figure S6 and S7). There were no further interactions with urbanization, age, physical activity, BMI, smoking, education (Supplementary Figure S8).

3.4. Association of environmental exposures with obesity – interaction sex

Apart from ozone and winter temperature, all associations of environmental exposures with BMI showed an interaction with sex (Table 4). The effects of environmental exposures on obesity were opposite for men and women. In men, we found no consistent association of any environmental exposure with obesity (Table 4 for the BMI-based and Supplementary Table S3 for the WC-based definition). However, trends showed higher BMI, WC and increased ORs of obesity with higher air pollution and air temperature. In contrast, higher levels of greenness indicated an inverse association with obesity in men (obesity: OR: 0.87 [95% CI: 0.74, 1.03]; BMI: −0.20 kg/m^2 [95% CI: −0.58, 0.18]). In women, IQR increases in NO_2, NO_x, PM_{10}, PM2$_{.5}$abs, and PNC were significantly associated with lower BMI and lower BMI obesity prevalence (BMI: NO_2: −0.60 kg/m^2 [95% CI: −0.96, −0.23], $PM_{2.5}$abs: −0.57 kg/m^2 [95% CI: −0.95, −0.19]; obesity: NO_2: OR: 0.81 [0.68, 0.95]; PM2.5 abs: OR: 0.80 [95% CI: 0.68, 0.95], Table 4). Additionally, we found significant negative associations between annual $PM_{2.5}$, air temperature, and summer temperature and BMI (Table 4). An increase in greenness resulted in significantly higher BMI (0.63 kg/m^2 [95% CI: 0.29, 0.98]) and was associated with higher obesity prevalence (OR: 1.27 [95% CI: 1.09, 1.48]). The results were similar for WC, but we did not observe any associations with obesity defined by WC (Supplementary Table S3).

We observed deviations from linearity for NO_2, PM_{10}, PM_{coarse}, $PM_{2.5}$abs and greenness with almost u-shaped functions in males and females and NOx and temperature in females only (Supplementary Figures S9 and S10). The exposure-response functions were similar for prevalent obesity and WC (data not shown). In addition, our results pointed to an effect modification by age, indicating partly stronger associations for participants younger than 65 years. However, there was no interaction between environmental exposures and physical activity, smoking or education (Supplementary Figure S11).

3.5. Association of environmental exposures with obesity – interaction urbanization

In line with the non-linear exposure-response functions, we found significant interactions between urbanization and NO_2, PM_{10}, PM_{coarse}, $PM_{2.5}$abs, winter temperature, and greenness in men. For women, the effects were similar but did not reach statistical significance (Fig. 2). Except for ozone, we observed significant positive associations between higher levels of air pollutants, lack of greenness and BMI in urban men. None of these associations were significant for urban women. In rural men and rural women, higher levels of NO_2, PM_{10}, $PM_{2.5}$abs, and temperature were suggestive of lower BMI but did not reach significance. Additionally, higher greenness was associated with higher BMI in rural residents and reached significance in rural women (men: 0.24 kg/m^2 [95% CI: −0.31, 0.79]; women: 0.68 kg/m^2 [95% CI: 0.03, 1.34]).

3.6. Exploratory analysis: two-exposure model for BMI

Based on the contradictive associations, particularly of air pollution and greenness with obesity, we explored potential confounding and interaction effects between these exposures on BMI in rural and urban areas. Firstly, to assess confounding effects, we applied a two-exposure model, adding the air pollution and greenness with an interaction term each for urbanization ($PM_{2.5}$abs by urbanization + greenness by urbanization) in our sex-stratified sample. As a representative for air pollution, we chose $PM_{2.5}$abs, for which the interaction effect with urbanization was strongest in men and women. The effect estimates from single- and two-exposure linear regression models can be compared in Fig. 3. In urban males, the adverse effect of $PM_{2.5}$abs did not change after adjusting for greenness (single: 0.99 kg/m^2 [95% CI: 0.41, 1.57], two-exposure: 0.94 kg/m^2 [95% CI: 0.03, 1.85]), whereas the protective effect of greenness disappeared after adjusting for $PM_{2.5}$abs (Fig. 3).

Table 2
Summary statistics of environmental exposures and Spearman's correlation coefficients.

	Mean ± SD	Median (IQR)	Min; Max	NO_2	NO_x	O_3	PM_{10}	PM_{coarse}	$PM_{2.5}$	$PM_{2.5}$abs	PNC	Annual temp.	Winter temp.	Summer temp.
NO_2 [μg/m^3]	13.6 ± 4.2	13.0 (6.3)	6.9; 28.3	–	–	–	–	–	–	–	–	–	–	–
NO_x [μg/m^3]	21.3 ± 7.0	22.0 (8.7)	3.9; 44.0	0.82	–	–	–	–	–	–	–	–	–	–
O_3 [μg/m^3]	39.1 ± 2.3	39.2 (3.5)	31.7; 45.7	−0.21	−0.17	–	–	–	–	–	–	–	–	–
PM_{10} [μg/m^3]	16.3 ± 1.4	16.0 (2.0)	12.9; 22.0	0.72	0.74	0.00	–	–	–	–	–	–	–	–
PM_{coarse} [μg/m^3]	4.8 ± 1.1	4.8 (1.4)	2.5; 8.2	0.81	0.69	0.17	0.80	–	–	–	–	–	–	–
$PM_{2.5}$ [μg/m^3]	11.6 ± 1.03	11.7 (1.4)	7.8; 14.2	0.74	0.81	−0.24	0.58	0.55	–	–	–	–	–	–
$PM_{2.5}$abs [10^{-5}m^{-1}]	1.2 ± 0.2	1.2 (0.3)	0.7; 1.7	0.86	0.73	−0.10	0.77	0.78	0.69	–	–	–	–	–
PNC [n/cm^3]	6960 ± 1692	6088 (1924)	2962; 13,656	0.75	0.92	−0.10	0.81	0.74	0.70	0.74	–	–	–	–
Annual temperature [°C]	10.2 ± 0.4	10.1 (0.6)	9.2; 11.2	0.74	0.47	−0.30	0.50	0.60	0.54	0.66	0.46	–	–	–
Winter temperature [°C]	1.5 ± 0.3	1.4 (0.4)	0.5; 2.2	0.65	0.40	−0.20	0.45	0.57	0.46	0.56	0.39	0.94	–	–
Summer temperature [°C]	19.0 ± 0.6	18.9 (0.8)	17.9; 20.4	0.76	0.50	−0.32	0.52	0.61	0.57	0.68	0.47	0.99	0.87	–
Greenness (NDVI)	0.4 ± 0.1	0.4 (0.1)	0.2; 0.7	−0.84	−0.79	0.09	−0.73	−0.75	−0.75	−0.81	−0.77	−0.62	−0.53	−0.64

Legend: Exposure levels are described as arithmetic mean and standard deviation (SD). Correlation coefficients were calculated using Spearman's rank correlation.
Abbreviations: SD = Standard deviation; PNC = Particle number concentration; NDVI = Normalized difference vegetation index.

Table 3
Associations of air pollution, air temperature and greenness with prevalent diabetes derived from logistic regression models with an interaction term for sex.

	IQR	Men	Women	$p_{interaction}$
		OR (95% CI)	OR (95% CI)	
NO_2 [μg/m^3]	6.3	1.49 (1.13, 1.95)	0.93 (0.70, 1.24)	0.020
NO_x [μg/m^3]	8.7	1.33 (1.05, 1.69)	0.98 (0.77, 1.25)	0.077
O_3 [μg/m^3]	3.5	0.89 (0.66, 1.18)	1.10 (0.82, 1.46)	0.305
PM_{10} [μg/m^3]	2.0	1.42 (1.11, 1.83)	0.96 (0.73, 1.26)	0.037
PM_{coarse} [μg/m^3]	1.5	1.38 (1.06, 1.79)	0.97 (0.74, 1.25)	0.056
$PM_{2.5}$ [μg/m^3]	1.4	1.41 (1.08, 1.84)	1.01 (0.77, 1.33)	0.091
$PM_{2.5}$abs [10^{-5}m^{-1}]	0.3	1.43 (1.08, 1.89)	0.92 (0.69, 1.23)	0.033
PNC [n/cm^3]	1924	1.30 (1.06, 1.61)	0.99 (0.80, 1.23)	0.075
Annual temperature [°C]	0.6	1.48 (1.15, 1.90)	0.96 (0.74, 1.25)	0.019
Winter temperature [°C]	0.4	1.39 (1.10, 1.75)	0.96 (0.75, 1.22)	0.027
Summer temperature [°C]	0.8	1.50 (1.17, 1.92)	0.97 (0.74, 1.26)	0.018
Greenness (NDVI)	0.1	0.78 (0.59, 1.01)	1.05 (0.80, 1.37)	0.118

Legend: Odds Ratios (OR) were calculated by single-exposure logistic regression models with an interaction term for sex.
Models were additionally adjusted for age, physical activity, alcohol, smoking, and education. ORs are given per interquartile range increase in exposure.
$P_{interaction}$ is the p-value derived from the interaction term between the respective exposure and sex.
Abbreviations: OR = Odds Ratio, 95% CI = 95% confidence interval, PNC = Particle number concentration, NDVI = Normalized difference vegetation index.

However, this pattern was not found in urban women or in rural men and women. Second, we further explored a possible interaction between PM2.5 abs and greenness considering non-linear effects. We aimed to evaluate the hypothesis that the association of air pollution or greenness with BMI is stronger with high or low levels of the other exposure, e.g., if the PM2.5 abs-BMI association is stronger with low levels of greenness and vice versa and if this interaction differs in urban and rural areas. Therefore, we applied a generalized additive model in our sex-stratified sample, where we specified a two-way multiplicative interaction ($PM_{2.5}$abs*greenness by urbanization) considering non-linear effects by modeling a thin plate spline. The sex- and urbanization-specific interaction effect between $PM_{2.5}$abs and greenness was visualized by a 3D surface plot (Fig. 4). While the 3D plot shows a complex surface in a 3D space for urban and rural men and rural women, we observed only a 2D surface standing diagonally in space for urban women, suggesting no interaction between exposures. This suggests a complex interaction between traffic-related air pollution and greenness, which appeared to differ between rural and urban areas and between sex.

3.7. Sensitivity analyses

Our results were robust in the different sensitivity analyses. First, adjusting for marital status instead of alcohol consumption, adjusting for education and neighborhood SES only, or adjusting for all proposed confounders did not change our results (Supplementary Table S4). We observed minor effect changes in models including neighborhood SES for obesity, but not for diabetes. Second, excluding participants who had moved in the last 10 years did not change the results (Supplementary Figure S12). Third, in a subsample adjusting for dietary factors instead of education, effect estimates were similar compared to our main model which we used in the final sample (Supplementary Figure S13). Lastly, our results were robust after excluding physical activity from the adjustment set (Supplementary Table S5).

Table 4
Associations of air pollution, air temperature and greenness body mass index (BMI) and BMI-based obesity derived from logistic or linear regression models with an interaction term for sex.

	IQR	BMI			Obesity (BMI)		
		Men	Women	$p_{interaction}$	Men	Women	$p_{interaction}$
		estimate (95% CI)	estimate (95% CI)		OR (95% CI)	OR (95% CI)	
NO_2 [μg/m³]	6.3	0.21 (−0.20, 0.61)	−0.60 (−0.96, −0.23)	0.004	1.13 (0.95, 1.34)	0.81 (0.68, 0.95)	0.006
NO_x [μg/m³]	8.7	0.17 (−0.16, 0.51)	−0.39 (−0.7, −0.07)	0.016	1.11 (0.96, 1.28)	0.86 (0.75, 0.99)	0.013
O_3 [μg/m³]	3.5	0.00 (−0.42, 0.41)	−0.07 (−0.44, 0.31)	0.822	1.03 (0.86, 1.24)	1.01 (0.85, 1.19)	0.823
PM_{10} [μg/m³]	2.0	0.32 (−0.07, 0.71)	−0.41 (−0.77, −0.06)	0.006	1.21 (1.02, 1.43)	0.82 (0.70, 0.97)	0.001
PM_{coarse} [μg/m³]	1.5	0.16 (−0.22, 0.54)	−0.42 (−0.76, −0.08)	0.024	1.16 (0.98, 1.36)	0.87 (0.75, 1.01)	0.012
$PM_{2.5}$ [μg/m³]	1.4	0.19 (−0.18, 0.56)	−0.34 (−0.69, 0.01)	0.039	1.08 (0.92, 1.27)	0.87 (0.75, 1.02)	0.059
$PM_{2.5}$abs [$10^{-5}m^{-1}$]	0.3	0.30 (−0.11, 0.71)	−0.57 (−0.95, −0.19)	0.002	1.15 (0.96, 1.37)	0.80 (0.68, 0.95)	0.004
PNC [n/cm³]	1924	0.23 (−0.08, 0.54)	−0.29 (−0.57, 0.00)	0.015	1.15 (1.00, 1.31)	0.86 (0.76, 0.98)	0.003
Annual temperature [°C]	0.6	0.19 (−0.19, 0.56)	−0.43 (−0.78, −0.09)	0.017	1.13 (0.96, 1.33)	0.91 (0.78, 1.06)	0.055
Winter temperature [°C]	0.4	0.11 (−0.24, 0.45)	−0.26 (−0.57, 0.06)	0.123	1.10 (0.94, 1.27)	0.96 (0.84, 1.11)	0.216
Summer temperature [°C]	0.8	0.21 (−0.17, 0.59)	−0.52 (−0.86, −0.17)	0.005	1.13 (0.96, 1.34)	0.88 (0.75, 1.02)	0.025
Greenness (NDVI)	0.1	−0.20 (−0.58, 0.18)	0.63 (0.29, 0.98)	0.001	0.87 (0.74, 1.03)	1.27 (1.09, 1.48)	0.001

Legend: Effect estimates and ORs were calculated by single-exposure linear (BMI) and logistic (obesity) regression models with an interaction term for sex. Models were additionally adjusted for age, physical activity, alcohol, smoking, and education. Estimates and ORs are given per interquartile range increase in exposure. $P_{interaction}$ is the p-value derived from the interaction term between the respective exposure and sex.
Abbreviations: OR = Odds Ratio, 95% CI = 95% confidence interval, PNC = Particle number concentration, NDVI = Normalized difference vegetation index.

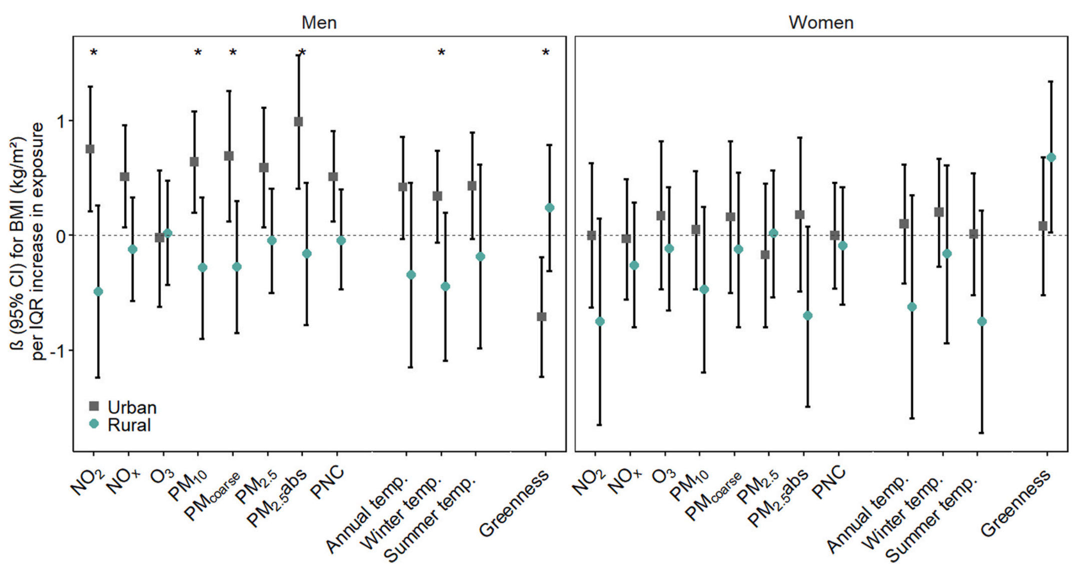

Fig. 2. Associations between BMI and environmental exposures considering effect modification by urbanization in sex-stratified samples. Urbanization-specific effect estimates are given as interquartile range increase in exposure adjusted for age, physical activity, alcohol, smoking, and education. Stars indicate significant interaction with a $p < 0.05$; error bars present 95 % confidence intervals.

4. Discussion

4.1. Summary

The present study analyzed effects of multiple environmental exposures on prevalent diabetes and obesity using cross-sectional data from 3034 middle-aged to older participants from a large population-based cohort. First, we identified higher air pollution and air temperature, and a lack of greenness to be associated with diabetes prevalence in men, but not in women. Second, the associations between environmental exposures and obesity showed a complex interplay with sex and urbanization, suggesting that direction and strength of associations depend on sex and degree of urbanization. Our exploratory analysis suggested a positive association of unfavorable levels of air pollutants and lack of greenness with BMI in urban men, whereas lack of greenness was suggestive of lower BMI in rural women. In addition, we observed a complex interaction between traffic-related pollution and greenness on BMI using a two-exposure model, suggesting that the association of air pollution with obesity may differ with the presence or absence of greenness and vice versa.

4.2. Sex- and urbanization-specific associations of environmental exposures with obesity

We did not expect to see protective effects of higher air pollution, air temperature and lack of greenness on obesity in women, nor did we hypothesize opposite associations of environmental exposures in rural and urban areas. These findings require discussion and further explanation. One explanation for the sex-specific associations could be residual confounding that occurs only in women, such as menopause, for which we could not adjust. Menopause is known to increase visceral fat and central obesity (Chang et al., 2018; Sowers et al., 2007). The age range of our population (53–74 years) reflects predominantly post-menopausal women, supporting the hypothesis that the higher BMI resulted from the transition of pre-to post-menopause.

In addition, we observed differences in obesity prevalence between

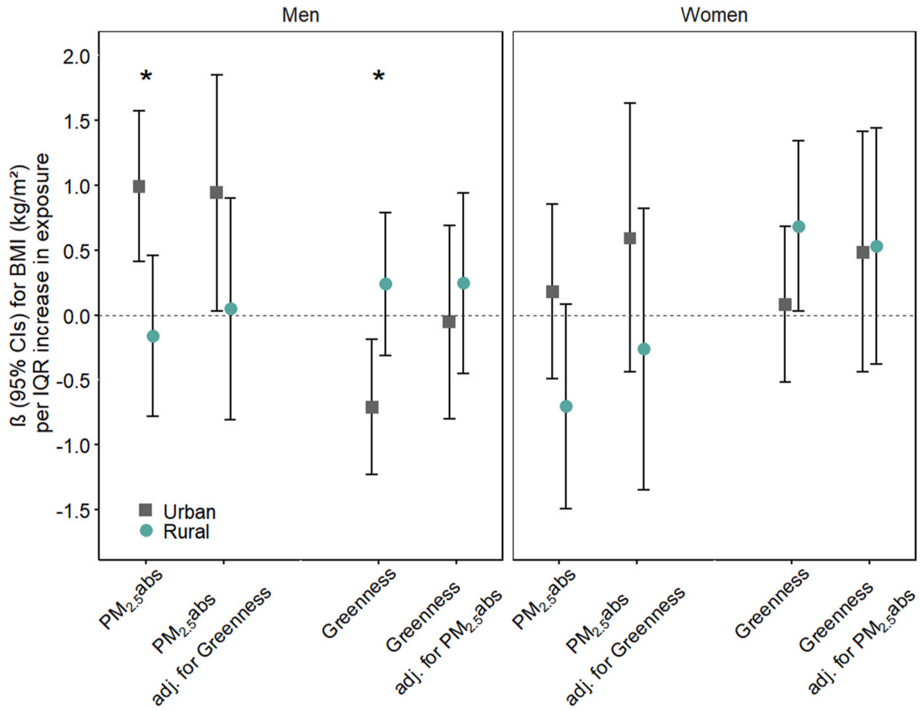

Fig. 3. Associations between BMI and selected environmental exposures from the single-exposure linear model and the two-exposure linear model, including an interaction term between exposures and urbanization. Effects estimates are given as interquartile range increase in exposure for BMI; error bars present 95 % confidence intervals. Abbreviations: adj. = adjusted.

urbanized regions. In our study, rural women were more likely to be obese than urban women, whereas obesity prevalence was similar in urban and rural men. This is consistent with global trends in obesity prevalence, which showed that in high-income countries, obesity prevalence is higher in rural areas than in urban areas; especially among women (NCD Risk Factor Collaboration, 2019). In contrast, environmental exposure concentrations were higher in urban than in rural areas, leading to the suggestive protective effects we observed in rural men and women. Rural areas may have additional factors contributing to obesity risk that we were not able to adjust for in our analyses, thus masking the effect of environmental exposures. For example, rural areas often lack public transportation within walking distance of the residents. This increases the reliance on motorized transport options, such as cars, which are often parked directly in front of homes, reducing walkways and physical activity levels (Wang et al., 2013). Therefore, monitoring the degree of active transportation in future studies could add important evidence on this potential pathway. Moreover, rural populations may have different eating habits including higher meat consumption and more hearty foods (Trivedi et al., 2015). Our results suggest that these obesogenic factors in rural areas may affect men and women unequally, as the suggested protective effects were more pronounced in rural women. This again indicates a complex interdependence of the effects of urbanization and sex on the association between environment and obesity. This is where the concept of sex/gender may come into play, taking into account the different life circumstances and roles of women and men in society, which may differ between urban and rural areas. As the concept of sex/gender is rarely explored in environmental epidemiology (Clougherty, 2010; Bolte et al., 2018, 2019), our findings call for more research in this area to disentangle our conflicting sex-specific associations between environment and obesity.

This complex interaction of both, sex and urbanization were most evident in the association between greenness and BMI. This may be explained by two different reasons. First, green spaces in urban areas are often parks used for recreational purposes. In contrast, high NDVI values occur mainly in rural areas, which are often forests or areas used for pasture or agriculture (Dempsey et al., 2018). Whether this type of greenness has the same positive effects on mental health or physical activity as parks in urban areas needs to be investigated. However, by accounting for urbanization, we may have automatically distinguished between these different vegetation types. This clearly indicates the need for improved measures of greenness to better characterize vegetation types and to be able to disentangle their different health effects. Second, sex-specific effects could also be due to differences in green space usage between men and women. While urban men in our study benefited from higher levels of greenness, this effect was not found for urban women. Recent studies have highlighted sex differences in the use of urban parks, showing that women are less likely to visit parks and to exercise in parks (Derose et al., 2018; Evenson et al., 2019; Lapham et al., 2016). Safety concerns and fear of crime are important factors in park use, and also contribute to sex differences, as women are more likely to have safety concerns (Sowers et al., 2007). Moreover, a study by Astell-Burt et al. (2014) showed that beneficial mental health effects of urban greenness vary over time, indicating an age and sex dependent effect of greenness. While women older than 40 years with moderate degree of greenness benefitted the most, men experienced protective effects in young adulthood (Astell-Burt et al., 2014).

Moreover, we note that the confounding and interaction between traffic-related air pollution and greenness differed by sex and urbanization, further complicating the association between environmental exposures and obesity. The beneficial effect of greenness in urban men seemed to be explained by $PM_{2.5}$abs, while we did not observe any confounding effect in urban women or in rural residents. Based on the interaction analysis in the two-exposure model, we hypothesize that the presence of greenness and air pollution result in different interactions that contribute differently to health risks in urban and rural areas. A possible explanation for these different interactions could be air pollution mitigation by greenness, which depends on vegetation type, tree species, diversity, age and size of the green space (van den Bosch et al., 2024; Nemitz et al., 2020), but to discuss this in detail is beyond the scope of this study. Further studies should explore this interplay of

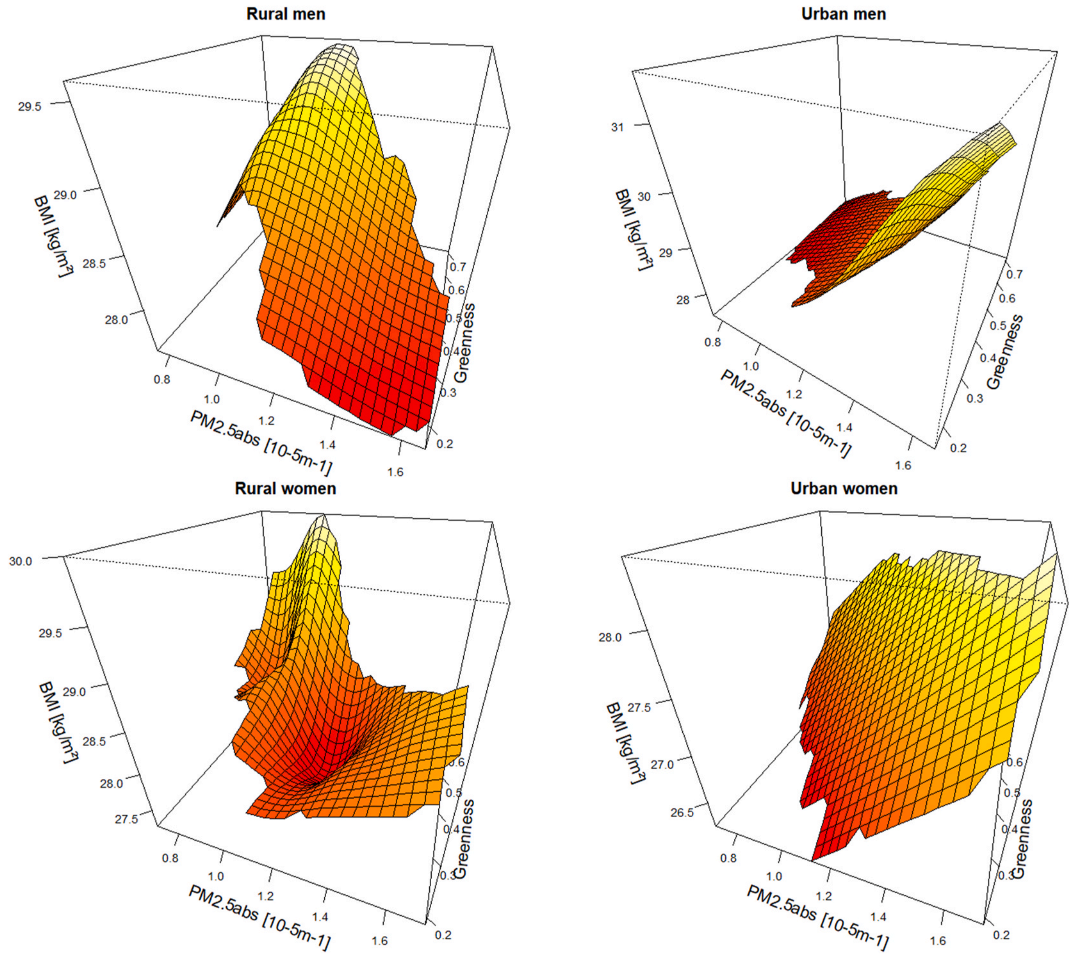

Fig. 4. 3D surface plots of the sex- and urbanization-specific associations between BMI and selected environmental exposures derived from two-exposure model with a thin plate spline and a multiplicative interaction term between $PM_{2.5}$abs and NDVI.

co-occurring environmental factors to corroborate our findings.

4.3. *Comparison to previous literature*

4.3.1. *Air pollution*

As summarized in the review by Rajagopalan and Brook (2012), there is strong evidence from animal studies demonstrating effects of air pollution on metabolism. Inhalation of $PM_{2.5}$ over several weeks resulted in increased insulin resistance, accretion of lipids and fatty degeneration of adipose tissue in mice (Rajagopalan and Brook, 2012). In our study, higher air pollution was associated with a higher diabetes prevalence in human males, which is in line with a previous meta-analysis and a systematic review (He et al., 2017; Yang et al., 2020). He et al. (2017) found a clear effect of $PM_{2.5}$ associated with a 1.25-fold higher risk of diabetes after pooling eleven studies. Furthermore, a meta-analysis in 2020 confirmed this association and additionally reported an increased risk of diabetes with increasing NO_2 and PM_{10} levels (Yang et al., 2020). We add evidence that even more air pollutants, such as NO_x, PM_{coarse}, and PNC appear to be associated with diabetes prevalence in men. An analysis of another German cohort study revealed a 10% higher risk for incident diabetes with increasing PM_{10}, which was more pronounced in men than in women and therefore, consistent with our results (Weinmayr et al., 2015). However, the study was also able to show effect modifications with age, education, and BMI, which we did not find. In addition, another meta-analysis reported potentially stronger effects in women, which contradicts to our results (Wang et al., 2014). Further studies are needed to examine sex-specific associations between environmental exposures and diabetes and to investigate possible biological differences in sex-specific susceptibility.

We found mixed results regarding the association of air pollution with obesity, but previous studies of this association have also been inconclusive. For example, Bowe et al. (2021) reported that $PM_{2.5}$ was associated with a higher weight gain and risk for obesity in a cohort of predominantly male participants, whereas we initially failed to show any association between environmental exposure and obesity in men. Only after controlling for urbanization, we observed similar effects in urban male residents. Furthermore, Bowe et al. (2021) found these associations to be non-linear, their exposure-response functions were positive and indicated a steeper slope for lower $PM_{2.5}$ levels, which is quite different from our findings. Hwang et al. (2019) did not observe any association between NO_2 or PM_{10} and obesity and these results were not modified by sex. In contrast, Li et al. (2015) reported significant associations of NO_2, PM_{10} and O_3 with obesity prevalence in Chinese adults, which remained only significant for women after stratification by sex. Results from the UK Biobank are partially consistent with our mixed findings (Furlong and Klimentidis, 2020). While exposure to PM was generally positively associated with BMI, they observed a negative association for NO_2. In fact, none of these studies tested for an effect modification by urbanization. Only Liu et al. (2021) demonstrated urbanization-specific associations of air pollution with obesity in China, with stronger adverse effects of air pollutants in rural areas compared to urban areas. The authors argued that the air pollutant composition may be more toxic in rural areas. However, these results are in contrast to our findings, where the effects appeared to be protective against obesity in rural areas.

4.3.2. Air temperature

We showed a positive association between air temperature exposure and prevalent diabetes in men. This is in line with previous studies that found a positive association of air temperature with glucose metabolism markers and prevalent diabetes (Valdes et al., 2019; Speakman and Heidari-Bakavoli, 2016). It is possible that lower temperature increases brown adipose tissue which is associated with improved glucose homeostasis and higher energy expenditure (Marlatt and Ravussin, 2017).

In contrast, we found a negative association of higher mean summer temperature with obesity in women and no association with obesity in men. This contradicts the findings of Yang et al. (2015) and Valdes et al. (2014), who observed higher odds for higher mean temperatures in a Korean and a Spanish cohort study. However, Speakman and Heidari-Bakavoli (2016) also could not show an association between temperature and obesity prevalence. In addition, a review claimed that the effect of low temperature on energy metabolism via brown adipose tissue stimulation is rather small (Marlatt and Ravussin, 2017). Moreover, these studies often focused on short-term exposure to low air temperature, therefore it is unclear whether long-term air temperature affects brown adipose tissue and if this leads to improved metabolic health (Marlatt and Ravussin, 2017). It is also possible that the temperature range in our study was too small. Compared to the other studies (Valdes et al., 2014, 2019; Yang et al., 2015; Speakman and Heidari-Bakavoli, 2016), the mean air temperature ranged only from a minimum of 9.2 °C to a maximum of 11.2 °C in our comparable small study area.

4.3.3. Greenness

In good agreement with our findings, a systematic review of seven studies on green spaces and diabetes observed that higher levels of green spaces and shorter distances to green spaces had protective effects on diabetes (De la Fuente et al., 2020). However, these studies did not analyze the effects separately for men and women, therefore, our results add sex-specific evidence on the beneficial effects of greenness on diabetes risk. Our results suggest that men benefitted more from higher greenness around their homes. Explanations such as sex-specific park use were already discussed above.

Comparable to our findings on greenness and obesity, Dempsey et al. (2018) found U-shaped exposure-response functions when investigating NDVI with obesity prevalence in an Irish cohort (Dempsey et al., 2018). As the lowest and highest NDVI quintiles were associated with higher odds of obesity, the authors argued that a lack of detailed characterization of greenness might be the reason, as we have discussed earlier. We provided evidence for this hypothesis by examining the effect modification by urbanization, which may have served as a proxy for differences in greenness. On the other hand, a study from Sweden reported lower odds of central obesity and reduced increase in WC with increasing NDVI levels only in women (Persson et al., 2018), which contradicts our results. However, compared to our sample, women were generally younger (aged 35–56) and exclusively from urban areas, so it could be hypothesized that greenness is less important for middle-aged to older adults.

4.4. Strengths and limitations

Our study has several strengths. First, the KORA-Fit study provides several environmental exposures in the year or prior to the year of the participants' examination. Second, the rich data set allowed us to adjust for multiple confounders and to investigate potential effect modifications. Furthermore, the KORA study region covered urban as well as rural areas, which enabled us to examine urbanization-specific effects. Finally, we were able to perform several sensitivity analyses to demonstrate the robustness of our results.

Nevertheless, several limitations must be acknowledged when interpreting the results of our study. First, we were unable to adjust for dietary factors, which are important independent risk factors for obesity and diabetes (Bellou et al., 2018; Schlesinger et al., 2019). However, our sensitivity analyses within a subpopulation that included dietary factors instead of education did not reveal major differences between models. Second, we could not distinguish between different types of diabetes, e.g., gestational diabetes or type 1 diabetes, because we did not have this information. However, only two participants reported an age at diagnosis of less than 20 years. If these were cases of type 1 diabetes, the effect on the associations would be negligible. Third, we must be cautious in interpreting the results of our exploratory analyses, such as secondary effect modifications and the two-exposure model. Regarding the secondary effect modification by urbanization, our sample size may have been underpowered; therefore, our subgroup analysis should be interpreted as an explanatory analysis and was not designed to formally test for significance. Moreover, because of the high correlation between exposures, the effect estimates resulting from the two-exposure models may be biased due to multicollinearity. Moreover, our study region was too small to show variability in air temperature levels and therefore, may not be able to detect associations with metabolic disease which also kept us from including air temperature in the two-exposure model. Larger studies with more exposure contrast are needed to confirm our findings. In addition, not all environmental factors were available in the year of examination and no longer exposure periods than one-year averages were considered. This may increase the risk of misclassification. However, we did not expect changes in spatial contrasts over the years and sensitivity analysis excluding movers within the last 10 years showed robust results. Lastly, due to a large number of missing data, we could not assess the effect of noise on metabolic disease, which is a relevant environmental risk factor, and few studies have been able to demonstrate an association with metabolic health (Gui et al., 2022; Sorensen et al., 2022; Eze et al., 2017).

5. Conclusion

We investigated the effects of air pollutants, air temperature, and surrounding greenness on metabolic outcomes in a population-based cohort of middle-aged to older adults. We showed that adverse environmental exposures were associated with higher diabetes prevalence in men. In addition, our results indicated a complex interaction of sex and urbanization on the association of environmental exposures with obesity. Finally, air pollution and greenness jointly influenced obesity in a complex manner. Therefore, our findings suggest that possible interactions among environmental exposures should be further investigated by taking into account differences between sex and urbanization, especially for study regions comprising urban and rural areas.

Ethics approval and consent to participate

The investigations were carried out in accordance with the Declaration of Helsinki, including written informed consent of all participants. All study methods were approved by the ethics committee of the Bavarian Chamber of Physicians, Munich [EC No. 17040].

Consent for publication

Not applicable, non-identifiable data only included.

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.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2024.118965.

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