Environmental Research 297 (2026) 124096

Contents lists available at ScienceDirect

Environmental Research

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

Sex-specific individual and joint associations of multiple environmental exposures with diabetes and obesity in the population-based German National Cohort (NAKO)

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https://doi.org/10.1016/j.envres.2026.124096
Received 24 November 2025; Received in revised form 18 February 2026; Accepted 22 February 2026
Available online 24 February 2026

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ARTICLE INFO

Keywords:
Metabolic disease
Environmental epidemiology
Urbanization
Exposure mixture

ABSTRACT

Recent studies have suggested a potential association of particulate matter (PM) and noise with diabetes and obesity, but studies examining other environmental exposures and their sex-specific and joint associations remain limited. Therefore, we investigated sex-specific individual and joint associations of annual exposure to multiple environmental factors with diabetes and obesity-related measures using cross-sectional data from the population-based multi-center German National Cohort (NAKO). Outcomes included self-reported diabetes mellitus, body mass index (BMI), obesity (BMI $\geq$30 kg/m^2), and waist circumference. Annual mean residential exposures included air pollutants, air temperature, day-evening-night road traffic noise (L_{den}) and surrounding greenness (normalized difference vegetation index (NDVI)). We used sex-stratified linear and logistic regression models to assess individual associations and quantile g-computation to assess joint associations. Among 174,955 adult participants (50.4% women), 5.6% reported a diabetes diagnosis and 20.9% were obese. An interquartile range increase in $PM_{2.5}$ and L_{den} was consistently associated with diabetes and obesity-related measures (e.g., $PM_{2.5}$-diabetes for men: odds ratio (OR) [95% confidence interval] = 1.12 [1.02; 1.22]; L_{den}-BMI for women: 0.22 kg/m^2 [0.16; 0.27]). Greenness showed non-linear (inverted U-shaped) with all outcomes. An interquartile range increase in multiple exposures simultaneously was associated with higher odds of diabetes, obesity and higher obesity-related measures (e.g., mixture ($PM_{2.5}$,L_{den}, lack of NDVI)-diabetes: OR = 1.20 [1.09; 1.33] for men; mixture ($PM_{2.5}$,L_{den}, lack of NDVI)-BMI: 0.33 kg/m^2 [0.21; 0.44] for women). While longitudinal studies need to confirm these findings, the study highlights that reducing multiple adverse environmental exposures could be potential targets for the prevention of diabetes and obesity.

Abbreviations

BMI	Body mass index
CI	Confidence Interval
CVD	Cardiovascular disease
DAG	Directed acyclic graph
EIONET	European Environment Information and Observation Network
ELAPSE	Effects of Low-Level Air Pollution: A Study in Europe
END	Environmental Noise Directive
ISCED	International Standard Classification of Education
L_{den}	Day–evening–night road traffic noise level
NAKO	German National Cohort
NDVI	Normalized Difference Vegetation Index
NO_2	Nitrogen dioxide
OR	Odds ratio
PM	Particulate matter
T_{mean}	Mean air temperature
SES	Socioeconomic status
WHO	World Health Organization

1. Introduction

With over 529 million people diagnosed with diabetes mellitus and 650 million affected by obesity (body mass index (BMI) $\geq$ 30 kg/m^2) in early 2020s (Global Burden of Disease, 2021 Diabetes Collaborators, 2023; Sorensen et al., 2022a), metabolic diseases represent a serious public health challenge worldwide. Moreover, obesity constitutes a risk factor for a wide range of other non-communicable diseases, including cardiovascular disease (CVD), cancer, and type 2 diabetes (Bluher, 2019). The incidence of metabolic diseases continues to rise globally (Global Burden of Disease, 2021 Diabetes Collaborators, 2023; Non-Communicable Disease Risk Factor Collaboration, 2024), despite the implementation of behavioral interventions designed to increase physical activity and to improve dietary habits, which are primary strategies in the prevention of metabolic diseases (Bluher, 2019). Low socioeconomic status (SES) has been identified as a crucial risk factor for diabetes and obesity (Schienkiewitz et al., 2022; Hoffmann et al., 2017), which often coincides with further socio-economic and environmental disparities due to more disadvantaged living conditions.

Environmental factors such as air pollution, traffic noise, ambient air temperature or lack of surrounding greenness are crucial health determinants (Global Burden of Disease Risk Factors Collaborators, 2024; Rojas-Rueda et al., 2021). In the latest update of the Global Burden of Disease Study in 2024, air pollution was identified as the most important risk factor attributable to deaths and disability-adjusted life years from diabetes, kidney disease, respiratory disease and CVD (Global Burden of Disease Risk Factors Collaborators, 2024). The World Health Organization (WHO) denoted traffic noise as the second most harmful environmental risk factor, evidencing levels above 53 dB(A) to adverse health effects. (WHO, 2018) As environmental risk factors can partly be controlled at the population level, for example by legally binding limit values for air pollution and traffic noise, or by considering re-vegetation of urban areas, these approaches could constitute powerful and essential public health interventions to prevent diabetes and obesity. Therefore, there is an urgent need to elucidate the potential impact of environmental factors on diabetes and obesity-related measures.

Growing evidence links high levels of air pollution, especially particulate matter (PM), and road traffic noise to diabetes prevalence and incidence (He et al., 2017; Yang et al., 2020a; Wang et al., 2020). However, the evidence on other air pollutants and environmental factors, including air temperature and greenness, are less clear and presently understudied (Valdes et al., 2019; De la Fuente et al., 2020). Furthermore, evidence on the association of environmental factors with obesity-related measures is inconclusive (An et al., 2018; Luo et al., 2020; Gui et al., 2022; Huang et al., 2020). For example, a meta-analysis from 2018 reported that 56% of the included studies did not find adverse associations of air pollution with obesity markers (An et al., 2018). High exposure to air pollutants and noise may contribute to diabetes and obesity by causing systemic inflammation, sleep disturbance, and constant release of stress hormones, while beneficial effects on mental

health and stress reduction are attributed to higher levels of greenness (Rajagopalan and Brook, 2012; Rajagopalan et al., 2024; Munzel et al., 2024; Fong et al., 2018).

In addition, studies have tended to focus on individual exposures, such as air pollution or greenness, rather than examining associations of multiple environmental exposures. This may not adequately capture the true health effects of these environmental factors, as they may confound and interact with each other (Klompmaker et al., 2019). It also ignores the fact that these factors co-exist, especially in urban areas (Nieuwenhuijsen, 2020). Due to the common traffic source, urban areas are often characterized by adverse levels of air pollution and road traffic noise while surrounding greenness is lacking, exposing urban residents to multiple environmental risk factors at the same time. There are only a few previous studies that looked at joint associations of multiple environmental exposures and metabolic diseases (Klompmaker et al., 2019; Sorensen et al., 2022b; Zhang et al., 2024). Although different methods were used, all studies indicated stronger adverse associations when exposures were considered jointly (Klompmaker et al., 2019; Sorensen et al., 2022b; Zhang et al., 2024). As study regions in previous studies were often restricted to urban areas (Pyko et al., 2017; Altug et al., 2024; Yang et al., 2019), there is insufficient evidence on which of these associations can still be observed in more rural and remote areas. Based on our previous analysis using data from another smaller German cohort (KORA-Fit), the associations of air pollutants and greenness with obesity-related measures varied by the degree of urbanization and sex (Niedermayer et al., 2024). As the previous study was limited to a smaller sample size (n = 3034), we aimed to confirm these observations in a larger population. Moreover, we observed interactions by sex, indicating potential sex-specific susceptibility to environmental factors. As biological differences in metabolic regulation between men and women are well established (Kautzky-Willer et al., 2023; Chew et al., 2023), studies explicitly examining sex-specific environmental associations with metabolic related outcomes remain scarce.

Earlier German cohort studies contributed substantially to understanding environmental determinants of health, primarily through single exposure analyses (Peters et al., 1997; Schikowski et al., 2010; Hoffmann et al., 2007). However, these studies lacked spatial variability due to their restricted study regions, and their comparatively small sample sizes reduced statistical power, particularly for subgroup analyses (Wolf et al., 2025). However, the German National Cohort (NAKO), which was initiated in 2014 and comprises more than 200,000 extensively characterized participants, provides a much stronger basis for comprehensive analyses by integrating individual-level data with a broad range of residential environmental exposures, including air pollution, road traffic noise, meteorology, and indicators of the built environment. Therefore, we investigated the sex-specific associations of various environmental exposures in single-exposure and multi-exposure models taking into account urbanicity. We analyzed cross-sectional data from a multi-center, population-based cohort study and addressed the following research questions:

1. How are higher annual levels of environmental exposures associated with diabetes and obesity-related measures in men and women?
2. Are there joint associations of multiple environmental exposures with diabetes and obesity-related measures in men and women?
3. Do these associations vary in urban, suburban and rural areas?

2. Methods

2.1. Study design and population

The German National Cohort (NAKO Gesundheitsstudie) is a nationwide, population-based, multi-center cohort that aims to investigate a range of chronic diseases, their risk factors, and etiology. A detailed description of the NAKO, including information on study design and participant recruitment, can be found elsewhere (Peters et al., 2022; Rach et al., 2025). Briefly, between 2014 and 2019, 205,415 participants aged 19-75 years underwent a baseline examination at one of 18 NAKO study centers within Germany. Participants were recruited in 16 different study center regions in Germany from the general population based on a sex and age-stratified designs (Rach et al., 2025), that comprised urban and rural living environments. Standardized, comprehensive interviews, medical and physical examinations were carried out by trained staff at the study centers. For the present analyses, we used cross-sectional data from 204,687 eligible participants who attended the baseline examination. The NAKO was approved by the local ethics committees and all participants gave written informed consent before study enrollment.

2.2. Outcomes

We used diabetes mellitus, obesity, BMI and waist circumference as outcome variables. The definition of diabetes mellitus was based on self-report. Participants were asked "Have you ever been diagnosed with diabetes mellitus by a physician?" during standardized, computer-assisted interviews at baseline examination (Jaeschke et al., 2020). BMI was calculated from standardized measurements of height and weight by dividing weight by the square of height (kg/m^2) (Fischer et al., 2020). If height and/or weight measurements were missing (<1%), values were filled in with self-reported height and weight information. Obesity was defined as BMI $\geq$30 kg/m^2 (WHO, 2000). Waist circumference was measured according to the WHO guideline using a measuring tape (Seca) placed midway between the lowest rib and the top of the iliac crest (WHO, 2008).

2.3. Exposures

We used the following environmental exposures: annual means of ambient air pollution, ambient air temperature, road traffic noise and greenness (Fig. S1). All environmental factors were assigned to the geocoded residential baseline addresses of participants at the time of the baseline examination. Detailed information on the exposure assessment, linkage, harmonization and data sources used can be found in Wolf et al. (2025).

Briefly, we used air pollution estimates from the ELAPSE (Effects of Low-Level Air Pollution: A Study in Europe) project, which provides annual levels of nitrogen dioxide (NO_2), particulate matter <2.5 μm in diameter ($PM_{2.5}$), and $PM_{2.5}$ absorbance ($PM_{2.5}$ abs), a proxy for black carbon, for Western Europe for the year 2010 (Wolf et al., 2025; de Hoogh et al., 2018). Land use regression models were developed to predict air pollution concentrations, incorporating measurements from ground-level monitoring stations, satellite observations, estimates from chemistry transport models, and further spatial predictors (de Hoogh et al., 2018). These models were then applied to compile country-wide maps with a resolution of 100m*100m (de Hoogh et al., 2018).

Data on annual mean, minimum and maximum air temperature were available for the years 2000-2020 with a resolution of 1 km*1 km. Air temperature measurements from ground-based measurement stations, satellite-derived land surface temperature and spatial factors were combined in a three-stage spatiotemporal model as described by Nikolaou et al. (2023). We assigned each participant the annual mean temperature (T_{mean}) in the examination year.

Road traffic noise data at a scale of 10m*10m for the year 2017 was available from the European Environment Information and Observation Network (EIONET) (Staab et al., 2025; European Comission, 2002). The maps provide day-evening-night levels (L_{den}) categorized into 5 groups: (55: 55-59 dB(A), 60: 60-64 dB(A), 65: 65-69 dB(A), 70: 70-74 dB(A), 75: $\geq$75 dB(A)). Participants with missing data or living in urbanized areas not covered by the Environmental Noise Directive (END) obligation 2002/49/EG Article 3 section k^{47} were set to 40 dB(A) defining a lower detection limit. We calculated mean values of grid cells within a 100m buffer size around residential addresses to obtain continuous

area-weighted noise levels (Wolf et al., 2025).

Lastly, we used the normalized difference vegetation index (NDVI) as indicator of surrounding greenness. Monthly data on a 1 km*1 km grid were gathered from the NASA Terra Moderate Resolution Imaging Spectroradiometer (MODIS), available on a 1 km*1 km grid, for the years 2014 to 2019 (Wolf et al., 2025). Briefly, the NDVI (= reflected radiation in the visible red minus in the near infrared divided by the sum of the two) takes values from −1 to 1. Prior to analysis, water pixels (values < 0) were excluded by masking the data with a mask layer, so values close to 0 indicate grey, less green areas, while values close to 1 indicate dense vegetation (Wolf et al., 2025). We assigned each participant the annual NDVI of the respective grid cell averaged over the vegetation period (March to October) of the examination year to reflect the whole vegetation period of this year.

2.4. Covariables

Information on sociodemographic, lifestyle factors, and SES were assessed by standardized interviews, questionnaires, and physical examinations at baseline. Alcohol consumption is provided as gram per day. Participants were categorized as never, former and current smoker based on their self-reported smoking behavior. Physical activity was assessed by the Global Physical Activity Questionnaire, evaluated according to the WHO analysis guide (Leitzmann et al., 2020). We winsorized implausible values to a maximum of 16 h a day per week (6720 min), and categorized into quintiles. We considered educational levels rather than income to reflect individual SES, as there were fewer missing values in this variable. Educational levels were classified by combining information on school and vocational training according to the International Standard Classification of Education (ISCED) 2011 (UNESCO Institute for Statistics, 2012) and we grouped participants still in education or training into a separate category.

Further geocoded variables assigned to the baseline residential addresses included neighborhood SES, population density and degree of urbanization. Neighborhood SES was represented by the unemployment rate at the district level for 2014 from the Federal Employment Agency (Bundesagentur für Arbeit). Population density, given as inhabitants per square meters within a 1 km buffer of participants' residencies, was available for the year 2018 from a private company (WiGeoGis (GmbH)). Information on the degree of urbanization was downloaded from EUROSTAT (statistical office of the European Union) for the year 2020 (population census data 2018), which provides a categorization of German municipalities into urban, suburban, and rural areas based on the proportion of densely populated grid cells in each municipality (European Union, 2018). We used this information to define the degree of urbanization of participants' municipalities of residence, which we considered as potential effect modifier.

2.5. Statistical analysis

We performed Spearman's rank correlation to assess correlations between environmental exposures and population density.

As our study aimed to report sex-specific associations, we applied linear and logistic regression models stratified by sex, adjusting for age, study center, lifestyle factors, SES and population density for our main analysis. Our basic model included outcome-related risk factors, such as age, smoking, physical activity, alcohol consumption, which explained some heterogeneity between our participants. We stepwise added the following confounders identified by directed acyclic graphs (DAG) (Fig. S2): study center, individual SES, neighborhood SES and population density. As neighborhood and study center region were relatively coarse, we hypothesized that these indicators may not fully capture socioeconomic heterogeneity within urban areas. Therefore, we included population density which may serve as a proxy for built environmental features. Degree of urbanization, however, was not included as a confounder. Instead, it was incorporated exclusively as an effect modifier to examine whether associations differed across levels of urbanicity. In addition, we examined the shape of the exposure-response functions between each exposure and outcome to identify non-linear associations. We fitted cubic splines for the exposure using the *gam* function of the R package *mgcv* (Wood, 2011). If there was a visual detection of non-linearity in the main exposure ranges (10^{th} – 90^{th} percentile), we present plots showing the non-linear exposure-response curve. In order to get a proximation of the association between each exposure range and the turning points, we applied piecewise linear and logistic regression models, which is described in detail in the supplement (supplementary methods S1). Odds ratios (OR) and absolute changes derived from the sex-stratified regression models are reported per interquartile range (IQR) increase in environmental exposure with 95% confidence intervals (95% CI) in the main text. We repeated the single-exposure analysis in the total sample and results are provided in the supplementary material.

Furthermore, we exploratory assessed joint associations of an environmental exposure mixture with diabetes and obesity-related measures in sex-stratified multi-exposure models using quantile g-computation. This method has been described by Keil et al. (2020) and is suitable for the environmental exposure setting (Zhang et al., 2024; Chen et al., 2024; Stevens et al., 2023). Briefly, exposures of interest are standardized and categorized into a predefined increment, such as quartiles. In a supervised approach, exposures are ranked according to their importance and contribution to the outcome of interest and a weighted sum index is created. The outcome is regressed on this single index so that the joint association can be interpreted as the change in outcome if all exposures were simultaneously increased by one pre-defined increment. Since our noise variable could not be divided into quartiles due to tied values in the lowest quartile, we turned off the quantization and standardized all environmental exposures by dividing them by their IQR. Consequently, the joint associations from the quantile g-computation approach can be interpreted as the change in outcome if all exposures were simultaneously increased by one IQR. In addition, the weights indicate the proportion to which an exposure contributes to the positive or negative joint association. We implemented quantile g-computation using the R package *qgcomp* (Keil et al., 2020) and considered two different exposure mixture sets: (1) including exposures that showed significant associations in single-exposure models, (2) including all exposures. The inverse of NDVI was used because it was negatively correlated with air pollution, air temperature and road traffic noise and because we expected negative associations with diabetes and obesity-related measures. In addition, we ran two sensitivity analyses for each exposure mixture set. (1) We dropped the exposure that displayed non-linear exposure-response functions from the exposure mixture set. (2) We used natural cubic splines for exposures that displayed non-linear exposure-response functions in single-exposure regression models. However, we need to note that for these exposure mixtures including splines, the method cannot derive weights attributed to each exposure. We also ran two-exposure models, mutually adjusting each environmental factor for another, to assess the independence of associations. Therefore, we paired exposures with Spearman correlation coefficients <0.7 to avoid multicollinearity.

We further assessed effect modification by adding an interaction term between exposure and degree of urbanization (urban/suburban/rural). In addition, we analyzed regression models stratified by study center region to identify between-center heterogeneity among associations.

We assessed the robustness of our results by performing several sensitivity analyses. Firstly, we used different adjustment sets: (1) we additionally adjusted for income and partnership, (2) we did not adjust for physical activity, as this could be a mediator in the association of NDVI with diabetes and obesity (De la Fuente et al., 2020), (3) we included BMI as a potential mediator in single-exposure models with diabetes as the outcome, in order to reflect the direct rather than total association between exposure and diabetes. Secondly, we excluded

participants who had self-reported a cancer or diabetes diagnosis when considering obesity-related outcomes. Thirdly, we excluded participants who reported living at the current residential address for less than five or ten years. Finally, we applied different definitions of diabetes on the associations: (1) we excluded all women who reported a diagnosis of diabetes onset during pregnancy (gestational diabetes) (n = 1157); (2) we excluded cases with probable type 1 diabetes (defined as age of diagnosis ≤30 years according to the DIAB-CORE (Schunk et al., 2012)), (3) we excluded cases which had only reported a diabetes diagnosis, but not the use of anti-diabetic medication.

All analyses were done with RStudio Version 4.3.1, and p-values <0.05 indicated statistical significance. All analyses were performed separately for each outcome.

3. Results

3.1. Sample characteristics

After excluding all individuals with missing data on any outcome, exposure or main covariates, our final analytic sample consisted of 174,955 participants (Fig. S3), of whom 50.4% were women, the mean age was 49.5 years, and more than 70% lived in urban areas (Table 1). In the present sample, 6.2% of the men and 5.0% of women reported a diabetes diagnosis, with a mean age at diagnosis of 50 and 45 years, respectively. For men, the mean BMI and waist circumference were 27.2 kg/m^2 and 96.5 cm, respectively, and 22% were obese. For women, the mean BMI and waist circumference were 26.0 kg/m^2 and 85.6 cm, respectively, and 19.8%, were obese. Women reported lower alcohol consumption, were less likely to be ex- or current smokers had lower levels of physical activity, were less likely to have a university degree and lived in more densely populated areas compared to men (Table 1). A comparison of the characteristics of the excluded and included participants can be seen in Table S1.

Environmental exposure levels were similar for men and women but differed according to the study region. Mean levels of NO_2, $PM_{2.5}$ and $PM_{2.5}$ abs were 26.8 μg/m^3, 17.3 μg/m^3, and 1.6 10^{-5} m^{-1}, respectively (Table S2). Mean air temperature was 10.9 °C, and the participants were exposed to a mean road traffic noise level of 44.6 dB(A) and a mean surrounding greenness cover of 0.5. Correlations were positive between air pollution, air temperature, and noise (r = 0.35 to 0.84), NDVI was negatively correlated with all other environmental exposures (r = −0.59 to −0.34) (Table S2). L_{den} showed the weakest correlation with $PM_{2.5}$ among the air pollutants (r = 0.35, compared with r = 0.61 for NO_2 and r = 0.56 for $PM_{2.5}$abs) and was only modestly negatively correlated with NDVI (r = −0.34).Population density was positively correlated with air pollution, air temperature, and noise (r = 0.42 to 0.72) and negatively with NDVI (r = −0.64).

3.2. Single-exposure models

Exposure-response functions showed linear forms in the main exposure ranges (10^{th} – 90^{th} percentile) for air pollution, temperature, and noise (Figs. S4–S7) with diabetes and obesity-related measures, therefore we show linear effect estimates (Tables 2–3). Estimates changed strongest when population density were included in the model, followed by study center region, and education (Tables S3–S4).

For men and women, an IQR increase in annual $PM_{2.5}$ was associated with higher odds of diabetes (e.g., men: OR = 1.12 [95% CI: 1.02; 1.22], women: OR = 1.11 [1.01; 1.22]; per 2.9 μg/m^3 increase). An association of higher NO_2 and $PM_{2.5}$abs was only found for diabetes in men (OR ranged from 1.08 to 1.10; Table 2). For women only, T_{mean} was associated with higher odds of diabetes, while an increase of 8.3 dB(A) in annual L_{den} was associated with 1.08-fold and 1.05-fold higher odds of diabetes in men and women, respectively. With regard to the obesity-related measures, an IQR increase in annual $PM_{2.5}$ was associated with higher obesity-related measures (Tables 2 and 3). For example, higher

Table 1
Participants' characteristics in the final analytical sample of the German National Cohort (NAKO), overall and stratified by sex.

	Overall (n = 174,955)	Men (n = 86,710)	Women (n = 88,245)
Sex, female n (%)	88,245 (50.4)	-	88,245 (100.0)
Age (years), mean (SD)	49.5 (12.8)	49.6 (12.8)	49.5 (12.7)
Diagnosis of diabetes, yes n (%)	9,747 (5.6)	5,352 (6.2)	4,395 (5.0)
Age at diabetes diagnosis, mean (SD)	47.6 (13.1)	49.9 (12.0)	44.9 (13.8)
Antidiabetic medication, n (%)	6,695 (3.8)	4,221 (4.9)	2,474 (2.8)
Obesity (≥ 30 kg/m^2) yes n (%)	36,579 (20.9)	19,096 (22.0)	17,483 (19.8)
Body Mass Index (kg/m^2), mean (SD)	26.6 (5.0)	27.19 (4.5)	26.0 (5.5)
Waist circumference (cm), mean (SD)	91.0 (14.3)	96.5 (12.9)	85.6 (13.5)
Physical activity (min/week), mean (SD)	1,440 (1,583)	1,466 (1,621)	1,415 (1,544)
Quintiles of physical activity, n (%)			
Q1	30,679 (17.5)	15,560 (17.9)	15,119 (17.1)
Q2	35,860 (20.5)	17,915 (20.7)	17,945 (20.3)
Q3	36,717 (21.0)	17,790 (20.5)	18,927 (21.4)
Q4	36,009 (20.6)	17,820 (20.6)	18,189 (20.6)
Q5	35,690 (20.4)	17,625 (20.3)	18,065 (20.5)
Alcohol consumption (g/day), mean (SD)	10.6 (16.7)	14.08 (19.4)	7.1 (12.6)
Smoking behavior, n (%)			
Never-smoker	81,151 (46.4)	36,374 (41.9)	44,777 (50.7)
Ex-smoker	56,988 (32.6)	30,547 (35.2)	26,441 (30.0)
Current smoker	36,816 (21.0)	19,789 (22.8)	17,027 (19.3)
Education (ISCED 2011), n (%)			
Primary	687 (0.4)	338 (0.4)	349 (0.4)
Lower secondary	3,527 (2.0)	1,274 (1.5)	2,253 (2.6)
Upper secondary	55,430 (31.7)	25,185 (29.0)	30,245 (34.3)
Post-secondary non-tertiary	15,700 (9.0)	6426 (7.4)	9274 (10.5)
Bachelor's	55,324 (31.6)	30,492 (35.2)	24,832 (28.1)
Master's	32,657 (18.7)	16,275 (18.8)	16,382 (18.6)
Doctoral	7,695 (4.4)	4,750 (5.5)	2,945 (3.3)
Still in education or training	3,935 (2.2)	1,970 (2.3)	1,965 (2.2)
Income (Euros), mean (SD)	3,721 (2,493)	3,975 (2,667)	3,466 (2,276)
Partnership, n (%)			
Single	32,807 (18.8)	14,051 (16.2)	18,756 (21.3)
Living with partner	124,039 (71.0)	63,983 (73.9)	60,056 (68.1)
Partner but living separately	17,894 (10.2)	8576 (9.9)	9318 (10.6)
Unemployment rate at district level (%), mean (SD)	8.62 (3.21)	8.60 (3.22)	8.63 (3.21)
Population density (n/m^2), 1 km buffer, mean (SD)	4652 (4363)	4628 (4350)	4675 (4375)
Degree of urbanization at municipality level, n (%)			
Urban	124,979 (71.4)	62,004 (71.5)	62,975 (71.4)
Suburban	27,923 (16.0)	13,771 (15.9)	14,152 (16.0)
Rural	22,045 (12.6)	10,933 (12.6)	11,112 (12.6)

*Q1: ≤210 min/wk for men, ≤200 min/wk for women, Q2: >210 - ≤ 540 min/wk for men, >200 - ≤ 530 min/wk for women, Q3: >540 - ≤ 1130 min/wk for men, >530 - ≤ 1110 min/wk for women, Q4: >1130 - ≤ 2490 min/wk for men, >1110 - ≤ 2370 min/wk for women, Q5: >2490 – 6720 min/wk for men, >2370 – 6720 for women. Abbreviations: ISCED = International Standard Classification of Education, N = number, SD = standard deviation.

Table 2
Associations of environmental exposures with existing diabetes and obesity from single-exposure logistic regression models in the German National Cohort (NAKO).

Exposure	IQR	Self-reported diagnosis of diabetes		Obesity (BMI ≥30 kg/m²)	
		Men (n = 86,710)	Women (n = 88,245)	Men (n = 86,710)	Women (n = 88,245)
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
NO_2 [μg/m³]	10.6	1.10 (1.02; 1.19)	1.04 (0.96; 1.13)	1.05 (1.01; 1.10)	1.05 (1.01; 1.10)
$PM_{2.5}$ [μg/m³]	2.9	1.12 (1.02; 1.22)	1.11 (1.01; 1.22)	1.07 (1.02; 1.13)	1.10 (1.04; 1.16)
$PM_{2.5}$abs [$10^{-5}m^{-1}$]	0.5	1.08 (1.01; 1.15)	1.03 (0.96; 1.11)	1.01 (0.97; 1.05)	0.98 (0.95; 1.02)
T_{mean} [°C]	1.1	0.96 (0.90; 1.04)	1.10 (1.02; 1.19)	0.98 (0.94; 1.02)	1.00 (0.96; 1.04)
L_{den} (100m) [dB(A)]	8.3	1.08 (1.03; 1.13)	1.05 (1.00; 1.10)	1.07 (1.04; 1.09)	1.08 (1.05; 1.11)

Legend: All models were adjusted for age, study center region, physical activity, alcohol consumption, smoking behavior, education, unemployment rate at district level and population density. ORs and confidence intervals are given per IQR increase in exposure. Diabetes was reported in n = 5352 men and n = 4395 women, and n = 19,096 men and n = 17,483 women were obese. Abbreviation: BMI = Body Mass Index, CI = confidence interval, IQR = interquartile range; L_{den} = day–evening–night noise level, NO_2 = nitrogen dioxide, OR = odds ratio, $PM_{2.5}$ = particulate matter with diameter <2.5 μm; $PM_{2.5}$abs = $PM_{2.5}$ absorbance, T_{mean} = annual mean temperature.

Table 3
Associations of environmental exposures with BMI and waist circumference from single-exposure linear regression models in the German National Cohort (NAKO).

Exposure	IQR	BMI		Waist circumference	
		Men (n = 86,710)	Women (n = 88,245)	Men (n = 86,710)	Women (n = 88,245)
		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
NO_2 [μg/m³]	10.6	0.06 (−0.02; 0.13)	0.13 (0.04; 0.22)	0.24 (0.04; 0.44)	0.25 (0.04; 0.47)
$PM_{2.5}$ [μg/m³]	2.9	0.11 (0.02; 0.20)	0.18 (0.07; 0.29)	0.40 (0.16; 0.64)	0.48 (0.21; 0.74)
$PM_{2.5}$abs [$10^{-5}m^{-1}$]	0.5	−0.02 (−0.09; 0.04)	−0.01 (−0.08; 0.07)	0.01 (−0.16; 0.18)	−0.05 (−0.24; 0.14)
T_{mean} [°C]	1.1	−0.06 (−0.12; 0.01)	−0.07 (−0.15; 0.01)	−0.25 (−0.43; −0.07)	−0.28 (−0.48; −0.08)
L_{den} (100m) [dB(A)]	8.3	0.11 (0.06; 0.15)	0.22 (0.16; 0.27)	0.26 (0.15; 0.38)	0.46 (0.34; 0.59)

Legend: All models were adjusted for age, study center region, physical activity, alcohol consumption, smoking behavior, education, unemployment rate at district level and population density. Betas and confidence intervals are given as IQR increase in exposure. Abbreviation: BMI = Body Mass Index, CI = confidence interval, IQR = interquartile range, L_{den} = day–evening–night noise level, NO_2 = nitrogen dioxide, $PM_{2.5}$ = particulate matter with diameter <2.5 μm, $PM_{2.5}$abs = $PM_{2.5}$ absorbance, T_{mean} = annual mean temperature.

annual $PM_{2.5}$ was associated with 0.11 kg/m² and 0.18 kg/m² higher BMI and 0.40 cm and 0.48 cm higher waist circumference in men and women, respectively. Except for T_{mean} and waist circumference, the associations were close to unity for NO_2, $PM_{2.5}$abs and T_{mean} for men and women. Higher annual L_{den} was associated with higher obesity-related measures for both men and women (e.g., men: 0.11 kg/m² [0.06; 0.15], 0.26 cm [0.15; 0.38]; women: 0.22 kg/m² [0.16; 0.27], 0.46 cm [0.34; 0.59]; per 8.3 dB(A) increase). Effect estimates for the total sample are provided in Table S5.

A deviation from linearity was observed for NDVI with all outcomes, suggesting an inverted U-shaped function and a turning point around the median (0.55) (Fig. 1). Thus, indicating that low NDVI (below the median) and high NDVI (above the median) were associated with lower odds of diabetes, obesity, and lower BMI and waist circumference in men and women (Fig. 1). The inverted u-shape was independent of the adjustment model (data not shown) and also observed in the total sample (Fig. S8).

3.3. Joint associations of environmental exposure mixtures

For diabetes, we observed positive joint associations for men and women (Table S6). Considering an IQR increase in annual $PM_{2.5}$, L_{den} and an IQR decrease in NDVI simultaneously, these exposures were associated with ORs of 1.20 [1.09; 1.33] and 1.13 [1.01; 1.27] for diabetes in men and women, respectively (Fig. 2). For men, the positive joint association was equally driven by all three exposures. In women, it was driven by $PM_{2.5}$ (70% of the positive weight attributed) (Fig. 2). Although the magnitudes are not directly comparable, ORs from quantile g-computation indicated joint associations of similar or slightly larger magnitude than the single-exposure associations (e.g., ORs in single-exposure models ranged from: 1.08 - 1.12 per IQR increase). When all six environmental exposures were considered, the joint association was attenuated but remained because T_{mean}, NO_2 and $PM_{2.5}$abs contributed to the negative side, especially for men (Table S6; Fig. S9). Multi-exposure sets that excluded NDVI also showed similar, albeit slightly weaker, ORs for exposure mixture effects (Table S6). As NDVI displayed non-linear associations in the single-exposure models, we used natural cubic splines for NDVI in the two different mixture sets. However, this resulted in large confidence intervals and changes in the estimates (Table S6).

For BMI, a IQR increase in annual $PM_{2.5}$, L_{den} and lack of NDVI was jointly associated with 0.12 kg/m² [0.03; 0.21] and 0.33 kg/m² [0.21; 0.44] higher BMI in men and women, respectively (Fig. 2). For men and women, this joint association was mainly driven by L_{den}, which accounted for more than 50% of the total positive association, followed by $PM_{2.5}$. Similarly, joint ORs of obesity and increases in BMI and waist circumference associated with an IQR increase across the exposure mixtures had a similar or slightly larger magnitude than those from the single-exposure models. When all six environmental exposures were considered, the joint association was attenuated but remained except for BMI in men (Table S6, Fig. S9). Excluding $NDVI_{inverse}$ from the exposure mixture sets did not markedly alter the joint associations (Table S6). Using splines for NDVI, we observed changes in the estimates and large CI that lead to null findings (Table S6). Similar results were observed for waist circumference and obesity (Table S6).

Two-exposure models confirmed the main contribution of L_{den}, as additional adjustments for other environmental exposures did not change the associations of L_{den} with diabetes or obesity-related measures (Fig. S10). In contrast, associations of air pollutants attenuated after adjustment for L_{den} (Fig. S10).

3.4. Exploratory analysis

3.4.1. Effect modification by degree of urbanization

Baseline characteristics stratified by sex and degree of urbanization can be found in Table S7. Briefly, we observed a higher frequency of diabetes and obesity in rural areas than in urban areas among men and women. For diabetes, interactions between degree of urbanization and exposures were observed for men (Fig. S11). In suburban and rural areas, higher annual air pollution was positively associated with diabetes in men. In addition, higher annual L_{den} in urban areas was associated with 1.05-fold and 1.06-fold higher odds of diabetes for men and women. For obesity-related measures, interactions between degree of urbanization and exposures were observed for men and women (e.g., BMI in Fig. 3). In urban and suburban areas, an IQR increase in annual

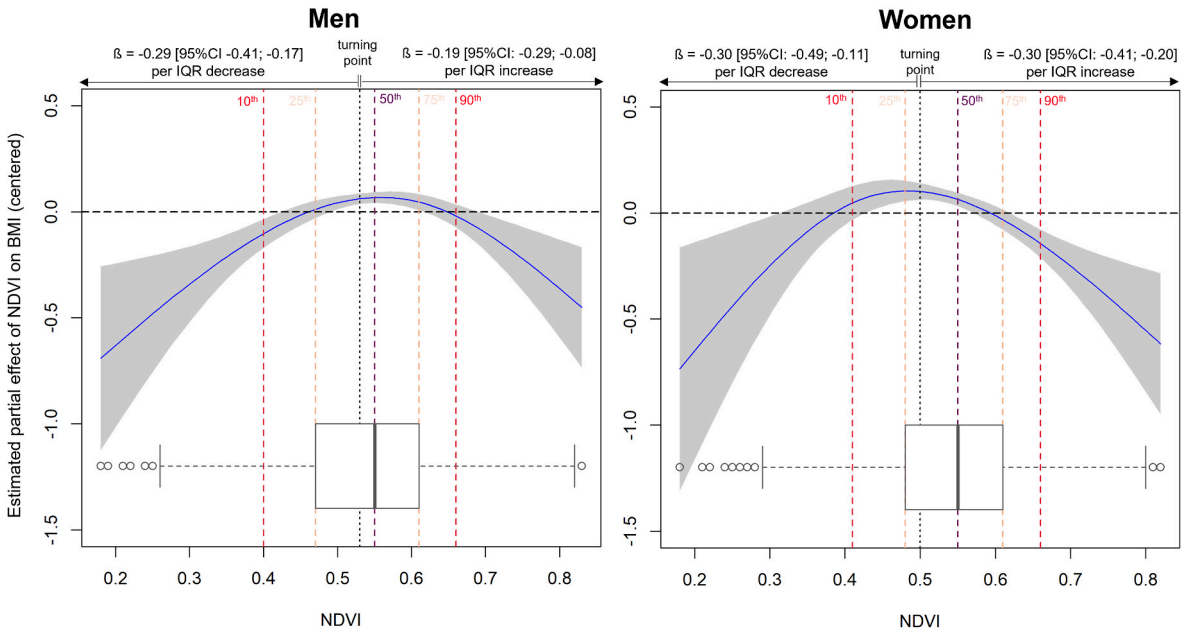

Fig. 1. Non-linear associations between NDVI and BMI in n = 86,710 men and n = 88,245 women from the German National Cohort (NAKO). Legend: Boxplots present distribution of exposure, vertical lines indicate NDVI percentiles (red, yellow, purple) and turning point (black). Models were fitted by cubic splines for the exposure and were additionally adjusted for age, study center region, lifestyle factors, education, unemployment rate at district level and population density. The betas and 95%-CI are given per IQR of 0.14 decrease in NDVI below the turning point (≤0.53 for men, ≤0.50 for women) and per IQR of 0.14 increase in NDVI above the turning point (>0.53 for men, >0.50 for women) derived from piecewise linear regression models. Abbreviations: BMI = Body Mass Index, CI = confidence interval, IQR = interquartile range, NDVI = Normalized difference vegetation index. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

air pollutants and L_{den} were associated with higher BMI, waist circumference and obesity in men and women. In rural areas, we found no association of environmental factors with obesity-related measures except for NO_2 in women. Non-linear associations between NDVI and obesity-related measures were driven by urban areas (e.g., BMI in Fig. S12).

3.4.2. Study center region-specific findings

The number of participants per study center region can be found in the Table S8. Radar plots showed different distribution patterns of environmental factors, BMI and population density across the study center regions (Fig. S13). Study center regions with a higher proportion of rural areas and lower population density had on average higher BMI and NDVI, but lower levels of air pollution, T_{mean} and L_{den} (e.g., Augsburg, Neubrandenburg, Saarbrücken, Regensburg). Study center regions with a large proportion of urban areas and high population density were characterized by lower mean BMI and NDVI, but higher air pollution and L_{den} (e.g., Berlin, Düsseldorf, Hannover, Mannheim). We observed a large heterogeneity in the associations when stratified by study center region (Figs. S14–15).

3.5. Sensitivity analyses

In sensitivity analyses, associations were robust. Using different confounder adjustment sets, consistent associations between adverse $PM_{2.5}$ levels and L_{den} were observed for all outcomes (Tables S9–10). The associations with obesity outcomes did not change when we excluded existing diabetes and cancer cases (Table S11). When restricting the sample to those living at least five or 10 years at their residencies, associations were robust (Tables S12–S13). For women, the associations were slightly stronger after excluding cases with gestational diabetes or cases which had only reported a diabetes diagnosis, but not the use of anti-diabetic medication (Table S14). For men, the associations slightly attenuated after excluding probable type 1 diabetes cases (Table S14).

4. Discussion

4.1. Summary and key points

In the current analyses, we assessed the associations of multiple environmental exposures with existing diabetes, obesity, BMI, and waist circumference using cross-sectional data from 174,955 participants of the multi-center NAKO study. We found consistent associations linking $PM_{2.5}$ and road traffic noise to diabetes and obesity-related measures, especially in urban and suburban areas. NDVI showed an inverted U-shaped exposure-response with diabetes and obesity-related measures. Environmental exposure mixtures, when considering an IQR increase across all exposures or only $PM_{2.5}$, road traffic noise and lack of greenness, were associated with higher joint odds of diabetes, obesity and higher BMI and waist circumference, assuming additivity. The interaction with degree of urbanization and the study center-specific heterogeneity suggested further variation and unknown factors contributing to diabetes and obesity risk in urban, suburban and rural areas.

4.2. Comparison to previous studies

4.2.1. Air pollution

Our findings on the association of adverse levels of $PM_{2.5}$ with metabolic diseases align with previous studies and analyses. Several meta-analyses found an overall association with PM and diabetes and obesity markers, whereas associations with other air pollutants such as NO_2, PM_{10}, or ozone were mixed (He et al., 2017; Yang et al., 2020a, 2020b; An et al., 2018; Huang et al., 2020). In our study, we show that the associations of NO_2 were reversed in two-exposure models, suggesting that $PM_{2.5}$ may have confounded the associations. In contrast, studies with higher levels of NO_2 or other air pollutants have observed positive associations with diabetes and obesity-related measures (Pan et al., 2023; Han et al., 2023; Li et al., 2022). This suggest that our findings may not be generalizable to highly pollutant areas. Nevertheless, annual mean residential levels of NO_2 and $PM_{2.5}$ exceeded the WHO

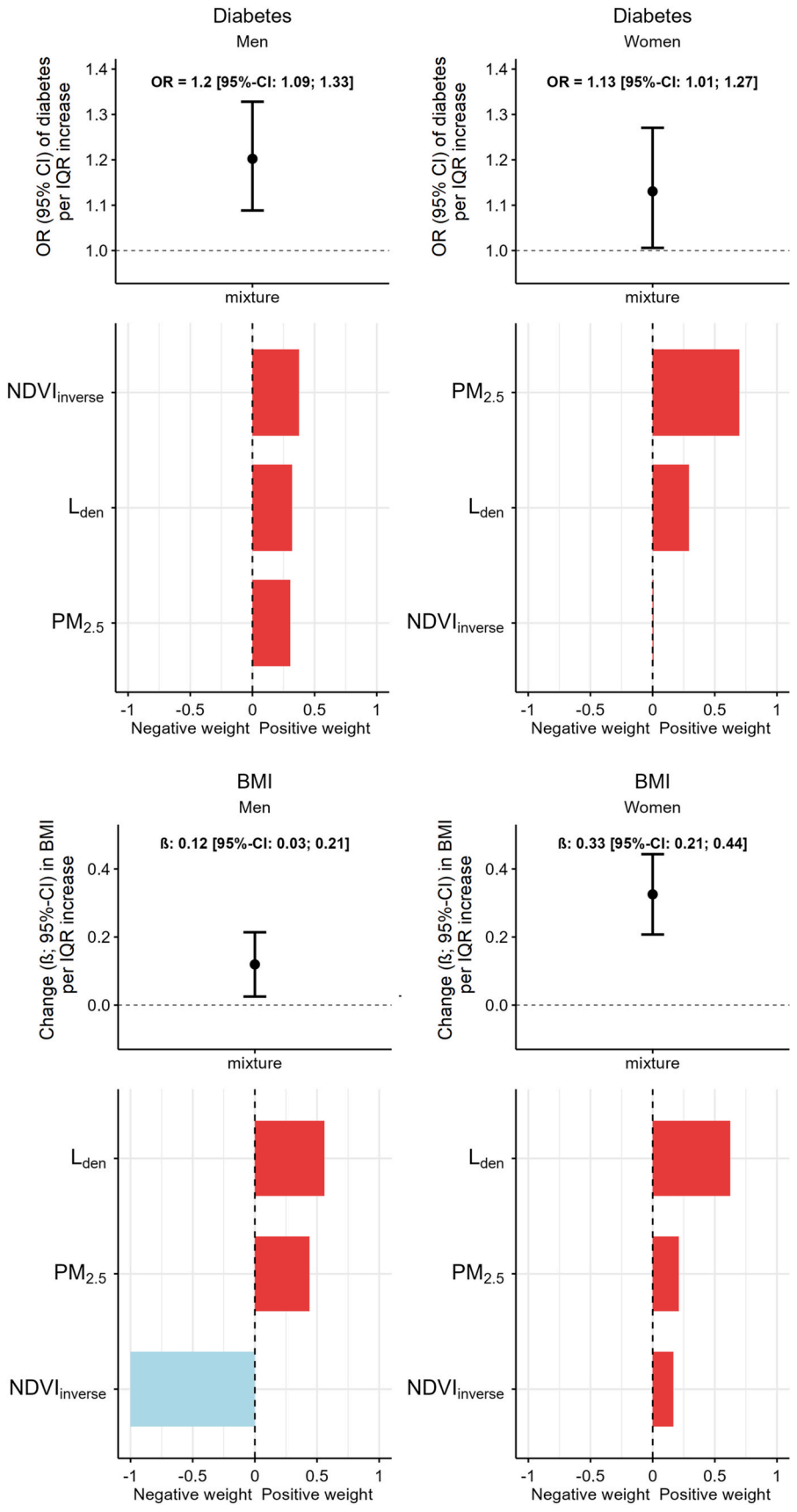

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Fig. 2. Joint associations of exposure to environmental mixture with diabetes and BMI for n = 86,710 men and n = 88,245 women from the German National Cohort (NAKO). Legend: Joint odds ratios and betas are given per IQR increase across all exposures derived from multi-exposure quantile g-computation models. We used the inverse of NDVI; and bars represent exposure weights, indicating the proportion of each exposure contributing to the overall positive and negative association. Models were additionally adjusted for age, study center region, lifestyle factors, education, unemployment rate at district level and population density. Abbreviations: BMI = Body Mass Index, CI = confidence interval, IQR = interquartile range, L_{den} = day–evening–night noise level, NDVI = normalized difference vegetation index, OR = Odds ratio, $PM_{2.5}$ = particulate matter with diameter <2.5 μm.

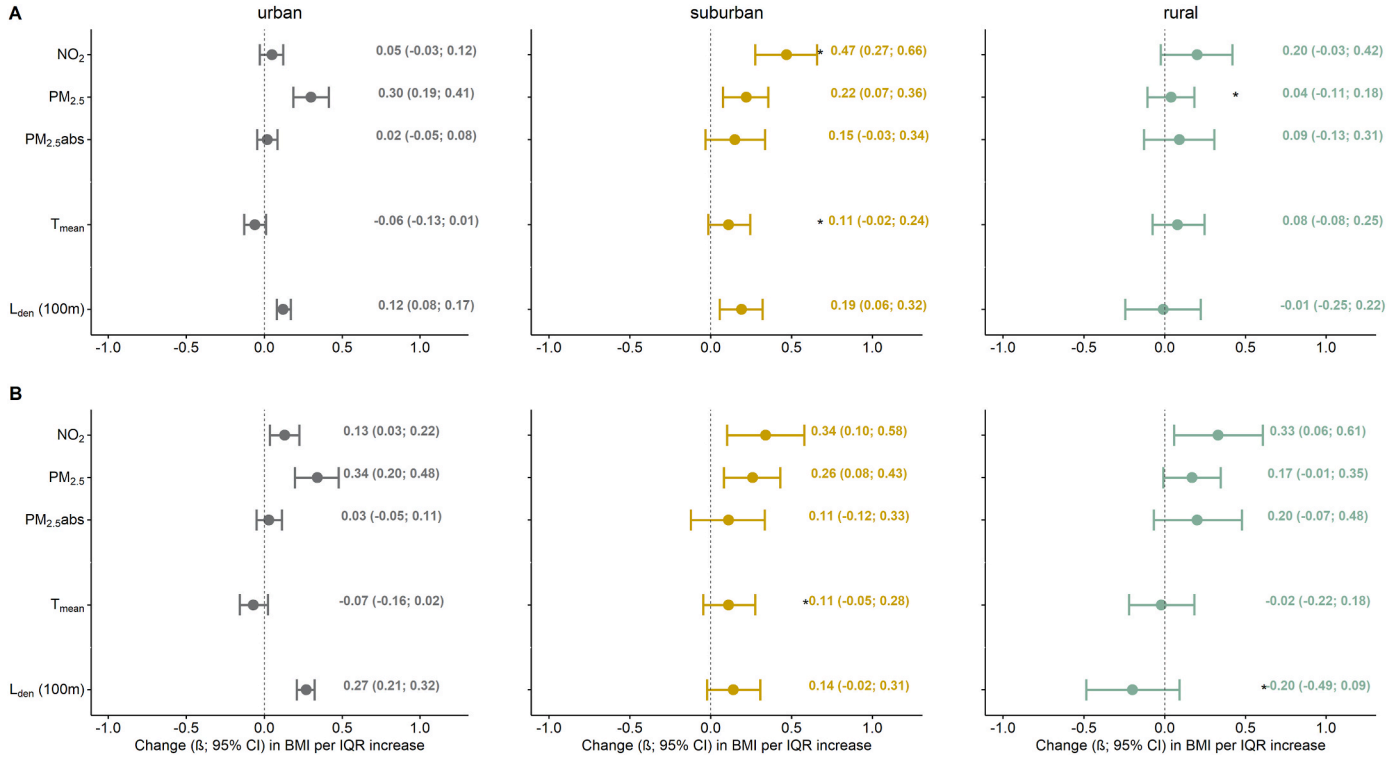

Fig. 3. Urbanization-specific associations of environmental exposures with diabetes for men (A) and women (B) in the German National Cohort (NAKO). Legend: Betas and 95%-CI were derived from linear regression models including an interaction term between exposure and degree of urbanization from EUROSTAT. Star indicates $p_{interaction} < 0.05$. All models were additionally adjusted for age, study center region, lifestyle factors, education, unemployment rate and population density. Urban: n = 62,004 men; n = 62,975 women, suburban: n = 13,771 men, n = 14,152 women, rural: n = 10,933 men, n = 11,112 women. Abbreviation: BMI = Body Mass Index, CI = confidence interval, IQR = interquartile range, L_{den} = day–evening–night noise level, NO_2 = nitrogen dioxide, OR = odds ratio, $PM_{2.5}$ = particulate matter <2.5 μm, $PM_{2.5}$abs = $PM_{2.5}$ absorbance, T_{mean} = mean air temperature.

recommended levels (WHO, 2021). Reviews by Rajagopalan et al. (Rajagopalan and Brook, 2012; Rajagopalan et al., 2024) gave a summary of the evident mechanistic insights of how air pollutants, in particular PM, affect human metabolism. For example, studies in humans and mice showed a deterioration of endothelial function and insulin sensitivity (Rajagopalan and Brook, 2012; Rajagopalan et al., 2024). Local inflammation in visceral adipose tissue and liver were reported, characterized by increased number of macrophages, oxidative stress, and mitochondrial dysfunction, all linking air pollution to diabetes and obesity (Rajagopalan and Brook, 2012; Rajagopalan et al., 2024).

4.2.2. Air temperature

For annual mean air temperature, our results were mixed and inconclusive, so we could not draw clear conclusions about its effect on diabetes and obesity-related measures. In contrast, two studies using data from the Spanish "Di@bet.es Study" found that an increase from the lowest to the highest quartile of annual air temperature was associated with 1.39 and 1.38 higher odds of diabetes and obesity, respectively (Valdes et al., 2014, 2019). However, Wallwork et al. (2017) and Speakman and Heidari-Bakavoli (2016) found that increases in air temperature were associated with diabetes prevalence, but not with obesity. These studies reported annual mean air temperature ranges of more than 10 °C, which shows a higher variability than in our study (6 °C). Previous studies on potential mechanistic pathways have focused on the effects of short-term exposure to air temperature, arguing that exposure to cold may increase activity of brown adipose tissue, which modulates triglyceride accumulation and is associated with improved insulin sensitivity (Valdes et al., 2014; Marlatt and Ravussin, 2017). Furthermore, air temperature may also act via lifestyle changes, as optimal temperatures may increase active transportation and physical activity compared to non-optimal temperatures. However, we assumed that air temperature variability in our study was limited and therefore, would not affect physical activity behavior of participants, as confirmed by our sensitivity analysis. Consequently, multi-country studies which provide more air temperature variability may give important insights into the association of air temperature with metabolic health.

4.2.3. Road traffic noise

We identified robust associations of road traffic noise with diabetes and obesity-related measures, independent of other environmental exposures. Furthermore, noise was the main contributor to the multi-exposure associations. This is in line with previous studies that have found consistent associations between noise exposure and several metabolic-related markers (Wang et al., 2020; Gui et al., 2022). In a subsample of the NAKO study, we also demonstrated an association of

road traffic noise exposure with adipose tissue depots and hepatic fat content measured by whole-body magnetic resonance imaging (Niedermayer et al., 2025). There are multiple reviews summarizing the harmful effects of noise exposure on human metabolism (Munzel et al., 2024; Sivakumaran et al., 2022). Noise, especially during night, can disrupt sleep and affects its quality (Smith et al., 2022; Cappuccio and Miller, 2017). This can result in metabolic abnormalities, characterized by an imbalance in hormones regulating appetite and satiety, which can further lead to an imbalance between energy intake and expenditure (Stevens et al., 2023). The other pathway involves an overactive hypothalamic-pituitary-adrenal axis and sympathetic nervous system that comes along with increased release of stress hormones such as adrenaline, cortisol or catecholamines, that in turn leads to increased oxidative stress and a constant state of inflammation (Munzel et al., 2024). We need to note that road traffic noise exposure is only available at urban areas with >100,000 inhabitants and along major roads with more than 3 million vehicles per year (European Comission, 2002). However, we were lacking adequate noise exposure assessment in rural and remote areas, nor were we able to take into account other potential sources of noise, such as aircraft or railway, which may have an additional impact on metabolic health (Bozigar et al., 2024).

4.2.4. Greenness

We observed non-linear associations of greenness with diabetes and obesity-related measures, which is comparable to numerous previous studies, although the described shape of the exposure-response function varied between studies (Dempsey et al., 2018; James et al., 2017; Klompmaker et al., 2018). Non-linear associations may account for previous mixed evidence on the effect of surrounding greenness on metabolic health (De la Fuente et al., 2020; Luo et al., 2020). In our study, we observed that these non-linear associations were driven by urban areas, suggesting potential residual confounding. We hypothesize that high NDVI levels in urban areas may be attributed to highly vegetated parks and areas on the outskirts of cities. On the other side, central urban areas may offer more opportunities for indoor physical activity with higher numbers of gyms, which may have resulted in the unexpected association of lower NDVI being related to lower odds of diabetes, obesity and lower BMI and waist circumference. Klompmaker et al. (2018) reported that natural greenness is associated with lower odds of overweight and higher physical activity levels, whereas contrary associations were found for urban green. In addition, NDVI as an indicator of greenness has some disadvantages, as it cannot distinguish between different types of greenness, such as parks, grassland, or agricultural areas - and therefore does not reflect the complexity or functional value of green spaces. It also does not provide information on accessibility or actual time spent in green spaces. These limitations may contribute to the observed inverted U-shape, as vegetation density alone may not fully capture the health-relevant characteristics of green spaces (Dempsey et al., 2018; Evenson et al., 2019).These aspects have shown to be important determinants of whether greenness positively affect mental health and physical activity behavior (Dempsey et al., 2018; Villeneuve et al., 2018; Astell-Burt et al., 2014).

4.2.5. Joint associations

Recently, the question of how multiple environmental exposures jointly contribute to disease risk has been raised, but only a few studies have investigated metabolic health outcomes (Klompmaker et al., 2019; Sorensen et al., 2022b; Zhang et al., 2024; Chen et al., 2024; Voss et al., 2021). A study by Klompmaker et al. (2019) used the cumulative risk index to quantify the cumulative effects of exposures to air pollution, noise and greenness and found a joint odds ratio of 1.13 for diabetes, which was higher than the associations found in single-exposure models. Similarly, a study from Denmark showed a cumulative risk index of 1.12 for diabetes when considering air pollution, greenness and noise together (Sorensen et al., 2022b). Applying a quantile-g computation that can handle multi-collinearity, and allows to explore non-additivity and non-linearity (Keil et al., 2020), we found joint associations of multiple adverse environmental exposures with diabetes and obesity-related measures. Similarly, Zhang et al. (2024) performed a quantile g-computation in two prospective US-based cohorts of female nurses. They observed a negative joint association between their environmental exposures, including air pollution, nighttime noise, greenness, light at night, air temperature, neighborhood SES, and BMI. However, this protective joint association was predominantly driven by neighborhood SES. After dropping the neighborhood SES variable from the models, the environmental exposure mixture was associated with 0.16 kg/m^2 and 0.06 kg/m^2 higher BMI in the two cohorts (Zhang et al., 2024). Partially consistent with our findings, the positive joint associations were mainly driven by the air pollutants NO_2, $PM_{2.5}$ and nighttime noise (Zhang et al., 2024). In contrast, NO_2 seemed to be confounded in our study in multi-exposure models, which resulted in a contribution of NO_2 to the negative joint associations with the outcome diabetes. In addition, we cannot explain why the contribution of weight differed for the joint association between environmental exposures and diabetes in women. Nevertheless, we need to be careful when interpreting the weights of each exposure, as these methods tend to give more weight to the exposure with the least measurement error (Zhang et al., 2024; Chen et al., 2024). Furthermore, we cannot derive weights from models that consider splines. Therefore, we should note that the weights were derived from models with NDVI as a linear predictor, which may not fully capture the complex exposure-response relationship for greenness in the exposure mixture. More research is therefore needed that examines multiple environmental factors together, investigating potential synergistic and interactive effects with methods that are more flexible than quantile g-computation. Methods such as Bayesian kernel machine regression and gradient boosting may be more appropriate for such complex mixture settings as it was observed in our study (Chen et al., 2024). Unfortunately, these methods are still too computationally intensive to be implemented in large cohort studies such as NAKO. Therefore, we need to strike a balance between the available methods that can assess joint associations. Quantile g-computation shares the simplicity of WQS regression, but relaxes several of its assumptions, including unidirectionality, linearity and the additivity of individual exposure effects (Keil et al., 2020). Consequently, we decided to implement this method in our cross-sectional study. By exploring different exposure mixture sets, we demonstrated the robustness of joint estimates when including or excluding NDVI as linear predictor. However, including NDVI as non-linear predictor led to changes in the effect estimates and larger CI.

4.2.6. Degree of urbanization

We observed that adjusting for population density had a strong impact on the associations of air pollution with obesity-related markers. Population density was included as a confounder, as we hypothesize related to both exposure variation and health outcomes through multiple behavioral and environmental pathways. For example, population density may be a proxy for several infrastructure-related variables such as a higher proportion of active travel options, increased walkability and connectivity, a diverse food environment (Ohanyan et al., 2022; Sun et al., 2022; Sarkar et al., 2017), or explain some population characteristics that differed by sex and SES and that may confound the association of some environmental factors with obesity. With regard to the present study, we hypothesized that study center region and unemployment rate at the district level may have been too coarse to capture these unmeasured confounders. Contributing to this, the associations of air pollution and road traffic noise were most pronounced in urban areas. Furthermore, study centers regions with a high proportion of urban areas tended to show expected associations of air pollution with diabetes and obesity-related measures, whereas study centers regions including a mixture of urban, suburban and rural areas contributed to unexpected protective or null findings. In addition to global trends of higher rates of obesity in rural area (Liu et al., 2021; Non-Communicable

Disease Risk Factor Collaboration, 2017; Lee and Um, 2021), these heterogeneous findings indicate that additional factors may contribute to the development of diabetes and obesity in rural areas, which require further investigation.

4.3. Outlook

Future analyses within NAKO will address several important questions that were beyond the scope of this cross-sectional study. As biomarker data becomes available, studies should investigate potential biological mechanisms through mediation analyses. Ideally, these analyses will use repeated measures of metabolic and inflammatory markers, such as hemoglobin A1c (HbA1c), lipids and C-reactive protein, to better establish temporal order and clarify the pathways linking environmental exposures with diabetes and obesity. Currently, the 10-year follow-up examination within the NAKO cohort is conducted collecting blood samples, anthropometric and clinical biomarkers. In this context, the role of BMI as a potential mediator in the association between environmental exposures and diabetes warrants further investigation in longitudinal studies. As we were primarily interested in the total association rather than the direct association between environmental exposures and diabetes, we did not include BMI in our main adjustment model. However, adjusting for BMI did not alter the results considerably (Table S9). Additionally, genotyping data from the entire cohort will enable the examination of gene–environment interactions, including the application of polygenic risk scores to determine if individuals with a higher genetic predisposition are more susceptible to adverse environmental influences. Once longitudinal follow-up data and genotyping is available, it will be possible to derive more robust causal estimates and calculate population attributable fractions in order to quantify the potential public health impact of reducing environmental exposures.

4.4. Strengths and limitations

Our study has several strengths. First, we used data from a large, deeply phenotyped, multi-center cohort study that provided sufficient exposure contrast, included participants from diverse socio-economic and urbanized environments, and provided several measures of metabolic function. In particular, BMI is critically discussed as measure of obesity (Rubino et al., 2025), but the NAKO study allowed us to compare associations across a range of different measures of adiposity. In addition, we used a novel, powerful method to assess the joint associations of environmental exposure mixtures with diabetes and obesity-related measures. Rather than assessing the association of one exposure while the other exposures are kept constant, the quantile g-computation assesses the associations of the mixture by increasing all exposures by the pre-defined increment (Zhang et al., 2024; Keil et al., 2020). As a result, this method may better reflect reality because it takes into account co-existing exposures and deals with multi-collinearity, thus reducing a potential bias of the association of environmental factors with diabetes and obesity.

We note the following limitations of our study. Firstly, misclassification in diabetes cases may be present as we had to rely on self-reported information on diabetes diagnosis. Although misclassification can bias associations towards or away from the null, our sensitivity analysis indicated a bias towards the null. Excluding participants who did not report the use of anti-diabetic medication tended to strengthen the association, particularly among women. Information on type of diabetes, blood markers, such as hemoglobin A1c, or oral glucose tolerance test results to identify undetected diabetes, was not available at the time of analysis, which would be interesting to investigate in future studies. Secondly, we cannot rule out residual confounding. The proxy of unemployment rate for neighborhood SES was only available at the district level, which was likely too coarse to adequately adjust for potential unmeasured spatial confounders. Thirdly, we did not have information on diet at the time of the study. However, we assumed that dietary factors might have explained some of the heterogeneity of our participants, but our previous findings in the KORA-Fit study did not show relevant confounding by diet (Niedermayer et al., 2024). In addition, environmental exposures were only available at residential addresses and information on workplace locations or commuting patterns were not available. However, previous studies examining the differences between environmental exposure levels at residential addresses and time-activity-integrated exposure levels have reported strong correlations between the two approaches (often exceeding 0.8), yielding nearly identical health effect estimates (Hoek et al., 2024). Therefore, we assume this will likely bias the associations towards the null. Adding to this, environmental exposures were available at different resolutions and for different exposure time windows. This temporal mismatch may introduce measurement error for different exposures. In our study, we assume that spatial, and for some exposures also temporal, distributions of environmental exposures are relatively stable, as shown in previous studies (Wolf et al., 2025; de Hoogh et al., 2018). Nevertheless, this measurement error for different exposures likely underestimates the true association between environmental exposures and health outcomes. Moreover, it may be a potential reason for null findings, which are hard to explain. Furthermore, measurement error for different exposures may have impacted the assessment of joint associations by quantile g-computation, that these methods tend to give more weight to the exposure with the least measurement error (Zhang et al., 2024; Chen et al., 2024). As mentioned above, weights were derived from models with NDVI as a linear predictor, which may not fully capture the complex exposure-response relationship for greenness in the exposure mixture. Additionally, it should be noted that including NDVI with a spline in the exposure mixture approach resulted in altered effect estimates and larger CIs. Furthermore, we only had cross-sectional data, which did not allow us to observe a temporal sequence of exposure and outcome. Consequently, we only observed associations and not causal effects, which is specifically true for quantile g-computation which aims to assess causal effects. Therefore, future longitudinal studies investigating the effects of multiple environmental exposures jointly on diabetes and obesity are warranted.

5 Conclusions

To conclude, we investigated the associations of six different environmental exposures with diabetes and obesity-related measures in this large multi-center cohort study. We observed that $PM_{2.5}$ and road traffic noise were consistently associated with diabetes and measures of obesity, particularly in urban areas, using single-exposure models. NDVI showed an inverted U-shaped exposure-response curve with all outcomes. In addition, joint associations were observed when multiple exposures were considered simultaneously. This suggests that reducing multiple adverse environmental exposures together could be a potential target for preventing diabetes and obesity. Longitudinal studies are needed to corroborate causal effects of co-existing environmental exposures on diabetes and obesity. Moreover, this study highlights the need to identify socio-economic and environmental drivers that can explain differences in diabetes and obesity-related measures between urban and rural areas in future studies.

CRediT authorship contribution statement

Fiona Niedermayer: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Barbara Hoffmann:** Writing – review & editing, Supervision, Resources, Methodology. **Boya Zhang:** Writing – review & editing, Methodology. **Jie Chen:** Writing – review & editing, Methodology. **Jaime E. Hart:** Writing – review & editing, Methodology. **Francine Laden:** Writing – review & editing, Methodology. **Gabriele Bolte:** Writing – review & editing, Resources. **Tobia Lakes:** Writing – review & editing, Resources. **Tamara Schikowski:** Writing – review & editing, Resources. **Karin Halina Greiser:** Writing – review & editing,

Resources. **Jeroen Staab:** Writing – review & editing, Resources, Data curation. **Nikolaos Nikolaou:** Writing – review & editing, Resources, Data curation. **Marco Dallavalle:** Writing – review & editing, Resources, Data curation. **Matthias B. Schulze:** Writing – review & editing, Resources. **Wolfgang Lieb:** Writing – review & editing, Resources. **Cara Övermöhle:** Writing – review & editing, Resources. **Thaddäus Tönnies:** Writing – review & editing, Resources. **Verena Katzke:** Writing – review & editing, Resources. **Heiko Becher:** Writing – review & editing, Resources. **Beate Fischer:** Writing – review & editing, Resources. **Michael Leitzmann:** Writing – review & editing, Resources. **Klaus Berger:** Writing – review & editing, Resources. **Fatemeh Mayvaneh:** Writing – review & editing, Resources. **Thomas Keil:** Writing – review & editing, Resources. **Lilian Krist:** Writing – review & editing, Resources. **Carolina J. Klett-Tammen:** Writing – review & editing, Resources. **Jana-Kristin Heise:** Writing – review & editing, Resources. **Tobias Pischon:** Writing – review & editing, Resources. **Ilais Moreno Velásquez:** Writing – review & editing, Resources. **Börge Schmidt:** Writing – review & editing, Resources. **Rajini Nagrani:** Writing – review & editing, Resources. **Stefan Rach:** Writing – review & editing, Resources. **Hermann Brenner:** Writing – review & editing, Resources. **Bernd Holleczek:** Writing – review & editing, Resources. **Volker Harth:** Writing – review & editing, Resources. **Nadia Obi:** Writing – review & editing, Resources. **Anna Köttgen:** Writing – review & editing, Resources. **Rafael Mikolajczyk:** Writing – review & editing, Resources. **Claudia Meinke-Franze:** Writing – review & editing, Resources. **Wolfgang Hoffmann:** Writing – review & editing, Resources. **Alexandra Schneider:** Writing – review & editing, Resources, Methodology, Data curation. **Kathrin Wolf:** Writing – review & editing, Resources, Methodology, Data curation. **Annette Peters:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization.

Notes

The authors have no conflicts of interest to declare.

Ethics approval and consent to participate

The German National Cohort (NAKO) was approved by the initial vote of the ethics committee of the Bavarian Medical Association ("Bayerische Landesärztekammer" (BLÄK), protocol code 13023), followed by votes from all local on-site institutional review boards, and written informed consent of all participants was obtained at the time of study enrollment. The study was conducted in accordance with the Declaration of Helsinki of 1975 (in the current, revised version).

Data sharing

The datasets analyzed during the current study are not publicly available. Access to and use of NAKO data and biosamples can be obtained via an electronic application portal (https://transfer.nako.de). Analysis codes are available from the authors upon request.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work the authors used DeepL in order to improve readability and language. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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.

Acknowledgements/Funding

The NAKO is funded by the Federal Ministry of Education and Research (BMBF) [project funding reference numbers: 01ER1301 A/B/C, 01ER1511D, 01ER1801 A/B/C/D and 01ER2301 A/B/C], the federal states and the Helmholtz Association, with additional financial support by the participating universities and the institutes of the Leibniz Association. The compilation of noise data was funded by the Helmholtz Association's Initiative and Networking Fund (ZT-I-PF-5-42). The manuscript was part of the NAKO data application NAKO-597.We thank all participants who took part in the NAKO and the staff of this research initiative.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2026.124096.

Data availability

The authors do not have permission to share data.

References

Altug, H., Ogurtsova, K., Breyer-Kohansal, R., Schiffers, C., Ofenheimer, A., Tzivian, L., et al., 2024. Associations of long-term exposure to air pollution and noise with body composition in children and adults: results from the LEAD general population study. Environ. Int. 189, 108799. https://doi.org/10.1016/j.envint.2024.108799.

An, R., Ji, M., Yan, H., Guan, C., 2018. Impact of ambient air pollution on obesity: a systematic review. Int. J. Obes. 42 (6), 1112–1126. https://doi.org/10.1038/s41366-018-0089-y.

Astell-Burt, T., Mitchell, R., Hartig, T., 2014. The association between green space and mental health varies across the lifecourse. A longitudinal study. J. Epidemiol. Community Health 68 (6), 578–583. https://doi.org/10.1136/jech-2013-203767.

Bluher, M., 2019. Obesity: global epidemiology and pathogenesis. Nat. Rev. Endocrinol. 15 (5), 288–298. https://doi.org/10.1038/s41574-019-0176-8.

Bozigar, M., Laden, F., Hart, J.E., Redline, S., Huang, T., Whitsel, E.A., et al., 2024. Aircraft noise exposure and body mass index among female participants in two Nurses' Health Study prospective cohorts living around 90 airports in the United States. Environ. Int. https://doi.org/10.1016/j.envint.2024.108660.

Bundesagentur für Arbeit [Federal Employment Agency], 04.03.2025. Available from: https://www.bmfsfj.de/bmfsfj/service/online-rechner/gleichstellungsatlas?view=.

Cappuccio, F.P., Miller, M.A., 2017. Sleep and cardio-metabolic disease. Curr. Cardiol. Rep. 19 (11), 110. https://doi.org/10.1007/s11886-017-0916-0.

Chen, J., Hart, J.E., Fisher, N.D.L., Yanosky, J.D., Roscoe, C., James, P., et al., 2024. Multiple environmental exposures and the development of hypertension in a prospective US-Based cohort of female nurses: a mixture analysis. Environ. Sci. Technol. 58 (32), 14146–14157. https://doi.org/10.1021/acs.est.4c03722.

Chew, N.W.S., Ng, C.H., Tan, D.J.H., Kong, G., Lin, C., Chin, Y.H., et al., 2023. The global burden of metabolic disease: data from 2000 to 2019. Cell Metab. 35 (3), 414–428 e3. https://doi.org/10.1016/j.cmet.2023.02.003.

de Hoogh, K., Chen, J., Gulliver, J., Hoffmann, B., Hertel, O., Ketzel, M., et al., 2018. Spatial PM2.5, NO2, O3 and BC models for Western Europe - evaluation of spatiotemporal stability. Environ. Int. 120, 81–92. https://doi.org/10.1016/j.envint.2018.07.036.

De la Fuente, F., Saldias, M.A., Cubillos, C., Mery, G., Carvajal, D., Bowen, M., et al., 2020. Green space exposure association with type 2 diabetes mellitus, physical activity, and obesity: a systematic review. Int. J. Environ. Res. Publ. Health 18 (1). https://doi.org/10.3390/ijerph18010097.

Dempsey, S., Lyons, S., Nolan, A., 2018. Urban green space and obesity in older adults: evidence from Ireland. SSM Popul Health 4, 206–215. https://doi.org/10.1016/j.ssmph.2018.01.002.

European Comission, 2002. Directive 2002/49/EC of the European parliament and of the council of 25 June 2002 relating to the assessment and management of environmental noise. Official Journal of the European Communities. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32002L0049.

European Union, 2018. Methodological Manual on Territorial Typologies. Publications Office of the European Union, Luxembourg. Report No.: 2315-0815.Last access: 23.12.2022. Available from: https://ec.europa.eu/eurostat/documents/3859598/9507230/KS-GQ-18-008-EN-N.pdf.

Evenson, K.R., Williamson, S., Han, B., McKenzie, T.L., Cohen, D.A., 2019. United States' neighborhood park use and physical activity over two years: the National Study of Neighborhood Parks. Prev. Med. 123, 117–122. https://doi.org/10.1016/j.ypmed.2019.03.027.

Fischer, B., Sedlmeier, A.M., Hartwig, S., Schlett, C.L., Ahrens, W., Bamberg, F., et al., 2020. Anthropometric measures in the German National Cohort-more than weight and height. Bundesgesundheitsblatt 63 (3), 290–300. https://doi.org/10.1007/s00103-020-03096-w.

Fong, K.C., Hart, J.E., James, P., 2018. A review of epidemiologic studies on greenness and health: updated literature through 2017. Curr. Environ. Health Rep. 5 (1), 77–87. https://doi.org/10.1007/s40572-018-0179-y.
Global Burden of Disease 2021 Diabetes Collaborators, 2023. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 402 (10397), 203–234. https://doi.org/10.1016/S0140-6736(23)01301-6.
Global Burden of Disease Risk Factors Collaborators, 2024. Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 403 (10440), 2162–2203. https://doi.org/10.1016/S0140-6736(24)00933-4.
Gui, S.Y., Wu, K.J., Sun, Y., Chen, Y.N., Liang, H.R., Liu, W., et al., 2022. Traffic noise and adiposity: a systematic review and meta-analysis of epidemiological studies. Environ. Sci. Pollut. Res. Int. https://doi.org/10.1007/s11356-022-19056-7.
Han, W., Xu, Z., Hu, X., Cao, R., Wang, Y., Jin, J., et al., 2023. Air pollution, greenness and risk of overweight among middle-aged and older adults: a cohort study in China. Environ. Res. 216 (Pt 1), 114372. https://doi.org/10.1016/j.envres.2022.114372.
He, D., Wu, S., Zhao, H., Qiu, H., Fu, Y., Li, X., et al., 2017. Association between particulate matter 2.5 and diabetes mellitus: a meta-analysis of cohort studies. J Diabetes Investig. 8 (5), 687–696. https://doi.org/10.1111/jdi.12631.
Hoek, G., Vienneau, D., de Hoogh, K., 2024. Does residential address-based exposure assessment for outdoor air pollution lead to bias in epidemiological studies? Environ. Health 23 (1), 75. https://doi.org/10.1186/s12940-024-01111-0.
Hoffmann, B., Moebus, S., Mohlenkamp, S., Stang, A., Lehmann, N., Dragano, N., et al., 2007. Residential exposure to traffic is associated with coronary atherosclerosis. Circulation 116 (5), 489–496. https://doi.org/10.1161/CIRCULATIONAHA.107.693622.
Hoffmann, K., De Gelder, R., Hu, Y., Bopp, M., Vitrai, J., Lahelma, E., et al., 2017. Trends in educational inequalities in obesity in 15 European countries between 1990 and 2010. Int. J. Behav. Nutr. Phys. Activ. 14 (1), 63. https://doi.org/10.1186/s12966-017-0517-8.
Huang, S., Zhang, X., Huang, J., Lu, X., Liu, F., Gu, D., 2020. Ambient air pollution and body weight status in adults: a systematic review and meta-analysis. Environ. Pollut. 265 (Pt A), 114999. https://doi.org/10.1016/j.envpol.2020.114999.
Jaeschke, L., Steinbrecher, A., Greiser, K.H., Dorr, M., Buck, T., Linseisen, J., et al., 2020. [Assessment of self-reported cardiovascular and metabolic diseases in the German National Cohort (GNC, NAKO Gesundheitsstudie): methods and initial results]. Bundesgesundheitsblatt - Gesundheitsforsch. - Gesundheitsschutz 63 (4), 439–451. https://doi.org/10.1007/s00103-020-03108-9.
James, P., Kioumourtzoglou, M.A., Hart, J.E., Banay, R.F., Kloog, I., Laden, F., 2017. Interrelationships between walkability, air pollution, greenness, and body mass index. Epidemiology 28 (6), 780–788. https://doi.org/10.1097/EDE.0000000000000724.
Kautzky-Willer, A., Leutner, M., Harreiter, J., 2023. Sex differences in type 2 diabetes. Diabetologia 66 (6), 986–1002. https://doi.org/10.1007/s00125-023-05891-x.
Keil, A.P., Buckley, J.P., O'Brien, K.M., Ferguson, K.K., Zhao, S., White, A.J., 2020. A quantile-based g-Computation approach to addressing the effects of exposure mixtures. Environ. Health Perspect. 128 (4), 47004. https://doi.org/10.1289/EHP5838.
Klompmaker, J.O., Hoek, G., Bloemsma, L.D., Gehring, U., Strak, M., Wijga, A.H., et al., 2018. Green space definition affects associations of green space with overweight and physical activity. Environ. Res. 160, 531–540. https://doi.org/10.1016/j.envres.2017.10.027.
Klompmaker, J.O., Janssen, N.A.H., Bloemsma, L.D., Gehring, U., Wijga, A.H., van den Brink, C., et al., 2019. Associations of combined exposures to surrounding green, air pollution, and road traffic noise with cardiometabolic diseases. Environ. Health Perspect. 127 (8), 87003. https://doi.org/10.1289/EHP3857.
Lee, G.Y., Um, Y.J., 2021. Factors affecting obesity in urban and rural adolescents: Demographic, socioeconomic characteristics, health behavior and health education. Int. J. Environ. Res. Publ. Health 18 (5). https://doi.org/10.3390/ijerph18052405.
Leitzmann, M., Gastell, S., Hillreiner, A., Herbolsheimer, F., Baumeister, S.E., Bohn, B., et al., 2020. [Physical activity in the German National Cohort (NAKO): use of multiple assessment tools and initial results]. Bundesgesundheitsblatt - Gesundheitsforsch. - Gesundheitsschutz 63 (3), 301–311. https://doi.org/10.1007/s00103-020-03099-7.
Li, Z.H., Zhong, W.F., Zhang, X.R., Chung, V.C., Song, W.Q., Chen, Q., et al., 2022. Association of physical activity and air pollution exposure with the risk of type 2 diabetes: a large population-based prospective cohort study. Environ. Health 21 (1), 106. https://doi.org/10.1186/s12940-022-00922-3.
Liu, M., Tang, W., Zhang, Y., Wang, Y., Baima, K., Li, Y., et al., 2021. Urban-rural differences in the association between long-term exposure to ambient air pollution and obesity in China. Environ. Res. 201, 111597. https://doi.org/10.1016/j.envres.2021.111597.
Luo, Y.N., Huang, W.Z., Liu, X.X., Markevych, I., Bloom, M.S., Zhao, T., et al., 2020. Greenspace with overweight and obesity: a systematic review and meta-analysis of epidemiological studies up to 2020. Obes. Rev. 21 (11), e13078. https://doi.org/10.1111/obr.13078.
Marlatt, K.L., Ravussin, E., 2017. Brown adipose tissue: an update on recent findings. Curr. Obes. Rep. 6 (4), 389–396. https://doi.org/10.1007/s13679-017-0283-6.
Munzel, T., Molitor, M., Kuntic, M., Hahad, O., Roosli, M., Engelmann, N., et al., 2024. Transportation noise pollution and cardiovascular health. Circ. Res. 134 (9), 1113–1135. https://doi.org/10.1161/CIRCRESAHA.123.323584.
Niedermayer, F., Wolf, K., Zhang, S., Dallavalle, M., Nikolaou, N., Schwettmann, L., et al., 2024. Sex-specific associations of environmental exposures with prevalent diabetes and obesity - results from the KORA Fit study. Environ. Res. 252 (Pt 3), 118965. https://doi.org/10.1016/j.envres.2024.118965.
Niedermayer, F., Rospleszcz, S., Matthiessen, C., Hoffmann, B., Stoecklein, S., Haueise, T., et al., 2025. Associations of road traffic noise with adipose tissue depots and hepatic fat content - results from the German National Cohort (NAKO). Environ. Int. 201, 109566. https://doi.org/10.1016/j.envint.2025.109566.
Nieuwenhuijsen, M.J., 2020. Urban and transport planning pathways to carbon neutral, liveable and healthy cities; A review of the current evidence. Environ. Int. 140, 105661. https://doi.org/10.1016/j.envint.2020.105661.
Nikolaou, N., Dallavalle, M., Stafoggia, M., Bouwer, L.M., Peters, A., Chen, K., et al., 2023. High-resolution spatiotemporal modeling of daily near-surface air temperature in Germany over the period 2000-2020. Environ. Res. 219, 115062. https://doi.org/10.1016/j.envres.2022.115062.
Non-Communicable Disease Risk Factor Collaboration, 2017. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet 390 (10113), 2627–2642. https://doi.org/10.1016/S0140-6736(17)32129-3.
Non-Communicable Disease Risk Factor Collaboration, 2024. Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. Lancet 403 (10431), 1027–1050. https://doi.org/10.1016/S0140-6736(23)02750-2.
Ohanyan, H., Portengen, L., Huss, A., Traini, E., Beulens, J.W.J., Hoek, G., et al., 2022. Machine learning approaches to characterize the obesogenic urban exposome. Environ. Int. 158, 107015. https://doi.org/10.1016/j.envint.2021.107015.
Pan, W., Wang, M., Hu, Y., Lian, Z., Cheng, H., Qin, J.J., et al., 2023. The association between outdoor air pollution and body mass index, central obesity, and visceral adiposity index among middle-aged and elderly adults: a nationwide study in China. Front. Endocrinol. 14, 1221325. https://doi.org/10.3389/fendo.2023.1221325.
Peters, A., Doring, A., Wichmann, H.E., Koenig, W., 1997. Increased plasma viscosity during an air pollution episode: a link to mortality? Lancet 349 (9065), 1582–1587. https://doi.org/10.1016/S0140-6736(97)01211-7.
Peters, A., German National Cohort, C., Peters, A., Greiser, K.H., Gottlicher, S., Ahrens, W., et al., 2022. Framework and baseline examination of the German National Cohort (NAKO). Eur. J. Epidemiol. https://doi.org/10.1007/s10654-022-00890-5.
Pyko, A., Eriksson, C., Lind, T., Mitkovskaya, N., Wallas, A., Ogren, M., et al., 2017. Long-term exposure to transportation noise in relation to development of Obesity-a cohort study. Environ. Health Perspect. 125 (11), 117005. https://doi.org/10.1289/EHP1910.
Rach, S., Sand, M., Reineke, A., Becher, H., Greiser, K.H., Wolf, K., et al., 2025. The baseline examinations of the German National Cohort (NAKO): recruitment protocol, response, and weighting. Eur. J. Epidemiol. 40 (4), 475–489. https://doi.org/10.1007/s10654-025-01219-8.
Rajagopalan, S., Brook, R.D., 2012. Air pollution and type 2 diabetes. Diabetes 61 (12), 3037–3045. https://doi.org/10.2337/db12-0190.
Rajagopalan, S., Brook, R.D., Salerno, P., Bourges-Sevenier, B., Landrigan, P., Nieuwenhuijsen, M.J., et al., 2024. Air pollution exposure and cardiometabolic risk. Lancet Diabetes Endocrinol. 12 (3), 196–208. https://doi.org/10.1016/S2213-8587(23)00361-3.
Rojas-Rueda, D., Morales-Zamora, E., Alsufyani, W.A., Herbst, C.H., AlBalawi, S.M., Alsukait, R., et al., 2021. Environmental risk factors and health: an umbrella review of meta-analyses. Int. J. Environ. Res. Publ. Health 18 (2). https://doi.org/10.3390/ijerph18020704.
Rubino, F., Cummings, D.E., Eckel, R.H., Cohen, R.V., Wilding, J.P.H., Brown, W.A., et al., 2025. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol. https://doi.org/10.1016/S2213-8587(24)00316-4.
Sarkar, C., Webster, C., Gallacher, J., 2017. Association between adiposity outcomes and residential density: a full-data, cross-sectional analysis of 419 562 UK Biobank adult participants. Lancet Planet. Health 1 (7), e277–e288. https://doi.org/10.1016/S2542-5196(17)30119-5.
Schienkiewitz, A., Kuhnert, R., Blume, M., Mensink, G.B.M., 2022. Overweight and obesity among adults in Germany - results from GEDA 2019/2020-EHIS. J Health Monit 7 (3), 21–28. https://doi.org/10.25646/10293.
Schikowski, T., Ranft, U., Sugiri, D., Vierkotter, A., Bruning, T., Harth, V., et al., 2010. Decline in air pollution and change in prevalence in respiratory symptoms and chronic obstructive pulmonary disease in elderly women. Respir. Res. 11 (1), 113. https://doi.org/10.1186/1465-9921-11-113.
Schunk, M., Reitmeir, P., Schipf, S., Volzke, H., Meisinger, C., Thorand, B., et al., 2012. Health-related quality of life in subjects with and without type 2 diabetes: pooled analysis of five population-based surveys in Germany. Diabet. Med. 29 (5), 646–653. https://doi.org/10.1111/j.1464-5491.2011.03465.x.
Sivakumaran, K., Ritonja, J.A., Waseem, H., AlShenaiber, L., Morgan, E., Ahmadi, S.A., et al., 2022. Impact of noise exposure on risk of developing stress-related metabolic effects: a systematic review and meta-analysis. Noise Health 24 (115), 215–230. https://doi.org/10.4103/nah.nah_21_22.
Smith, M.G., Cordoza, M., Basner, M., 2022. Environmental noise and effects on sleep: an update to the WHO systematic review and meta-analysis. Environ. Health Perspect. 130 (7), 76001. https://doi.org/10.1289/EHP10197.
Sorensen, T.I.A., Martinez, A.R., Jorgensen, T.S.H., 2022a. Epidemiology of obesity. Handb. Exp. Pharmacol. 274, 3–27. https://doi.org/10.1007/164_2022_581.
Sorensen, M., Poulsen, A.H., Hvidtfeldt, U.A., Brandt, J., Frohn, L.M., Ketzel, M., et al., 2022b. Air pollution, road traffic noise and lack of greenness and risk of type 2 diabetes: a multi-exposure prospective study covering Denmark. Environ. Int. 170, 107570. https://doi.org/10.1016/j.envint.2022.107570.
Speakman, J.R., Heidari-Bakavoli, S., 2016. Type 2 diabetes, but not obesity, prevalence is positively associated with ambient temperature. Sci. Rep. 6, 30409. https://doi.org/10.1038/srep30409.

Staab, J., Droin, A., Weigand, M., Dallavalle, M., Wolf, K., Schady, A., et al., 2025. Pixels, chisels and contours - technical variations in European road traffic noise exposure maps. J. Environ. Manag. 385. https://doi.org/10.1016/j.jenvman.2025.125475.

Stevens, D.R., Rosen, E.M., Van Wickle, K., McNell, E.E., Bommarito, P.A., Calafat, A.M., et al., 2023. Early pregnancy phthalates and replacements in relation to fetal growth: the human placenta and phthalates study. Environ. Res. 229, 115975. https://doi.org/10.1016/j.envres.2023.115975.

Sun, B., Yao, X., Yin, C., 2022. An N-Shaped Association between population density and abdominal obesity. Int. J. Environ. Res. Publ. Health 19 (15). https://doi.org/10.3390/ijerph19159577.

UNESCO Institute for Statistics, 2012. International Standard Classification of Education ISCED 2011. UNESCO Institute for Statistics, Montreal, Canada.. Available from: https://uis.unesco.org/sites/default/files/documents/international-standard-classification-of-education-isced-2011-en.pdf

Valdes, S., Maldonado-Araque, C., Garcia-Torres, F., Goday, A., Bosch-Comas, A., Bordiu, E., et al., 2014. Ambient temperature and prevalence of obesity in the Spanish population: the Di@bet.es study. Obesity 22 (11), 2328–2332. https://doi.org/10.1002/oby.20866.

Valdes, S., Doulatram-Gamgaram, V., Lago, A., Garcia Torres, F., Badia-Guillen, R., Olveira, G., et al., 2019. Ambient temperature and prevalence of diabetes and insulin resistance in the Spanish population: di@bet.es study. Eur. J. Endocrinol. 180 (5), 273–280. https://doi.org/10.1530/EJE-18-0818.

Villeneuve, P.J., Jerrett, M., Su, J.G., Weichenthal, S., Sandler, D.P., 2018. Association of residential greenness with obesity and physical activity in a US cohort of women. Environ. Res. 160, 372–384. https://doi.org/10.1016/j.envres.2017.10.005.

Voss, S., Schneider, A., Huth, C., Wolf, K., Markevych, I., Schwettmann, L., et al., 2021. ENVINT-D-20-01309: Long-term exposure to air pollution, road traffic noise, residential greenness, and prevalent and incident metabolic syndrome: results from the population-based KORA F4/FF4 cohort in Augsburg, Germany. Environ. Int. 147, 106364. https://doi.org/10.1016/j.envint.2020.106364.

Wallwork, R.S., Colicino, E., Zhong, J., Kloog, I., Coull, B.A., Vokonas, P., et al., 2017. Ambient fine particulate matter, outdoor temperature, and risk of metabolic syndrome. Am. J. Epidemiol. 185 (1), 30–39. https://doi.org/10.1093/aje/kww157.

Wang, H., Sun, D., Wang, B., Gao, D., Zhou, Y., Wang, N., et al., 2020. Association between noise exposure and diabetes: meta-analysis. Environ. Sci. Pollut. Res. Int. 27 (29), 36085–36090. https://doi.org/10.1007/s11356-020-09826-6.

WHO (World Health Organization), 2000. Obesity : Preventing and Managing the Global Epidemic : Report of a WHO Consultation. WHO, Geneva, Switzerland. Available from: https://iris.who.int/handle/10665/42330.

WHO (World Health Organization), 2008. Waist Circumference and Waist–Hip Ratio: Report of a WHO Expert Consultation Geneva, 8–11 December 2008 Geneva. WHO. Available from: http://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491_eng.pdf?sequence=1.

WHO (World Health Organization), 2021. WHO Global Air Quality Guidelines: Particulate Matter (PM2.5 and PM10), ozone, nitOogen dNoxide, sDlfur dioSide anD carbon monCxide. World Health Organization, Meneva. Last access: 23.01.2025. Available from: https://www.who.int/publications/i/item/9789240034228/.

WIGeoGIS Gesellschaft für digitale Wirtschaftsgeographie GmbH. Last access: 04.03.2025. Available from: https://www.wigeogis.com/de/impressum.

Wolf, K., Dallavalle, M., Niedermayer, F., Bolte, G., Lakes, T., Schikowski, T., et al., 2025. Environmental exposure assessment in the German National Cohort (NAKO). Environ. Res. 273, 121259. https://doi.org/10.1016/j.envres.2025.121259.

Wood, S.N., 2011. Fast stable restricted maximum likelihood and marginal likelihood estimation of semiparametric generalized linear models. J. Roy. Stat. Soc. B 73, 3–36. https://doi.org/10.1111/j.1467-9868.2010.00749.x.

Yang, Z., Song, Q., Li, J., Zhang, Y., 2019. Air pollution as a cause of obesity: micro-level evidence from Chinese cities. Int. J. Environ. Res. Publ. Health 16 (21). https://doi.org/10.3390/ijerph16214296.

Yang, B.Y., Fan, S., Thiering, E., Seissler, J., Nowak, D., Dong, G.H., et al., 2020a. Ambient air pollution and diabetes: a systematic review and meta-analysis. Environ. Res. 180, 108817. https://doi.org/10.1016/j.envres.2019.108817.

Yang, M., Cheng, H., Shen, C., Liu, J., Zhang, H., Cao, J., et al., 2020b. Effects of long-term exposure to air pollution on the incidence of type 2 diabetes mellitus: a meta-analysis of cohort studies. Environ. Sci. Pollut. Res. Int. 27 (1), 798–811. https://doi.org/10.1007/s11356-019-06824-1.

Zhang, B., Hart, J.E., Laden, F., Bozigar, M., James, P., 2024. Environmental mixtures and body mass index in two prospective US-based cohorts of female nurses. J. Hazard Mater. 480, 135794. https://doi.org/10.1016/j.jhazmat.2024.135794.

WHO (World Health Organization), 2018. Environmental Noise Guidelines for the European Region. Available from: https://www.euro.who.int/_data/assets/pdf_file/0008/383921/noise-guidelines-eng.pdf.