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The association of specific industry-related air pollution with occurrence of chronic diseases: A register-based study

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ABSTRACT

Air pollution may contribute to onset and progression of chronic diseases such as cardiovascular and respiratory diseases. Most studies have focused on the contribution of traffic-related exposure to PM_{10} or $PM_{2.5}$. Our aim was to investigate the association of different components of industry-related air pollution on the occurrence of chronic diseases.

A register-based repeated cross-sectional study was conducted among 89,714 subjects (2012) with 536,599 annual observations (2012–2017) living in the vicinity of a large industrial area in the Netherlands. Information from the dispensed medication registration was linked with a dispersion model to characterize annual individual-level exposure of all subjects at place of residence. Associations between annual exposure (concentration and duration) to particulate matter (PM_{10}), nitrogen oxides (NO_X), sulphur dioxide (SO_2), and volatile organic compounds (VOC) with annual dispensed medication for cardiovascular diseases, respiratory diseases, diabetes mellitus, and inflammatory conditions were investigated by multivariate logistic regression analysis with generalized estimating equations (GEE) while controlling for confounders.

Exposure to PM_{10} and to NO_X (per $\mu g/m^3$) were significantly associated with medication for cardiovascular diseases (OR 1.06, 95CI% 1.06–1.06 and OR 1.01, 95%CI 1.01–1.01 respectively). Exposures to PM_{10} and SO_2 (per $\mu g/m^3$) were significantly associated with medication for inflammatory conditions (OR 1.05, 95%CI 1.00–1.09 and OR 1.07, 95%CI 1.01–1.14 respectively). Exposure to SO_2 was inversely associated with respiratory diseases (OR 0.91, 95%CI 0.86–0.97). Except for inflammatory conditions, exposure duration (years) was significantly associated with the other three chronic diseases (OR varying from 1.01 to 1.03).

This study indicates that specific air pollution components caused by industry may contribute to the occurrence of cardiovascular diseases, respiratory diseases, diabetes mellitus, and inflammatory conditions.

1. Introduction

Air pollution is a complex mixture of different gaseous and particulate components and can cause several adverse health effects, such as respiratory and cardiovascular diseases (Mannucci et al., 2015). A review of recent studies showed a positive association between outdoor air pollution and the incidence and severity of COVID-19 (Marquès and Domingo, 2022). This makes outdoor air pollution even more important than in the past.

A study of Liu et al. (2019) about air pollution from 652 cities in 24 countries showed that an increase of 10 $\mu g/m^3$ (2-day average) in particulate matter with diameters of less than 10 μm (PM_{10}) concentration was associated with 0.36–0.47% increases in daily all-cause, cardiovascular, and respiratory mortality. Recently, a prospective cohort study in Germany showed that PM_{10} (per interquartile range of 3.8 $\mu g/m^3$) was associated with an increased risk of diabetes mellitus (RR: 1.25, 95% CI 1.02 to 1.53). Exposure to nitrogen dioxide (NO_2) from industrial sources was associated with an increased risk of diabetes mellitus (RR: 1.21, 95% CI 1.06 to 1.37 per interquartile range of 1.9 $\mu g/m^3$) (Lucht et al., 2020).

Most epidemiologic studies have used data about patients with disease episodes severely enough to seek direct medical care, such as admissions to hospital or emergency care use (Environmental Protection Agency (EPA), 2019, 2016a, 2016b). These studies may underestimate

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the impact of air pollution on the actual occurrence of chronic diseases in the general population. Information from health insurances on dispensed medicine by general practitioner (GP) or specialist care can be used to identify persons with both severe and non-severe diseases.

An ecological study in de UK about air pollution and respiratory medication (salbutamol) prescribed by 63 primary care practices showed that higher monthly average exposure to PM_{10} (per 10 μg/m^3) was associated with an increase of salbutamol prescribing in the same month (1%, 95% CI 0.1 to 2%) (Sofianopoulou et al., 2013). A prospective cohort study among children in Sweden showed that exposure in 2010 to NO_2 (per μg/m^3), considered to reflect exposure during the follow-up period, was associated with at least two prescribed asthma medications during follow up period from 2005 to 2010 (OR 1.02, 95% CI 1.01 to 1.03). There was no evidence that stressors linked to socio-economic or mental health problems increased susceptibility to the effects of air pollution on the development of asthma (Oudin et al., 2017). A prospective cohort study among asthmatic individuals in the United States showed that a weekly exposure increase to particulate matter (of 1 μg/m^3) with diameters of less than 2.5 μm ($PM_{2.5}$) increased weekly inhaler use (0.82%, $p < 0.05$) (Williams et al., 2019).

To our best knowledge, studies about the association between specific air pollution components and medication for chronic diseases are rare, often address only one specific disease, and mostly focus on traffic-related air pollution. Therefore, the aim of this study is to investigate the association of several components of air pollution from a large industrial area on dispensed medication for a variety of chronic diseases with a high prevalence. This study targets a region in the Netherlands with a unique situation of a concentrated presence of industries with low traffic density. In addition, the register-based approach ensures complete coverage of the entire population, due to mandatory health insurance in the Netherlands.

2. Methods

2.1. Study design and population

A register-based repeated cross-sectional study (2012–2017) on the association of industry-related air pollution with dispensed medication for chronic diseases was conducted among inhabitants in the vicinity of the large industrial area. At individual level, annual mean exposure to air pollution from a dispersion model was linked to dispensed medicine in the same year. All subjects were followed for a maximum of six years between 2012 and 2017, resulting in a maximum of six observations per subject. Observations were only included when a subject did not move outside the study area within a given year. When a subject changed home inside the study area within a given year, the annual exposure for that individual was calculated relative to exposure level at both residences during that year. The study area (see Fig. 1) covered the canal from the cities Terneuzen to Sas van Gent in the Southwest of the Netherlands (municipality Terneuzen) and surrounding areas without heavy industries (municipalities Hulst and Sluis). The total number of inhabitants of the study area was 89,714 in 2012. At the time of the study several heavy industries were active in this area, such as a large petrochemical factory, fertiliser factories, a bromine plant, and terminals for storing and shipping of dry bulk products, including among others, fertiliser. The study area borders on an area of Belgium where heavy industry is also present.

A database was developed with information on air pollution exposure at home address and subsequently linked with registers on dispensed medication, prescribed by general practitioner or specialist, and demographic characteristics of the Statistics Netherlands (CBS). In order to safeguard the privacy of individuals, the linkage between different databases was conducted with a random unique identification number (RIN) and information about the home addresses was removed. All analyses were conducted within a secure workspace at CBS. Results of the analyses were carefully checked for identifiability by CBS before they could be published. This research proposal has been approved by the medical ethical committee from the Erasmus MC, University Medical Centre, the Netherlands (reference MEC-2020-0386).

2.2. Exposure assessment

For the exposure assessment the same method was used as in an earlier study about birth-outcomes in the same study area and time period (see Bergstra et al., 2020). In short, emission data from all the heavy industry in and around the study area were collected from the Emission Register in the Netherlands (http://www.emissieregistratie.nl/) and the Flanders Environment Agency in Belgium (https://en.vmm.be/).

From 22 air pollution components emitted by the plants, three air pollution compounds with the highest ratios of emission over immission limit were selected, namely: PM_{10}, nitrogen oxides (NO_X), and sulphur dioxide (SO_2). Volatile organic compounds (VOC, no limit value available) was also chosen because this component was emitted in non-negligible quantities. For PM_{10}, NO_X, SO_2, and VOC a total of 149 (23 plants), 488 (52 plants), 219 (33 plants) and, 848 (75 plants) emission sources were used respectively as input.

The Operational Priority Substances (OPS) dispersion model (version 4.5.2.1) (Van Jaarsveld, 2004) was used to calculate annual concentration levels at x,y coordinates of the individual homes with a resolution of 1 m. This model estimates the exposure attributable to industry, against background exposure due to other sources. For a more detailed description of all steps in the exposure assessment we refer to our previous publication (Bergstra et al., 2020).

2.3. Chronic diseases and sociodemographic information

CBS manages an extensive collection of healthcare data collected by Dutch healthcare insurance companies. In the Netherlands, health insurance is mandatory, therefore the CBS database contains for the entire Dutch population information about the annually dispensed medication (by GP or specialist) per home dwelling citizen. The database covers the period 2012–2017. CBS also has data on the year of birth, sex, marital status, family composition, income, and ethnicity.

2.3.1. Chronic diseases

CBS uses the 4 digit Anatomical Therapeutic Chemical Classification System (ATC code) according to the *Guidelines for ATC classification and DDD assignment 2020* from the World Health Organisation (WHO Collaborating Centre for Drug Statistics Methodology, 2019) to categorize the dispensed medication. Specific chronic diseases were identified based on these ATC-codes, according to guidance by a previous study (Huber et al., 2013). The following four chronic diseases were identified for the current study based on the integrated science assessments of EPA for particulate matter, NO_X and SO_2 (Environmental Protection Agency (EPA), 2019, 2016a, 2016b): cardiovascular diseases, respiratory diseases, diabetes mellitus, and inflammatory conditions. Other chronic diseases of interest, e.g. lung cancer and dementia, remain outside the scope of this study. General cardiovascular (CV) medication was defined as drugs included in the ATC codes B01A and C04A (Antithrombotic agents and peripheral vasodilators), C01 (Cardiac agents), C03A and C08 (low-ceiling diuretics & calcium channel blockers), and C07, C09A, and C09B (beta blocking agents & ACE inhibitors). Respiratory illness (asthma, COPD, wheezing disorder) was defined as drugs included in the ATC code R03 (drugs for obstructive airway diseases). Diabetes mellitus was defined as drugs included in the ATC codes A10A and A10B (insulins and analogues and blood glucose lowering drugs), and A10X (other drugs used in diabetes). Inflammatory conditions was defined as drugs included in the ATC codes M01 (anti-inflammatory and anti-rheumatic products) and M02 (topical products for joint and muscular pain).

2.3.2. Sociodemographic variables

The following individual characteristics were taken into account as confounders: age, sex, ethnicity, marital status, family composition and income. Age was categorized into six age groups (0–4, 5–9, 10–17, 18–44, 45–64, and 65 years and older). Ethnicity (first generation) was categorized as native Dutch, and immigrants from Western and non-Western origin. Western immigrants are persons with a migration background in Europe (excluding Turkey), North America and Oceania, and Indonesia and Japan. Studies have linked lower socioeconomic position (SEP) with disproportionate access to health care and poorer health outcomes. SEP may be gauged by various measures such as marital status and income (Sahni et al., 2017). Marital status was categorized into 1) single, 2) married or living with partner 3) divorced, 4) widow. Family composition was categorized into households without and with children.

The registration of the highest educational level of CBS is incomplete. The linkage of school diplomas with education level was implemented in the early 1970s by the CBS, and, thus, for many older persons educational level is not available (Robroek et al., 2020). Therefore, household spendable income was used as indicator of socio-economic position. The disposable income of a household consists of gross income minus premiums and taxes. Household disposable income was categorized into quartiles. Besides individual socioeconomic position also neighbourhood socioeconomic position may influence health (behaviour) (Forsberg et al., 2018; Kim et al., 2020). Neighbourhood household income was used as the mean disposable household income per neighbourhood, categorized into four groups. In the study area a neighbourhood has on average 850 inhabitants.

Since health of people in rural areas may differ from people in cities due to differences in social and physical environment and lifestyles (Aerts et al., 2020a; Trabelsi et al., 2019), the population density (number of inhabitants per km^2) was also included.

2.3.3. Drug prescribing behaviour general practitioner

Drug prescribing can differ considerable across GPs (Muijrers et al., 2004). The CBS database with annually dispensed medication has no information about which GP or specialist prescribed the drugs. In order to be able to take GP prescription behaviour as confounder into account, the nearest GP practice per home address was identified and used as an estimator. The geographic information system QGIS (version 2.18) was used to geocode (by means of the PDOK BAG Geocoder plugin) the addresses of the GP practice. The nearest GP practice per home address was determined by use of the QGIS NNJoin Plugin. GP practices close to each other (e.g. in one village) were clustered because it is not possible to determine the preference of a citizen for a particular GP practice.

2.4. Statistical analyses

Multivariate logistic regression analyses, utilizing generalized estimating equations (GEE), were used to analyse associations of pollutants with chronic diseases. In this repeated measurement analysis an unstructured covariance structure (least restrictive) was applied to take into account residual correlation. The unstructured covariance structure had a better goodness of fit than the compound symmetry covariance structure. In the main analysis, the exposure in a particular year is associated with dispensed medication in the same year. Besides exposure concentration also the exposure duration (number of years lived in the study area from 2012) and an interaction term (exposure concentration X exposure durantion) were examined. Centering methodology was used to reduce multicolinearity.

Exposure correlation matrix figures were constructed to calculate the correlation between the four air pollution compounds, in order to identify potential confounding or collinearity effects in the regression analyses.

The statistical analyses were conducted with the statistical package IBM SPSS version 25 (SPSS Inc., Chicago, IL, USA). Results are presented with 95% confidence intervals (CI). The RStudio statistical software, version 1.4.113, was used to provide the graphs.

3. Results

From January 1, 2012 to December 31, 2017 in the study region 648,330 observations were registered. Subjects without a successful link of air pollution data to their home address (n = 44,011) and subjects with a home address close to major urban roads/freeways (more than 5000 vehicles per day and the distance between road and house is less than 100 m) and waterways (distance between the axis of the waterway and home address was less than 250 m) (n = 67,720) were excluded, leaving 536,599 observations in the current study. The prevalence of chronic diseases between the included subjects and excluded subjects were similar (Supplementary Table S1). The number of observations per subject ranged from one to six, and 72 percent of the subjects had six observations.

At the start of the study the largest age group was 45–65 years (32%) and the largest ethnic group was native Dutch (86%) (see Table 1). For all covariates the number of missings was 2.2% (GP, data not shown in Table 1) or less.

The prevalence of cardiovascular diseases (CVD) and diabetes mellitus among children was very low (see Fig. 2). Inflammatory diseases, unlike the other chronic diseases, decreased from the age of 60 and were consistently more present in women. CVD with inflammatory conditions and CVD with diabetes mellitus had the highest co-occurrence (5.4% and 3.6% respectively, see Supplementary Fig. S1). The prevalence of cardiovascular diseases has increased slightly over the years of study, and the prevalence of inflammatory conditions has decreased over these years (Supplementary Fig. S2).

Table 2 shows that most of the subjects in the study population had a modestly increased exposure to PM_{10}, NO_X, SO_2 and VOC from industrial emissions compared to the background concentration from all other sources. The geographical exposure pattern is depicted in Fig. 1 for NO_X and for other compounds in the supplementary file (Supplementary Figs. S3–S5). The air pollution compounds were (highly) correlated (Pearson correlation coefficients ranged from 0.40 to 0.83, see Fig. 3). The density plots show clusters in the air pollution distribution. The x-y plots shows several scatter patterns.

Table 3 shows that adjustment for covariates in logistic regression analyses with GEE reduced the observed associations towards null for most comparisons. Adjusted logistic regression analyses with GEE showed that exposures to PM_{10} and NO_X (per $\mu g/m^3$) were significantly associated with CVD (OR 1.06, 95CI% 1.06–1.06 and OR 1.01, 95%CI 1.01–1.01 respectively). Exposures to PM_{10} and SO_2 (per $\mu g/m^3$) were significantly associated with inflammatory conditions (OR 1.05, 95%CI 1.00–1.09 and OR 1.07, 95%CI 1.01–1.14 respectively). Exposure to SO_2 was inversely associated with cardiovascular diseases (OR 0.91, 95%CI 0.86–0.97). Except for inflammatory conditions exposure duration (years) was significantly associated with the other three chronic diseases (OR varying from 1.01 to 1.03). The models for PM_{10}, NO_X, SO_2 and VOC showed inverse associations between exposure duration and inflammatory conditions (OR varying from 0.98 to 0.99). The interaction terms of exposure concentration and exposure duration were close to 1 in all statistical models (data not shown in Table 3).

Additional analyses with two-pollutants in one logistic regression analysis with GEE showed that associations compared to single pollutant models generally were reduced (Supplementary Table S2).

GPs' prescribing behaviour may influence the results as the proportion of dispensed medicine between GP locations in this study differed as much as a factor of 2 (Supplementary Table S3). Logistic regression analyses with GEE with and without GP location as adjustment variable showed small differences in presented associations (Supplementary Table S4).

Table 1
Statistical summary of social-demographical characteristics and selected chronic diseases of the subjects in the study area (2012, n = 89714).

Characteristic	
Sex, n (%)	
Male	44666 (49.8)
Female	45048 (50.2)
Age (years), n(%)	
0 - 4	3206 (3.6)
5 - 9	4623 (5.2)
10 - 17	8719 (9.7)
18 - 44	25316 (28.2)
45 - 64	28630 (31.9)
≥ 65	19220 (21.4)
Ethnicity, n (%)	
Native Dutch	76788 (85.6)
Immigrant western	10850 (12.1)
Immigrant non western	2076 (2.3)
Marital status, n (%)	
Married or living with partner	50985 (56.8)
Widow	5000 (5.6)
Divorced	4547 (5.1)
Single	28340 (31.6)
Missing	842 (0.9)
Single parenthood, n (%)	
Yes	5738 (6.4)
No	41122 (45.8)
Household without children	42763 (47.7)
Missing	91 (0.1)
Household with children, n (%)	
No	44853 (50.0)
One child	16504 (18.4)
Two children	20149 (22.5)
Three or more	8174 (9.1)
Missing	34 (0.0)
Gross household income, n (%)	
<34,000 euro	19508 (21.7)
34,000–60,000 euro	22628 (25.2)
60,000–91,000 euro	23576 (26.3)
>91,000 euro	23627 (26.3)
Missing	375 (0.4)
Gross neighbourhood household income, n (%)	
< 62,500 euro	18376 (20.5)
62,500–66,000 euro	23412 (26.1)
66,000–73,500 euro	24374 (27.2)
>73,500 euro	23552 (26.3)
Population density, n (%)	
< 1400 inhabitants per km^2	24858 (27.7)
1400–2300 inhabitants per km^2	23683 (26.4)
2300–2700 inhabitants per km^2	22096 (24.6)
> 2700 inhabitants per km^2	19077 (21.3)
Locations of general practices, n	18
Chronic diseases, n (%)	
Cardiovascular diseases	19377 (21.6)
Respiratory diseases	7915 (8.8)
Diabetes mellitus	4508 (5.0)
Inflammatory conditions	17375 (19.4)

Table 2
Modelled exposure to industry-related air pollution at the residential addresses of the subjects in the study area (2012–2017, 536,599 observations).

Component	Median	Interquartile range	Minimum - Maximum
PM_{10} (μg/m^3)	0.31	0.40	0.05–4.21
NO_X (μg/m^3)	2.44	1.19	0.45–12.25
SO_2 (μg/m^3)	0.77	0.57	0.19–3.05
VOC (μg/m^3)	1.89	1.04	0.31–11.05

4. Discussion

This study showed that higher exposure levels to PM_{10} and to NO_X from industrial sources were significantly associated with higher occurrence of CVD. PM_{10} and SO_2 from industrial sources were significantly associated with presence of inflammatory conditions. Exposure duration of all specific air pollutants was associated with CVD, respiratory diseases, and diabetes mellitus.

An unexpected finding in this study was the inverse association between SO_2 exposure with respiratory diseases. We can only speculate on possible explanations for this inverse association. First, SO_2 had the lowest range of all 4 compounds and also the most scattered exposure pattern. Hence, the limited discriminatory power may have contributed to the unexpected finding. Second, the observed inverse association may reflect confounding by for example differences in prescribed medication between GPs or other unmeasured variables, resulting in lower prescribed medication in areas with a higher exposure of SO_2 air pollution. Ecological studies in Belgium showed also unexpected inverse associations between air pollution and medication sales, which suggest that the observed geographical distribution may be driven by differences in medical/pharmaceutical practices, rather than by environmental realities (Aerts et al., 2020a, 2020b; Trabelsi et al., 2019). However, the fact that we did not observe this for other compounds, despite the fact that these were correlated to SO_2, points towards a more exposure-specific explanation. Third, the immission of PM_{10} and NO_X in the study area comes mainly from sources in the Netherlands, while the emission of SO_2 mainly comes from sources in Belgium (see Supplementary Fig. S4). It is unknown whether the geographical differences in sources of exposure reflect also differences in other relevant characteristics. Another contradictory observation was that exposure levels were, in general, associated with an increased risk on inflammatory diseases, but for duration of exposure we observed risk estimates consistently below 1, suggesting risk reductions of 1%–2%. This is possibly due to the fact that the prevalence of inflammatory conditions has decreased slightly over the years in the Dutch population, which may have created an artificial inverse association.

This study indicates that specific air pollutants caused by industry may contribute to the occurrence of selected chronic diseases. In a previous study, we found an association between industry-related air pollution and adverse birth outcomes in the same area and time period (Bergstra et al., 2020). Higher exposures to PM_{10}, NO_X, SO_2 and VOC were among others associated with reduced birth weight.

Comparable studies about the influence of industry-related air pollution on different health effects are rare. Most studies focus on air pollution in general (road traffic, smog and urban or regional differences) and mortality from chronic diseases. To the best of our knowledge there are no other studies that have described associations of individual-level modelled air pollution exposure from industry and the onset and aggravation of chronic diseases in the general population.

This study has certain strengths and limitations. First, a strength of the study is the use of dispensed medication as objective register-based measure with linkage to exposure estimates from a dispersion model. This prevents reporting bias by subjects in presented associations. The data were provided by CBS, based on healthcare data on paid medication by Dutch healthcare insurance funds. In the Netherlands, health insurance is mandatory, therefore, the CBS database contains the entire Dutch population. A second strength is that exposure to air pollution was based on a dispersion model with many industrial sources. A validation study showed a good agreement for both SO_X and NO_X between measured and modelled concentrations with the OPS dispersion model (Van Jaarsveld, 2004). A dispersion model takes many relevant factors into account, such as stack height, exact distance between stack and the home address of the subjects, weather, wind direction, and temperature. Third, also emissions from foreign industries were included in this study. Fourth, extensive emission data was used for the dispersion calculations. Although available information only allowed estimation of annual mean concentrations, this is probably a fair reflection of industry-based air pollution.

A limitation is the fact that outdoor air pollution estimations at the home address were used without considering, for example, exposure at the workplace and during travel. Second, the air pollution components were highly correlated and therefore it is possible that the effect of a

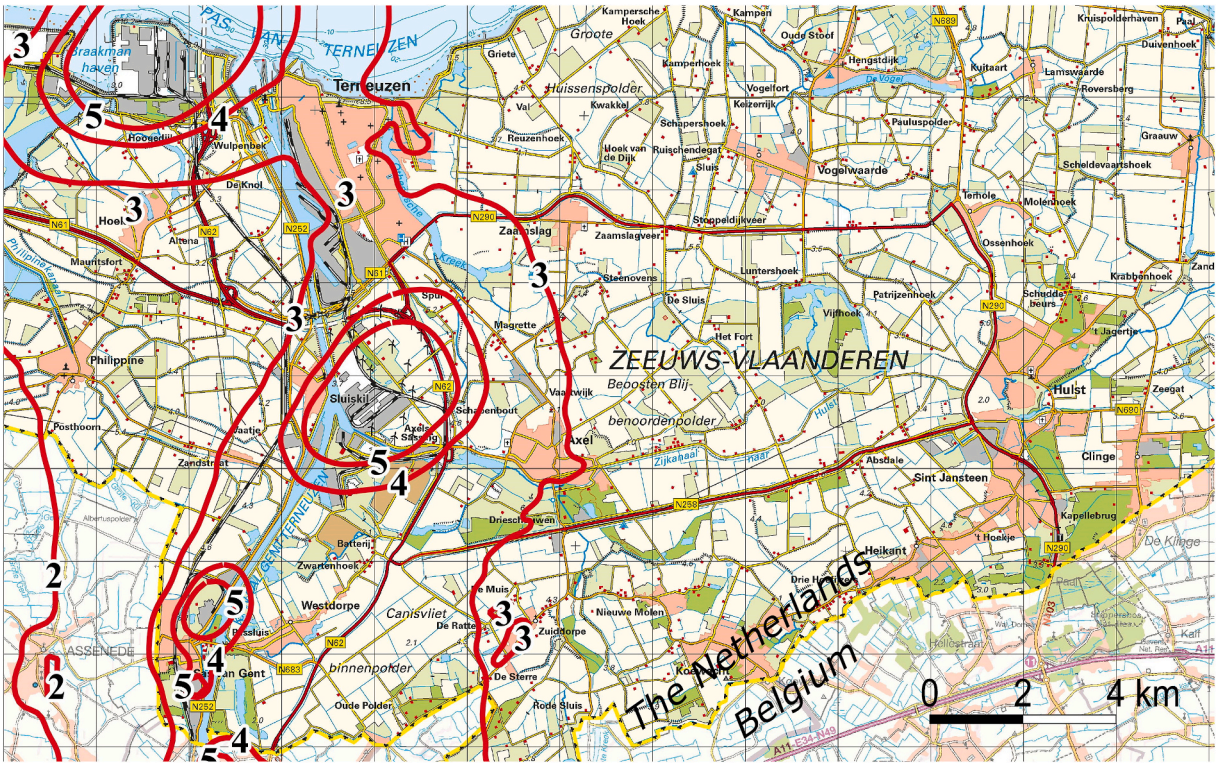

Fig. 1. Modelled NO_X iso-concentration contours (per $\mu g/m^3$), depicted with red solid lines. Numbers presents the mean annual industry-related exposure without background concentration (2012–2017). Map reprinted from Kadaster in the Netherlands (https://nationaalgeoregister.nl/) under a CC-BY-4.0 license, 2019.

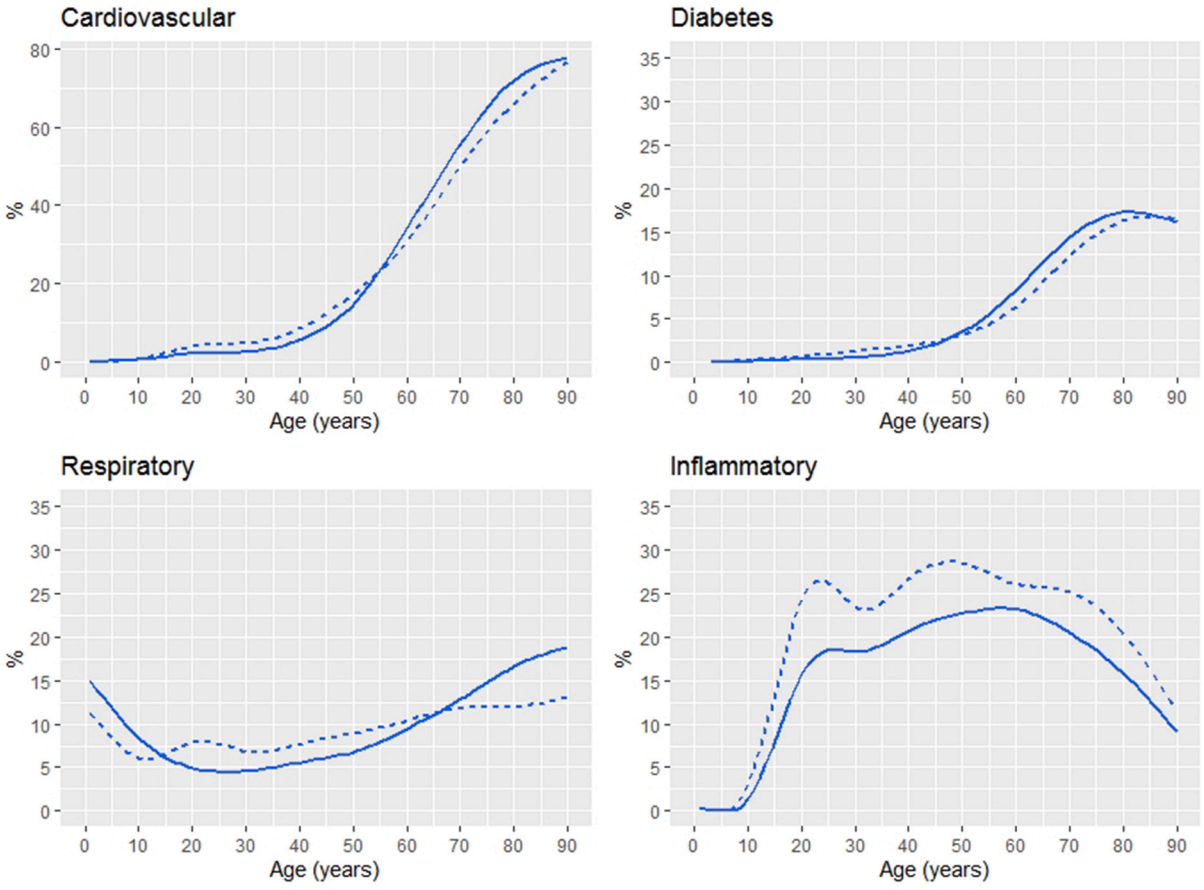

Fig. 2. Prevalence of four chronic diseases by age among male (solid line) and female (dashed line) (2012, n = 89,714).

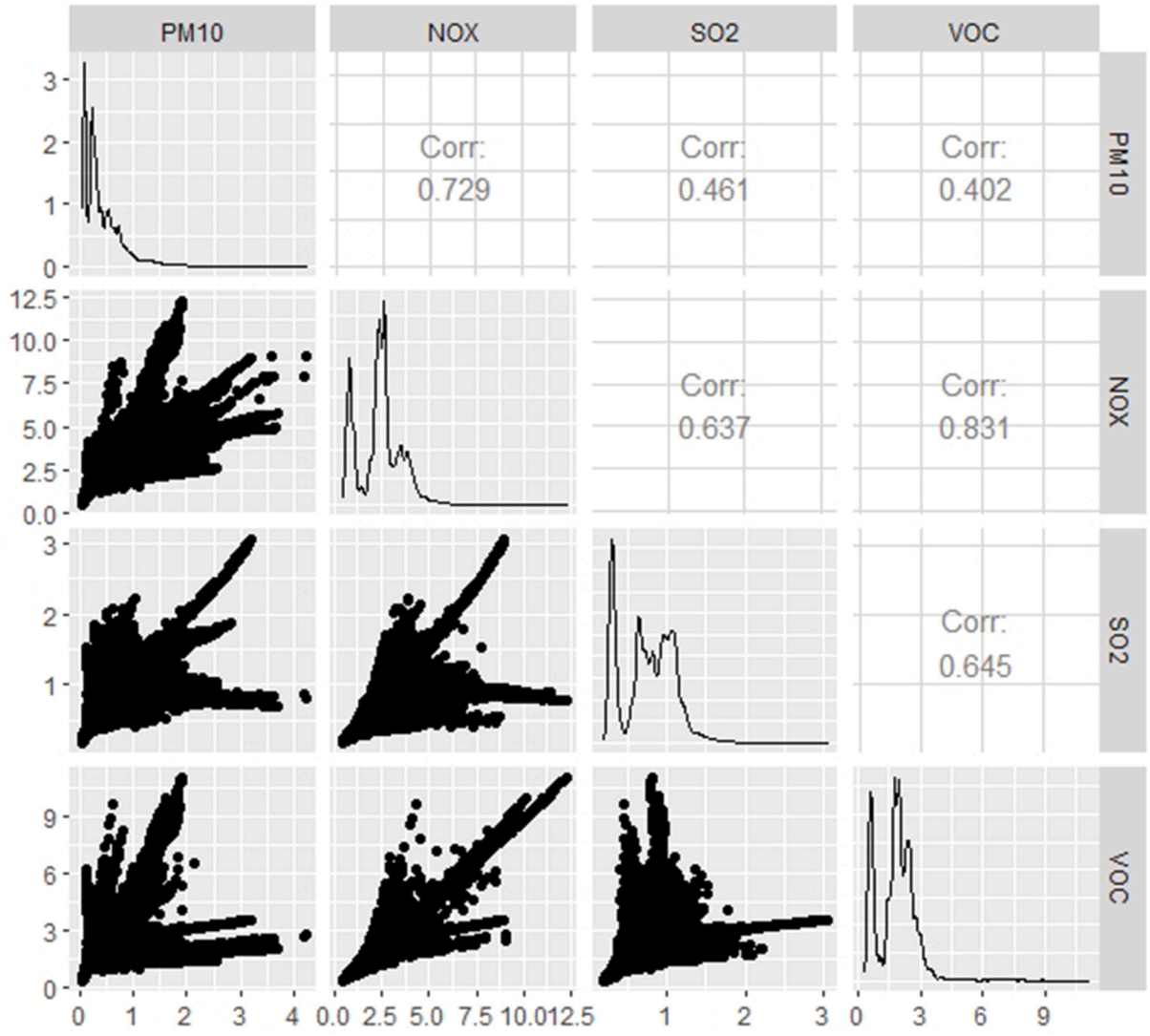

Fig. 3. XY plot, density plot and correlation (Pearson) matrix for specific air pollution components (2012–2017, 536,599 observations).

particular pollutant is confounded by the effect of another pollutant(s). The pollutants should be considered more as indicators of the air pollution mixture and not as uniquely identifiable causal factors for the occurrence of chronic diseases. In addition, specific chronic diseases may be particularly sensitive to various components (e.g. organic compounds, nitrate, elemental carbon, trace metals) from different sources of pollution. The industry in the study area with its different processes emit PM_{10}, NO_X, SO_2 and VOC in different ratios and regarding PM_{10} and VOC also with different compositions. The xy plots (see Fig. 3) suggest areas with different emission compositions. This may have influence the results. Third, analyses with and without covariates showed that the covariates influenced the results. In general, covariates in regression analyses provide better estimators. Fourth, in this registered-based study information about lifestyle at individual level such as smoking and physical activity, was not available for the entire population. Although the statistical models were adjusted for socio-economic position as important predictor for unhealthy behaviour, residual confounding cannot be completely ruled out. Fifth, prescribed medication for a chronic illness may be different for children and adults. This can bias the results. For most associations this will be limited as the results for cardiovascular diseases (CVD), diabetes mellitus, and inflammatory conditions are mainly determined by adults and/or elderly. Sixth, medication prescribing differs considerable across GPs (Supplementary Table S3). Logistic regression analyses with and without GP as covariate showed small differences (Supplementary Table S4). The nearest GP practice for each home address was used as proxy for the GP location (GP locations close to each other were clustered) where medication was prescribed. The actual distribution of patients among GP practices may differ and thus may introduce some error. Also, a GP practice may employ different GPs each with their own medicine prescription behaviour. An analysis with detailed information on GP and specialist prescribing the medication may improve the accuracy of studies about air pollution and dispensed medication for chronic diseases.

5. Conclusion

This study indicates that specific air pollution components caused by industry may contribute to the occurrence of cardiovascular diseases, respiratory diseases, diabetes mellitus, and inflammatory conditions.

Author contributions

Arnold Bergstra: Conceptualization, Methodology, Software, Formal analysis, Investigation, Writing – original draft, Visualization. Jasper Been: Writing- Reviewing and Editing. Alex Burdorf: Conceptualization, Methodology, Investigation, Writing- Reviewing and Editing,

Table 3
Associations between exposure (concentration and exposure duration) to specific industry-related air pollutants and selected chronic diseases in logistic regression analysis with GEE (536,599 observations).

	Cardiovascular diseases	Respiratory diseases	Diabetes mellitus	Inflammatory conditions
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Unadjusted regression models				
Model for PM_{10}				
PM_{10} (μg/m^3)	**0.96 (0.94–0.99)**	**1.08 (1.04–1.12)**	0.99 (0.94–1.05)	**1.22 (1.19–1.24)**
Exposure duration (years)	**1.06 (1.05–1.06)**	**1.01 (1.01–1.02)**	**1.04 (1.04–1.05)**	**0.99 (0.99–1.00)**
Model for NO_X				
NOX (μg/m^3)	1.00 (0.99–1.00)	1.00 (0.99–1.01)	1.00 (0.99–1.01)	**1.04 (1.03–1.05)**
Exposure duration (years)	**1.06 (1.05–1.06)**	**1.01 (1.01–1.02)**	**1.04 (1.04–1.05)**	1.00 (1.00–1.00)
Model for SO_2				
SO2 (μg/m^3)	**0.94 (0.91–0.97)**	**0.87 (0.83–0.91)**	1.01 (0.95–1.07)	1.02 (0.99–1.05)
Exposure duration (years)	**1.05 (1.05–1.06)**	**1.01 (1.01–1.02)**	**1.04 (1.04–1.05)**	1.00 (1.00–1.00)
Model for VOC				
VOC (μg/m^3)	**0.99 (0.98–0.99)**	**0.98 (0.96–0.99)**	1.01 (0.99–1.02)	**1.02 (1.01–1.03)**
Exposure duration (years)	**1.06 (1.05–1.06)**	**1.01 (1.01–1.02)**	**1.04 (1.04–1.05)**	1.00 (1.00–1.01)
Adjusted regression models[a]				
Model for PM_{10}				
PM_{10} (μg/m^3)	**1.06 (1.06–1.06)**	1.00 (0.95–1.05)	0.99 (0.94–1.05)	**1.05 (1.00–1.09)**
Exposure duration (years)	**1.02 (1.02–1.02)**	**1.01 (1.01–1.02)**	**1.02 (1.01–1.02)**	**0.98 (0.98–0.99)**
Model for NO_X				
NO_X (μg/m^3)	**1.01 (1.01–1.01)**	1.00 (0.99–1.01)	1.00 (0.99–1.01)	1.01 (1.00–1.02)
Exposure duration (years)	**1.02 (1.02–1.02)**	**1.01 (1.01–1.02)**	**1.02 (1.01–1.02)**	**0.99 (0.98–0.99)**
Model for SO_2				
SO_2 (μg/m^3)	0.99 (0.95–1.03)	**0.91 (0.86–0.97)**	1.00 (0.95–1.06)	**1.07 (1.01–1.14)**
Exposure duration (years)	**1.02 (1.02–1.03)**	**1.01 (1.01–1.02)**	**1.02 (1.01–1.02)**	**0.99 (0.98–0.99)**
Model for VOC				
VOC (μg/m^3)	1.01 (1.00–1.02)	1.00 (0.98–1.02)	1.00 (0.98–1.01)	1.02 (1.00–1.03)
Exposure duration (years)	**1.03 (1.02–1.03)**	**1.01 (1.01–1.02)**	**1.02 (1.01–1.02)**	**0.99 (0.99–0.99)**

Bold text indicates logistic regression coefficient is statistical significant ($p < 0.05$). [a]Adjusted for: sex, age, ethnicity, marital status, single parenthood, number of children in household, gross household income, gross neighbourhood household income, population density and general practice.

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Medical ethical committee

This research proposal has been approved by the medical ethical committee from the Erasmus MC, University Medical Centre, the Netherlands (reference MEC-2020-0386).

Data statement

The research data is confidential according to CBS, RIVM and the Flanders Environment Agency (Belgium) regulations.

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.

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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.2022.112872.

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