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The association between air pollution and type 2 diabetes in a large cross-sectional study in Leicester: The CHAMPIONS Study

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ABSTRACT

Background: Observational evidence suggests there is an association between air pollution and type 2 diabetes; however, there is high risk of bias.
Objective: To investigate the association between air pollution and type 2 diabetes, while reducing bias due to exposure assessment, outcome assessment, and confounder assessment.
Methods: Data were collected from 10,443 participants in three diabetes screening studies in Leicestershire, UK. Exposure assessment included standard, prevailing estimates of outdoor nitrogen dioxide and particulate matter concentrations in a 1×1 km area at the participant's home postcode. Three-year exposure was investigated in the primary analysis and one-year exposure in a sensitivity analysis. Outcome assessment included the oral glucose tolerance test for type 2 diabetes. Confounder assessment included demographic factors (age, sex, ethnicity, smoking, area social deprivation, urban or rural location), lifestyle factors (body mass index and physical activity), and neighbourhood green space.
Results: Nitrogen dioxide and particulate matter concentrations were associated with type 2 diabetes in unadjusted models. There was no statistically significant association between nitrogen dioxide concentration and type 2 diabetes after adjustment for demographic factors (odds: 1.08; 95% CI: 0.91, 1.29). The odds of type 2 diabetes was 1.10 (95% CI: 0.92, 1.32) after further adjustment for lifestyle factors and 0.91 (95% CI: 0.72, 1.16) after yet further adjustment for neighbourhood green space. The associations between particulate matter concentrations and type 2 diabetes were also explained away by demographic factors. There was no evidence of exposure definition bias.
Conclusions: Demographic factors seemed to explain the association between air pollution and type 2 diabetes in this cross-sectional study. High-quality longitudinal studies are needed to improve our understanding of the association.

1. Introduction

Diabetes is one of the leading causes of death in lower-middle-income economies, upper-middle-income economies, and high-income economies (World Health Organization, 2017). The global prevalence of diabetes has risen from 4.7% in 1980 to 8.5% in 2014, with the majority of cases being type 2 diabetes (World Health Organization, 2016). Experimental evidence in humans and animals suggests that it is plausible that air pollution is a risk factor for type 2 diabetes (Rao et al., 2015). Exposure to the traffic-related air pollutant nitrogen dioxide (NO_2) and the associated particulate matter ≤ 2.5 µm ($PM_{2.5}$) and ≤ 10.0 µm (PM_{10}) pollutants is related to inflammation and insulin resistance (Rao et al., 2015), which are the hallmarks of type 2 diabetes (DeFronzo, 2010). Experimental evidence in humans suggests that short-term exposure to low levels of $PM_{2.5}$ increases systemic insulin resistance (Brook et al., 2013). Experimental evidence in mice suggests

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that oxidative stress in the lungs may be an intermediate step between exposure to $PM_{2.5}$ and systemic insulin resistance (Haberzettl et al., 2016). Observational evidence also suggests that there is an association between air pollution and type 2 diabetes; however, there is a high risk of bias (Eze et al., 2015).

It is important to investigate the association between air pollution and type 2 diabetes while reducing bias. Bias due to exposure assessment, bias due to outcome assessment, and bias due to confounder assessment were addressed in the present study in Leicester, Calculating How Air Pollution Impacts Our Society (The CHAMPIONS Study).

2. Methods

2.1. Participants

The present study included participants from three diabetes screening studies that were conducted in Leicestershire in the United Kingdom using identical standard operating procedures: ADDITION-Leicester (ClinicalTrials.gov registration number: NCT00318032), Let's Prevent Diabetes ('Let's Prevent', NCT00677937), and Walking Away from Diabetes ('Walking Away', NCT00941954). Research ethics committees approved the studies and all participants gave written, informed consent.

The original studies are described in detail elsewhere (Gray et al., 2012b; Webb et al., 2010; Yates et al., 2012). Briefly, ADDITION-Leicester (2004–2009) was a population-based study in which people were screened for type 2 diabetes (Webb et al., 2010). Individuals selected at random from participating general practices who met the eligibility criteria were invited to participate. Eligibility criteria included age 40–75 years (white Europeans) or 25–75 years (other ethnicities) and no diagnosis of diabetes; thus, all type 2 diabetes cases were screen-detected. Let's Prevent (Gray et al., 2012b) (2009–2011) and Walking Away (Yates et al., 2012) (2010) used similar recruitment methods and inclusion criteria, except that individuals in Walking Away were at high risk of type 2 diabetes according to the Leicester Practice Risk Score (Gray et al., 2012a). Participants in all three studies attended a clinic visit where they provided a fasting blood sample, underwent an oral glucose tolerance test, had anthropometric measurements recorded, and completed questionnaires. Participants were excluded from the present analysis if their postcode was missing or invalid, if their postcode could not be reconciled with an air pollution value, or if their diabetes values were missing. The most recent record was used if participants took part in more than one of the studies. The original cohorts are also described in detail elsewhere; briefly, age was similar in each cohort, the proportion of males was similar, the proportion of whites was similar, physical characteristics were similar, cardiovascular disease risk factors were similar, the proportion with abnormal glucose tolerance was similar, and the proportion with type 2 diabetes was similar (Gray et al., 2012a).

2.2. Explanatory variables

The Department for Environment, Food & Rural Affairs (DEFRA) in the United Kingdom publishes 1×1 km grids of pollutant concentrations using data from around 9000 representative roadside values (Department for Environment Food and Rural Affairs, 2015). Air pollution data were derived from the DEFRA Pollution Climate Mapping (PCM) model, which is described elsewhere (Department for Environment Food and Rural Affairs, 2015). There is one model per pollutant and the models are run by Ricardo Energy & Environment (Oxfordshire, UK) on behalf of DEFRA. Exposure to air pollution in the present study was defined as the three-year average, including the year in which the participant entered the study and the preceding two years. The list of participants' postcodes was run through a script which binned each postcode into a 1×1 km grid of the same size and shape as that used in the PCM model. The NO_2, $PM_{2.5}$ and PM_{10} concentrations for each of the 5394 unique postcodes could then be combined with the diabetes data for that postcode.

2.3. Outcomes measures

Type 2 diabetes diagnoses were based on World Health Organisation 2011 criteria, using the oral glucose tolerance test (fasting glucose ≥ 7.0 mmol·L^{-1} or two hour glucose ≥ 11.0 mmol·L^{-1}).

2.4. Potential confounders

We recorded age, sex, smoking habit, urban or rural location (Bibby and Shepherd, 2004), and area social deprivation score [The English Indices of Deprivation 2010 provides a relative measure of deprivation at small area level across England, and its measure of multiple deprivation was used in the present study (DATA.GOV.UK, 2013)]. Ethnicity was self-reported using United Kingdom census categories and grouped as white European, South Asian and other due to the small number of participants in some ethnic groups. Trained staff measured height and weight and body mass index (BMI) was calculated as weight (kg)/height (m) squared. Cholesterol concentration was measured in the fasting blood sample. Self-reported physical activity was assessed using the International Physical Activity Questionnaire and published standards were used to calculate the number of metabolic equivalents (METs) per day for total activity (The IPAQ Group, 2005). Green space was defined as the percentage of green space in the participant's home neighbourhood. The geographic information system, ArcGIS 9.3, was used (ESRI, 2009). To delineate neighbourhood boundaries, each participant's postcode was geolocated using the UK Ordnance Survey Code-Point database (2004–2013) (Ordnance Survey, 2016), which provides a set of coordinates depicting the average latitude and longitude of all mail delivery locations within each postcode, which contains 15 addresses on average. Neighbourhood was delineated based on distance around these coordinates. Neighbourhood was defined as the straight-line distance of 3 km, as it is thought that people will travel such a distance to access resources and be physically active (Boruff et al., 2012; Dalton et al., 2013; Hurvitz and Moudon, 2012). Estimates of green space were from the Centre for Ecology and Hydrology Land Cover Map of the United Kingdom (Centre for Ecology and Hydrology, 2011), which is derived from satellite images and digital cartography, and records the dominant land use type, based on a 23 class typology, per 25×25 m grid cell. Broadleaved and coniferous woodland, arable, improved grassland, semi-natural grassland, mountain, heath, bog, and freshwater (including rural Lakeland environments) were classed as green space. Each participant's exposure was computed by overlaying the mapped green space with the neighbourhood boundary in the geographic information system software to calculate the percentage of each neighbourhood area that contained these land cover types.

2.5. Statistical analysis

The distributions of the air pollutants were considered using histograms (not shown). The odds of type 2 diabetes were investigated using generalized estimating equations, with pollutant concentrations expressed per 10 μg·m^3. It has been argued that models should include variables that are thought to be important from the literature, whether or not they reach statistical significance in a particular data set (Collins et al., 2011). The models in the present study included variables that Eze et al. (2015) identified as potential confounders of the association between air pollution and type 2 diabetes. Neighbourhood green space