Land cover and air pollution are associated with asthma hospitalisations: a cross-sectional study

Ian Alcock[1]; Mathew White[1]; Mark Cherrie[2,1]; Benedict Wheeler[1]; Jonathon Taylor[3]; Rachel McInnes[4,1]; Eveline Otte im Kampe[5]; Sotiris Vardoulakis[6,1]; Christophe Sarran[4]; Ireneous Soyiri[2]; Lora Fleming[1]

[1]University of Exeter; [2]University of Edinburgh; [3]University College London; [4]MetOffice; [5]London School of Hygiene and Tropical Medicine; [6]Public Health England

Abstract

Background

There is increasing policy interest in the potential for vegetation in urban areas to mitigate harmful effects of air pollution on respiratory health. We aimed to quantify relationships between tree and green space density and asthma-related hospitalisations, and explore how these varied with exposure to background air pollution concentrations.

Methods

Population standardised asthma hospitalisation rates (1997-2012) for 26,455 urban residential areas of England were merged with area-level data on vegetation and background air pollutant concentrations. We fitted negative binomial regression model using maximum likelihood estimation to obtain estimates of asthma-vegetation relationships at different levels of pollutant exposure.

Results

Green space and gardens were associated with reductions in asthma hospitalisation when pollutant exposures were lower but had no significant association when pollutant exposures were higher. In contrast, tree density was associated with reduced asthma hospitalisation when pollutant exposures were higher but had no significant association when pollutant exposures were lower.

Conclusions

We found differential effects of natural environments at high and low background pollutant concentrations. These findings can provide evidence for urban planning decisions which aim to leverage health co-benefits from environmental improvements.

Keywords

Ecosystem management; Air pollutants; Green space; Urban land use; Pollen; Allergy

1 **Introduction**

Asthma is a chronic inflammatory condition of the airways of the lungs which causes hyper-responsiveness to specific triggers, and leads to a variety of respiratory symptoms (GINA 2017). Persistent low-level symptoms can be exacerbated by exposure to stressors such as influenza, air pollution and environmental allergens. In the UK, 18% of adults report asthma in the previous 12 months (To et al. 2012), and symptoms are reported by 21% of 6-7 year olds and 25% of 13-14 year olds (Asher et al. 2006). Over 5.4 million people are currently receiving treatment in the UK, at an annual cost to the National Health Service of around £1 billion (www.asthma.org.uk).

Exposure to higher levels of outdoor air pollutants such as nitrogen dioxide (NO2), particulate matter less than 2.5 μm (PM2.5) and sulphur dioxide (SO2) has been associated with the onset of wheeze and asthma in pre-school infants (Clark et al. 2010), school-aged children (Khreis et al. 2017; Gasana et al. 2012) and adults (Anderson et al. 2013). Exacerbation in those who already have asthma has also been linked to exposure to outdoor air pollution. For example, short-term increases in pollutant exposure are associated with increased asthma symptoms and asthma-related emergency room visits (Zheng et al. 2015; Weinmayr et al. 2010); and long-term background pollutant exposure is associated with increased asthma-related hospitalisations (Roberts et al. 2012). Indoor air quality (and other indoor environmental factors) are also important for asthma prevalence (Kanchongkittiphon et al. 2015).

The potential for vegetation to mitigate the negative health impacts of air pollution has received considerable interest from urban planners (Escobedo et al. 2011). Trees and plants reduce ambient particulate concentrations by capturing particles on their leaf surfaces (Wuyts et al. 2008; Roy et al. 2012), and leaf stomata can absorb gaseous pollutants (Chaparro-Suareza 2011). Models of urban area airsheds (ground to atmospheric boundary layer) suggest that reductions in particulates from deposition on urban trees are modest (Tallis et al. 2011). Importantly, however, localised improvements to air quality for those living in close proximity to urban trees may be both much higher and of medical significance (McDonald et al. 2016). Trees can also influence wind turbulence and thus the dispersion of air pollutants (Janhäll 2015). Urban trees may increase pollutant concentrations in some street canyon configurations (Salmond et al. 2013; Vos et al. 2013), but reduce pollutant concentrations when winds are parallel to street canyons (Amorim et al. 2013; Abhijith and Gokhale 2015).

The potential impacts on asthma of tree cover and green spaces in general are further complicated by their generation of allergenic pollen. Even though not all asthmatics react to pollen, short-term variation in local pollen concentrations are associated with allergy medication purchases (Ito et al. 2015), asthma symptoms (DellaValle 2012), and asthma-related emergency department visits (Ito et al. 2015; Jariwala et al. 2011; Orazzo et al. 2009). Moreover, there is evidence from laboratory and field experiments to suggest that environmental air pollutant and allergenic pollen exposures may interact (Motta et al. 2006; Ghiani et al. 2012). For example, studies show that NO2 can impact on pollen morphology (Chassard et al. 2015; Zhao et al. 2015), as well as change the pollen protein content or protein release processes, although effects are species and concentration dependent (Frank and Ernst 2016). There is also evidence that grass pollen allergen molecules can bind to other fine particles in polluted air and become concentrated (Namork et al. 2006). In addition, airways damaged by air pollutant exposure may be more susceptible to hyper-responsiveness with allergen exposure (Amato et al. 2010). Consistent with these mechanisms, there is evidence of the interactive effects of pollen and other aeroallergens with air pollutants on increased hospitalisation for asthma (Cakmak et al. 2012; Hebbern and Cakmak 2014).

The net effects of urban trees and green spaces on asthma exacerbation are likely therefore to result from opposing influences which are not easily separated in empirical investigation, and are necessarily compounded in the experience of asthma sufferers in their contacts with natural environments. Indeed, a wider variety of exacerbating and mitigating environmental factors than those discussed above may be involved. Even as they remove particulate and gaseous pollutants, urban woodlands and green spaces may reduce air quality through the emission of biogenic volatile organic compounds which contribute to the formation of ozone (Domm et al., 2008). Effects on asthmatics may also result from exposure fungal spores and moulds (Sharpe et al., 2014), saprophytic bacteria, and polyphenolic compounds (Rook 2013). Exposure to natural environments may also impact on asthma through effects on human skin proteobacteria, which can in turn affect atopic sensitisation (Ruokolainen et al. 2015). In addition, green space can promote physical activity and reduce stress (Hartig et al. 2014), which may in turn reduce the risk of asthma attacks, given the potential for overweight/obesity (Beuther et al. 2006) and stress (Vliagoftis 2014) to exacerbate the condition.

Few studies have investigated the net effect of these multiple and potentially conflicting influences of urban trees and green space on asthma. Findings from the limited previous investigations are inconsistent, possibly due to differences between studies in the spatial resolution or local characteristics of vegetation, or in asthma outcome measure, sampled population, or covariate controls. Individual level analyses of the effects of green land cover measures on asthma outcomes have suggested beneficial (Maas et al., 2009; Sbihi et al., 2015), null (Lovasi et al., 2013; Dadvand et al., 2014; Andrusaityte et al., 2016) and even harmful relationships (Lovasi et al., 2013; Dadvand et al., 2014; Andrusaityte et al., 2016); and ecological level analyses have suggested both beneficial (Ayres-Sampaio et al., 2014; Erdman et al., 2015; Lovasi et al., 2008) and null relationships (Ayres-Sampaio et al., 2014; Erdman et al., 2015; Lovasi et al., 2008; Pilat et al., 2012).

Importantly, previous studies are generally at relatively low spatial resolution (leading to imprecision in exposure estimation), and there are almost no examples of large population studies which relate asthma surveillance data at high geographic resolution with local natural environment characteristics. The current study aimed to address this issue by examining emergency hospitalisations for asthma in a small-area ecological analysis of all urban residential areas in England and testing associations with two green space land use measures (neighbourhood green space and domestic gardens), and with tree density. Furthermore, we also recognised the importance of potential interactions between natural environment and air pollutant exposures, driven by processes of pollutant deposition, pollutant dispersion, pollen allergen development and the bio-availability of pollen allergens, as well as direct synergistic exposure effects for asthma sufferers. We therefore aimed to examine not only how asthma hospitalisations are associated with natural environments when adjusted for the effects of air pollutants, but also how the associations between hospitalisations and natural environment exposure might vary at different levels of air pollutant exposure. An understanding of these relationships is needed to inform targeted interventions, public health policies, and urban planning.

2 **Methods**

2.1 Overview

English Hospital Episode Statistics (http://www.content.digital.nhs.uk/hes) were used in a cross-sectional ecological analysis to examine associations between emergency hospitalisations for asthma (ICD-10 J45/J46), natural environments and background air pollutant concentrations. Hospitalisations (n =660,505) for the study period 1st April 1997 to 31st March 2012 amongst

residents of urban areas in England were summed by geographical areas called 'Lower-layer Super Output Areas' (LSOAs, defined by the UK government for statistical reporting for England). LSOAs encompass similar sized populations and have a mean physical area of c. 0.9 km2 in urban areas (n=26,455, with a total population in 2001 of c. 41M). Period (1997-2012) population standardised emergency hospitalisations for asthma for each urban LSOA was linked to other data at LSOA level, specifically: area level measures of public green spaces, domestic gardens, and tree cover (collectively referred to as '*natural environments*' henceforth); air pollution; and Indices of Deprivation (IOD). Negative binomial regression models were used to explore associations between asthma and these factors. Analyses were performed in Stata 14 (StataCorp, College Station TX).

2.2 Asthma data

Standardised hospitalisation rates for asthma (1997-2012) were calculated for each urban LSOA from the area total hospitalisations, and from data on the (2001) area population size. Using data on the (2001) age structure of the population of each of the LSOAs, a direct standardisation was undertaken of these LSOA crude rates, to the 2013 European Standard Population (ESP). These standardised hospitalisation rates (per 100,000 ESP, referred to as the '*asthma rate*' henceforth) enabled comparison between areas.

2.3 Natural environment data

Two measures of 'natural' environment density, 1) LSOA percentage of green space and 2) LSOA percentage of gardens, were derived from the Generalised Land Use Database (GLUD, Department for Communities and Local Government, 2007), which divides the total land in each LSOA into nine categories of use: green space; domestic gardens; freshwater; domestic buildings; non-domestic buildings; roads; paths; railways and other (largely hard standing). GLUD data were collected in 2005 and were then accurate to approximately 10 m^2. Within urban areas, green space is largely publicly accessible, whereas gardens are largely privately owned. Regression models were specified to estimate the change in the asthma dependent variable associated with a percentage point increase in green space and in gardens; it is important to note that such a percentage point increase involves a corresponding percentage point decrease in the omitted reference category, comprising all land uses that are not green space or gardens (i.e. the classes of built land use listed above, and water).

A third natural environment measure used was the density of mature (i.e. over 3 meters high) trees, or closely grouped tree crowns where clustered canopies were at the same height. This variable was derived from tree count data obtained from the Bluesky International, National Tree Map (www.emapsite.com/downloads/product_guides/NTM-Specification.pdf) by aggregating 25 m raster data to LSOA boundaries using ArcGIS (ESRI, Redlands CA). Tree density was calculated from tree count and LSOA surface area data. A scale point increase on the tree density scale represents an increase of 50 trees/clustered crowns per km^2. The green space and gardens land use categories are mutually exclusive (i.e. land parcels are one, or the other, or neither), whereas the tree density measure 'cuts across' the land use classification, in that tree density is derived for all land, irrespective of its land use classification.

2.4 Air pollution data

Period mean levels of modelled background concentrations of NO2, SO2 and PM2.5 at 1 x 1 km spatial resolution (available online from DEFRA https://uk-air.defra.gov.uk/data/pcm-data) were aggregated by areal interpolation to LSOAs using the Geospatial Modelling Environment/ArcGIS (www.spatialecology.com). The outdoor background air pollution data were obtained from Pollution Climate Mapping (PCM) model simulations. PCM is based on dispersion modelling techniques,

national atmospheric emission inventory data, meteorological data, and terrain characteristics (Brookes et al. 2016). It has been calibrated using measurements from the Automatic Urban and Rural Network (AURN) of air quality monitoring sites. Due to limitations in the data available from DEFRA, the range of years over which mean concentrations could be derived did not include the early years of the 1997-2012 period, and also varied slightly between pollutants: NO2 μg/m^3 2001-2012; SO2 μg/m^3 2002-2012; PM2.5 μg/m^3 2002-2012. To avoid the implication that the modelled pollutant data has the accuracy of measured data, quintiles of the period mean outdoor background air pollutant concentrations in urban LSOAs were used as independent variables in regression models. The use of quintiles also allowed non-linear relationships to be evident. (Ozone was not examined in this study since the DEFRA annual summary data gave the number of days exceeding 120 μg/m^3, rather than detailed information on background concentration levels.)

Given that people spend on average 70% of their time in their own homes (Lader et al. 2006), their exposure to residential area outdoor air pollution is, arguably, heavily influenced by the extent of its penetration of domestic buildings. For use in a sensitivity analysis, the urban LSOA mean outdoor concentrations were adjusted to account for the ratio of NO2, SO2 and PM2.5 from outdoor sources estimated to penetrate indoors, based on domestic housing types within each LSOA. Briefly, concentrations of outdoor pollution penetrating indoors depend on the airtightness of the dwelling; the dwelling built form, including exposed surface area and internal volume; wind exposure; occupant ventilation behaviour; and deposition and penetration behaviour of the pollutants. Spatial variation of housing and surrounding environment may therefore lead to regional variations in exposure to outdoor pollution indoors. To account for this, we employed building physics estimates of indoor/outdoor ratio of NO2, SO2 and PM2.5 from outdoor sources only for over 1 million individual dwellings across the UK in the Homes Energy Efficiency Database, averaged for each LSOA (Taylor et al. 2016). These adjusted pollutant measures will be referred to as '*penetrating pollutants*' to distinguish them from the outdoor background concentrations used in the main analysis; quintiles of the period mean penetrating pollutant concentrations were derived. Although they are likely to be important contributors to indoor pollution exposure, pollution from indoor sources and other indoor environment factors are excluded from this sensitivity analysis.

The interval scale measures of NO2 and PM2.5 had a Pearson correlation coefficient of 0.82, and the quintile categories showed a substantial degree of overlap (see Appendix, Part 1). Therefore, to avoid estimates being biased by collinearity, the NO2 and PM2.5 categories were not included simultaneously in the same model. Regression models estimated effects of both NO2 and SO2 in combination, and PM2.5 and SO2 in combination; and then the findings were compared.

2.5 Socio-economic deprivation and region control variables

Socio-economic deprivation is strongly associated with asthma (Uphoff 2015) and was controlled for using data from the English Indices of Deprivation (IOD) 2007, which are Census based statistics at LSOA level compiled from 2005 data (Noble et al. 2008). Principal components analysis was carried out of indices across five domains of deprivation: income; employment; education; barriers to housing and services; and risk of crime. Two IOD domains were not included: health/disability, and living environment. The former included hospital admission rates in its component indicators, and therefore risked conflation with the dependent variable; the latter included air quality in its component indicators, and therefore risked conflation with the air pollution variables of interest. Two principal components had eigenvalues above 1, which together explained 0.818 of the variance in the indices, and scores on these deprivation components, referred to as *DC1* and *DC2*, were included in regression models as covariate controls. Although data on smoking prevalence rates were not available, the deprivation control variables will limit any bias to estimates which may be

due to differential exposure to tobacco smoke, a major cause of asthma exacerbation, since area smoking rates in the UK increase as deprivation increases (Wise 2014). Categorical variables identifying Government Office Region (GOR), 9 large regions of England, were also included in regression models to control for potential regional variation in, for example, climate and health care culture. Although we have no direct data on area rates of diagnosed versus undiagnosed asthma, or adherence to prescribed medication regimes, differences in health care culture across regions and socio-economic strata are believed to be a principal mechanism for relationships between asthma and deprivation, and our covariate controls are designed to limit bias from this source.

2.6 Statistical Analysis

In a series of models, negative binomial regression using maximum likelihood estimation was used to estimate the effects of natural environments and air pollutants on the rate of asthma hospitalisations. One series of models included NO2 and SO2; another series included PM2.5 and SO2. Using the nbreg command in STATA 14 software, a negative binomial distribution (and log link function) was specified to account for over-dispersion due to unobserved heterogeneity in the hospitalisation rate data. Standard errors were estimated using the Huber/White/sandwich estimator, which is robust to heteroscedasticity in error terms.

Before examining how the associations between asthma and natural environments might vary with coexisting air pollution, initial exploratory analyses examined: 1) the direct (unadjusted) effects of the natural environments and the three air pollutant variables with adjustment for the deprivation and GOR covariates (i.e., models with only one predictor-of-interest were specified, referred to as '*single predictor models*'); and 2) the combined effects of natural environments and air pollutants with mutual adjustment and with adjustment for the deprivation and GOR covariates (i.e., two multivariable predictors-of-interest models were specified, referred to as the '*multivariable model, NO2/SO2*' and the '*multivariable model, PM2.5/SO2*', to show the effects of the three natural environments, NO2/PM2.5 and SO2 when they were simultaneously mutually adjusted).

The main analysis examined the effects of natural environments on asthma rate at different levels of background air pollutant exposure. Following examination of descriptive statistics and the correlations between predictors, our final model, referred to as the '*PM2.5/SO2 model with interaction terms',* was developed from simpler models by the inclusion of further blocks of interaction terms to account for correlations amongst predictors, informed by test statistics and comparisons of model fit. Asthma rate was regressed against pollutant quintiles (NO2/PM2.5; SO2); natural environments (green space; gardens; trees); deprivation components 1 and 2; GOR; all two way natural environment by pollutant quintile interactions; the NO2/PM2.5 by SO2 two way interaction; all two way interactions and the three way interaction between natural environments; all two way pollutant quintile by deprivation component interactions; all two way natural environment by deprivation component interactions, i.e., the following model:

$$\text{Hospitalisation rate\_i} = \exp(\alpha + \beta NO2/PM2.5\_i + \beta SO2\_i + \beta Greenspace\_i + \beta Gardens\_i + \beta Trees\_i + \beta DC1\_i + \beta DC2\_i + \beta GOR\_i + \beta Greenspace*NO2/PM2.5\_i + \beta Gardens*NO2/PM2.5\_i + \beta Trees*NO2/PM2.5\_i + \beta Greenspace*SO2\_i + \beta Gardens*SO2\_i + \beta Trees*SO2\_i + \beta NO2/PM2.5*SO2\_i + \beta Greenspace*Gardens\_i + \beta Greenspace*Trees\_i + \beta Gardens*Trees\_i + \beta Greenspace*Gardens*Trees\_i + \beta NO2/PM2.5*DC1\_i + \beta NO2/PM2.5*DC2\_i + \beta SO2*DC1\_i + \beta SO2*DC2\_i + \beta Greenspace*DC1\_i + \beta Greenspace*DC2\_i + \beta Gardens*DC1\_i + \beta Gardens*DC2\_i + \beta Trees*DC1\_i + \beta Trees*DC2\_i) + \varepsilon\_i$$

Results are expressed for our variables of interest as average marginal effects, which report derivatives of the response. This approach to the communication of findings is particularly helpful where models include interaction terms. With the categorical pollutant quintiles, the average marginal effects measure discrete change, i.e., how the mean predicted hospitalisation rate changes as the variable changes from the 1st to other pollutant quintiles, with all other variables held as observed. With the interval scale natural environment variables, the average marginal effects measure the instantaneous rate of change, which is an approximation of the effect on the mean predicted hospitalisation rate of a one unit increase in the measures, with all other variables held as observed. In the models with interaction terms between pollutant quintiles and natural environment measures, the average marginal effects of the natural environment measures were further calculated conditional on the values of the pollutant quintiles.

The sensitivity of results from the models with interaction terms was examined including only those aged 15-79 in the calculation of the hospitalisation rate, as children and older adults may be especially vulnerable to health risks associated with air pollution (Makri and Stilianakis 2008). Further supplementary analyses examined the sensitivity of the findings from models with interaction terms to the substitution of background pollutant concentration quintiles for quintiles of penetrating pollutant concentration (referred to as '*penetrating NO2*'; '*penetrating SO2*' and '*penetrating PM2.5*'; see 2.4 above). Both the NO2/SO2 and the PM2.5/SO2 models with interaction terms were re-specified using these adjusted background concentration measures.

3 **Results**

Descriptive data on the asthma rate and the natural environment variables for the urban LSOAs are presented in Table 1. The asthma rate varied greatly across urban LSOAs, ranging from 0 to nearly 20,000. On average, approximately a third of land cover was used for green space, with an additional 29% used for gardens. The average number of mature trees per km^2 within urban LSOAs was 581 (11.62 x 50). Descriptive data on pollutant concentrations in the quintile categories are presented in Table 2. (Further data on the variables used in this study are given in Appendix.)

Table 1. Descriptive data on the asthma rate and the natural environment variables, urban LSOAs (n = 26,455)

Variable	Mean	S.D.	10th %	25th %	50th %	75th %	90th %	Min.	Max.
asthma rate	1645.7	1047.4	610	933	1422	2100	2936	0	19434
green space %	33.36	24.05	6.33	13.96	27.55	48.83	71.40	0	97.47
gardens %	29.02	15.85	7.86	15.89	28.46	41.28	50.87	0	75.07
tree density 50/km^2	11.62	5.97	5.10	7.48	10.66	14.60	19.14	0	60.03

Table 2. Descriptive data on pollutant concentrations in the quintile categories

	NO2 µg/m^3				SO2 µg/m^3				PM2.5 µg/m^3			
	Mean	**S.D.**	**min**	**max**	**Mean**	**S.D.**	**min**	**max**	**Mean**	**S.D.**	**min**	**max**
1st quintile[a]	14.14	2.17	6.43	16.90	1.95	0.37	0.42	2.38	9.60	0.73	6.67	10.57
2nd quintile	18.84	1.04	16.90	20.58	2.60	0.13	2.38	2.82	11.15	0.30	10.57	11.61
3rd quintile	22.13	0.89	20.58	23.71	3.11	0.19	2.82	3.45	11.99	0.22	11.61	12.37
4th quintile	25.81	1.27	23.71	28.23	3.85	0.22	3.45	4.23	12.87	0.33	12.37	13.52

5th quintile[b]	33.28	4.59	28.23	56.39	5.25	1.07	4.23	12.35	14.63	0.84	13.52	18.09

[a] Least polluted quintile. [b] Most polluted quintile.

Results from the three stages of regression modelling are presented for the natural environment and air pollutant variables of interest (average marginal effects estimates for covariate control variables are not reported). Regression results for natural environment variables are expressed as associations with a 1 unit increase in predictors (1% green space; 1% gardens; 50 trees/km^2). Regressions were also specified using standardised variables for the natural environments (Mean = 0; S.D. = 1) and results are also given for 1 S.D. increases in predictors. These alternative presentations of the results allow different comparisons of effects across the three classes of natural environment: unit increases reflect the types of choices facing urban planners, whereas S.D. increases reflect equivalent relative increases across the three classes. Results for air pollutant quintiles show the effects of a category change from the least polluted quintile (quintile 1) to other categories.

3.1 Single predictor models

Results from the single predictor-of-interest models are presented in Table 3. Increases in all three natural environments were associated with decreases in the asthma rate. The effects on the asthma rate of S.D. increases in green space and gardens were similar to each other, and greater than the reduction associated with trees. Whilst increased asthma rate was associated with NO2 and PM2.5 at quintile 5 compared to quintile 1, there was no clear evidence of trend across the quintiles. For SO2, while there was evidence of a higher asthma rate in areas in quintiles 3 and 4 compared to quintile 1, there was no clear trend.

Table 3. Results of the single predictor models,[a] marginal effects with other variables held as observed (*n* = 26,455). Note that natural environment effects are presented both for a scale point increase and for an estimation sample S.D. increase.

Single predictor-of-interest		**Mean change to asthma rate, p value, (95% CI)**
Green space[b]	+1 %	-5.18, p<0.001, (-5.9, -4.47)
Gardens	+1 %	-5.89, p<0.001, (-7.02, -4.76)
Trees	+50/km^2	-11.19, p<0.001, (-13.18, -9.2)
Green space	*+1 S.D.*[c]	*-124.64, p<0.001, -141.84, -107.46)*
Gardens	*+1 S.D.*[d]	*-93.35, p<0.001, (-111.29, -75.41)*
Trees	*+1 S.D.*[e]	*-66.8, p<0.001, (-78.66, -54.94)*
NO2[f]	2nd quintile	+38.56, p=0.145, (-7.46, +84.58)
	3rd quintile	+12.75, p=1.0, (-30.57, + 56.07)
	4th quintile	+68.05, p=0.001, (+20.65, + 115.45)
	5th quintile	+181.83, p=0.004, (+119.8, +243.86)
SO2[f]	2nd quintile	-7.44, p=1.0, (-53.12, +38.24)
	3rd quintile	+159.64, p<0.001, (+109.65, +209.63)
	4th quintile	+101.67, p<0.001, (+45.28, +158.06)
	5th quintile	-28.67, p=0.623, (-79.12, +21.79)

PM2.5[f]	2nd quintile	-12.36, p=1.0, (-60.48, +35.75)
	3rd quintile	+37.96, p=0.466, (-22.43, +98.34)
	4th quintile	+37.19, p=0.631, (-28.58, +102.95)
	5th quintile	+209.47, p<0.001, (+119.54, + 299.41)

[a] Adjusted for deprivation component variables and government office region. [b] Note that green space and gardens were entered simultaneously in a single model so that the reference category remained 'built land' for both estimates. [c] +24.1%. [d] +15.9%. [e] +298.5 trees/km^2. [f] The 1st (least polluted) quintile is the reference for all comparisons; C.I. and p values Bonferroni adjusted for 4 comparisons. Fit statistics: **Green space/Gardens** (Log pseudolikelihood = -211851.91, Wald (df=12) = 8535.48 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.021, Cox-Snell/ML = 0.288, Cragg-Uhler/Nagelkerke = 0.288; BIC (df=14) = 423846.39); **Trees** (Log pseudolikelihood = -211894.71, Wald (df=11) = 8378.66 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.02, Cox-Snell/ML = 0.285, Cragg-Uhler/Nagelkerke = 0.285; BIC (df=13) = 423921.81); **NO2** (Log pseudolikelihood = -211933.11, Wald (df=14) = 8294.96 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.02, Cox-Snell/ML = 0.283, Cragg-Uhler/Nagelkerke = 0.283; BIC (df=16) = 424029.14); **SO2** (Log pseudolikelihood = -211878.45, Wald (df=14) = 8475.61 (p<0.001); Pseudo-R2 McFadden (adjusted) = 0.021, Cox-Snell/ML = 0.286, Cragg-Uhler/Nagelkerke = 0.286; BIC (df=16) = 423919.83); **PM2.5** (Log pseudolikelihood = -211936.22, Wald (df=14) = 8341.12 (p<0.001); Pseudo-R2 McFadden (adjusted) = 0.02, Cox-Snell/ML = 0.283, Cragg-Uhler/Nagelkerke = 0.283; BIC (df=16) = 424035.38)

3.2 Multivariable predictors-of-interest models

Results from the NO2/SO2 and PM2.5/SO2 versions of the multivariable model are presented in Table 4. The three natural environments remained associated with reduced asthma rate with mutual adjustment and adjustment for the effects of air pollutants in these models, though compared to the single predictor models, the associated asthma reductions were smaller. The effects of natural environments (and SO2) were broadly consistent in both versions of the multivariable model. The patterns of association of pollutant quintiles with asthma rate in the NO2 and PM2.5 versions of the multivariable model were consistent with those observed in the single predictor models.

3.3 Models with interaction terms

Estimates of the average marginal effects of predictors from the NO2/SO2 and PM2.5/SO2 versions of the model with interaction terms are presented in Table 5. The three natural environments remained associated with reduced asthma rate when adjusting for their interactions with pollutants in addition to their main effects, and when accounting for other interactions amongst predictors. The magnitude of these associated reductions in asthma rate were highly consistent in the NO2/SO2 and PM2.5/SO2 versions of the model with interaction terms.

Of more interest, however, than the average change in asthma rate associated with increases in natural environment and background air pollutant exposure, are the changes in rate associated with increases in natural environment exposure at different levels of air pollutant exposure. Plots of the marginal effects of natural environments at each NO2 and SO2 pollutant quintile, derived from the NO2/SO2 model with interaction terms, are presented in Figure 1 and 2 respectively; as with previous presentations, results are shown for both a scale point increase and a 1 S.D. increase in natural environments. Plots of the average marginal effects of natural environments at each PM2.5 and SO2 pollutant quintile, derived from the PM2.5/SO2 model with interaction terms, are presented in Figure 3 and 4 respectively. (The results illustrated in Figure 1-4 are tabulated in

Appendix. Pairwise Wald tests of equivalence of marginal effects of natural environments conditional on pollutant quintiles were carried out and results are also presented in Appendix; unadjusted p values and p values with Bonferroni adjustment for ten comparisons are displayed.)

In the NO2/SO2 model with interaction terms, green space was associated with significantly reduced asthma rate at all NO2 quintiles except at the 5th (most polluted) quintile, where its association was non-significant (Figure 1). Gardens showed the same pattern with NO2, though the association at the 1st quintile was also non-significant (Figure 1). However, there was no evidence of trend in the effects of gardens and green space across the NO2 quintiles (Table A10, A11) , although in both cases, asthma rate was significantly *lower* at the 4th than the 3rd quintiles. In contrast, trees were associated with significantly reduced asthma rate at the 3rd and 5th NO2 quintiles (Figure 1), and the reduction at the 5th quintile was significantly greater than that at all less polluted quintiles (Table A12). Green space and gardens were associated with reduced asthma rate at all SO2 quintiles, though the effect for gardens at the 3rd quintile was non-significant (Figure 2), and there was no evidence of trend in the effects of gardens and green space across the SO2 quintiles (Table A13, A14). Trees were associated with reduced asthma rate at the 3rd-5th SO2 quintiles, and there was evidence of a trend effect, with reductions at the 3rd-5th quintiles greater than the 1st quintile, and reductions at the 4th and 5th quintiles greater than the 2nd quintile (Table A15).

In the PM2.5/SO2 model with interaction terms, the associations between the natural environments and asthma rate at different PM2.5 quintiles were very similar to those observed in the NO2 version between the environments and the asthma rate at different NO2 quintiles. Green space and gardens were associated with reduced asthma rate at all PM2.5 quintiles, though the effect for gardens was non-significant at the 5th quintile (Figure 3). There was no evidence of trend in effects of green space and gardens across the PM2.5 quintiles (Table A16, A17). Trees were associated with reduced asthma rate at the 3rd and 5th PM2.5 quintiles (Figure 3) and effects at the 5th quintile were significantly different from effects at all less polluted quintiles (Table A18). Green space and gardens were also associated with reduced asthma rate at all SO2 quintiles, though effects were non-significant at the 3rd quintile (Figure 4), with no evidence of trend across the quintiles (Table A19, A20). Trees were associated with reduced asthma rate with SO2 at the 3rd-5th quintiles (Figure 4) with effects at the 4th and 5th quintiles significantly different from the 1st and 2nd quintiles (Table A21).

3.4 Sensitivity Analyses

A supplementary analysis tested the robustness of the findings from NO2/SO2 and PM2.5/SO2 models with interaction terms to the inclusion of emergency asthma hospitalisations only amongst the 15-79 age group. Substantive findings on changes in hospitalisations associated with increases in natural environment exposure at different levels of air pollutant exposure (see 3.3 above) were replicated (see Appendix, Figure A1-A4).

A further sensitivity analysis explored the robustness of the findings from the models with interaction terms, to re-specification using quintiles of penetrating air pollutants (see 2.4 above): penetrating NO2 and penetrating SO2 in the NO2/SO2 model with interaction terms, and penetrating PM2.5 and penetrating SO2 in the PM2.5/SO2 version. Full results of these robustness checks are presented in Appendix, where relevant descriptive statistics are also given. Despite substantial differences in the ranking of LSOAs between the pollutant quintiles used in the main analysis and the penetrating pollutant quintiles used in this sensitivity analysis (Table A26-A28), the interactions observed between the natural environments and the pollutants (Figure 1-4) were

Table 4. Results of the multivariable models,[a] marginal effects with other variables held as observed (*n* = 26,455). Note that natural environment effects are presented both for a scale point increase and for an estimation sample S.D. increase.

		Multivariable model, NO2/SO2 **Mean change to asthma rate, p value, (95% CI)**	**Multivariable model, PM2.5/SO2** **Mean change to asthma rate, p value, (95% CI)**
Greenspace	**+1 %**	-3.8, p<0.001, (-4.56, -3.04)	-3.89, p<0.001, (-4.65, -3.14)
Gardens	**+1 %**	-4.26, p<0.001, (-5.42, -3.1)	-4.35, p<0.001, (-5.5, -3.19)
Trees	**+50/km²**	-9.14, p<0.001, (-11.19, -7.09)	-8.78, p<0.001, (-10.81, -6.75)
Greenspace	***+1 S.D.***[b]	*-91.39, p<0.001, (-109.74, -73.03)*	*-93.64, p<0.001, (-111.85, -75.42)*
Gardens	***+1 S.D.***[c]	*-67.58, p<0.001, (-86.01, -49.14)*	*-68.89, p<0.001, (-87.26, -50.52)*
Trees	***+1 S.D.***[d]	*-54.57, p<0.001, (-66.8, -42.33)*	*-52.42, p<0.001, (-64.53, -40.31)*
NO2[e]	**2nd quintile**	+50.32, p=0.03, (+3.26, +97.38)	
	3rd quintile	+30.12, p=0.476, (-18.12, +78.37)	
	4th quintile	+67.92, p=0.007, (+14.04, +121.79)	
	5th quintile	+146.8, p<0.001, (+77.09, +216.5)	
PM2.5[e]	**2nd quintile**		+10.52, p=1, (-38.95, +59.99)
	3rd quintile		+57.62, p=0.071, (-3.07, +118.3)
	4th quintile		+52.96, p=0.249, (-18.01, +123.93)
	5th quintile		+179.93, p<0.001, (+84.62, +275.25)
SO2[e]	**2nd quintile**	-40.62, p=0.124, (-87.67, +6.43)	-33.52, p=0.279, (-79.7, +12.66)
	3rd quintile	+111, p<0.001, (+58.54, +163.46)	+122.9, p<0.001, (+71.78, +174.03)
	4th quintile	+48.61, p=0.208, (-13.88, +111.11)	+64.83, p=0.028, (+4.9, +124.76)
	5th quintile	-91.69, p<0.001, (-148.28, -35.1)	-79.75, p=0.001, (-133.79, -25.71)

[a] Adjusted for deprivation component variables and government office region. [b] +24.1%. [c] +15.9%. [d] +298.5 trees/km². [e] The 1st (least polluted) quintile is the reference for all comparisons; C.I. and p values Bonferroni adjusted for 4 comparisons. Fit statistics: **NO2/SO2** (Log pseudolikelihood = -211706.89, Wald (df=21) = 9094.54 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.021, Cox-Snell/ML = 0.296, Cragg-Uhler/Nagelkerke = 0.296; BIC (df=23) = 423647.99); **PM2.5/SO2** (Log pseudolikelihood = -211706.29, Wald (df=21) = 9146.14 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.021, Cox-Snell/ML = 0.296, Cragg-Uhler/Nagelkerke = 0.296; BIC (df=23) = 423646.8)

Table 5. Results of the models with interaction terms,[a] mean marginal effects with other variables held as observed (*n* = 26,455). Note that natural environment effects are presented both for a scale point increase and for an estimation sample S.D. increase.

Predictors of interest		**NO2/SO2 model with interaction terms** **Mean change to asthma rate, p value, (95% CI)**	**PM2.5/SO2 model with interaction terms** **Mean change to asthma rate, p value, (95% CI)**
Greenspace	**+1 %**	-4.63, p<0.001, (-5.66, -3.61)	-4.77, p<0.001, (-5.79, -3.76)
Gardens	**+1 %**	-5.01, p<0.001, (-6.45, -3.57)	-5.16, p<0.001, (-6.59, -3.72)
Trees	**+50/km²**	-7.61, p<0.001, (-10.14, -5.08)	-7.88, p<0.001, (-10.35, -5.41)
Greenspace	***+1 S.D.***[b]	*-111.48, p<0.001, (-136.17, -86.79)*	*-114.8, p<0.001, (-139.2, -90.38)*
Gardens	***+1 S.D.***[c]	*-79.42, p<0.001, (-102.26, -56.58)*	*-81.78, p<0.001, (-104.51, -59.05)*
Trees	***+1 S.D.***[d]	*-45.42, p<0.001, (-60.52, -30.32)*	*-47.03, p<0.001, (-61.79, -32.27)*
NO2[e]	**2nd quintile**	+63.28, p=0.106, (-7.99, +134.55)	
	3rd quintile	+17.21, p=1, (-51.31, + 85.73)	
	4th quintile	+94.04, p=0.005, (+20.94, +167.14)	
	5th quintile	+188.12, p<0.001, (+100.73, +275.5)	
PM2.5[e]	**2nd quintile**		+43.8, p=0.241, (-14.42, +102.02)
	3rd quintile		+110.48, p<0.001, (+46.72, +174.24)
	4th quintile		+108.18, p=0.001, (+35.33, +181.04)
	5th quintile		+253.21, p<0.001, (+156.07, +350.36)
SO2[e]	**2nd quintile**	-8.43, p=1, (-79.44, + 62.58)	-3.68, p=1, (-64.9, +57.54)
	3rd quintile	+31.71, p=0.97, (-36.06, + 99.49)	+46.38, p=0.215, (-13.7, +106.46)
	4th quintile	-25.71, p=1, (-100.65, +49.23)	+25.17, p=1, (-42.57, +92.91)
	5th quintile	-168.28, p<0.001, (-241.16, -95.39)	-129.27, p<0.001, (-192.46, -66.09)

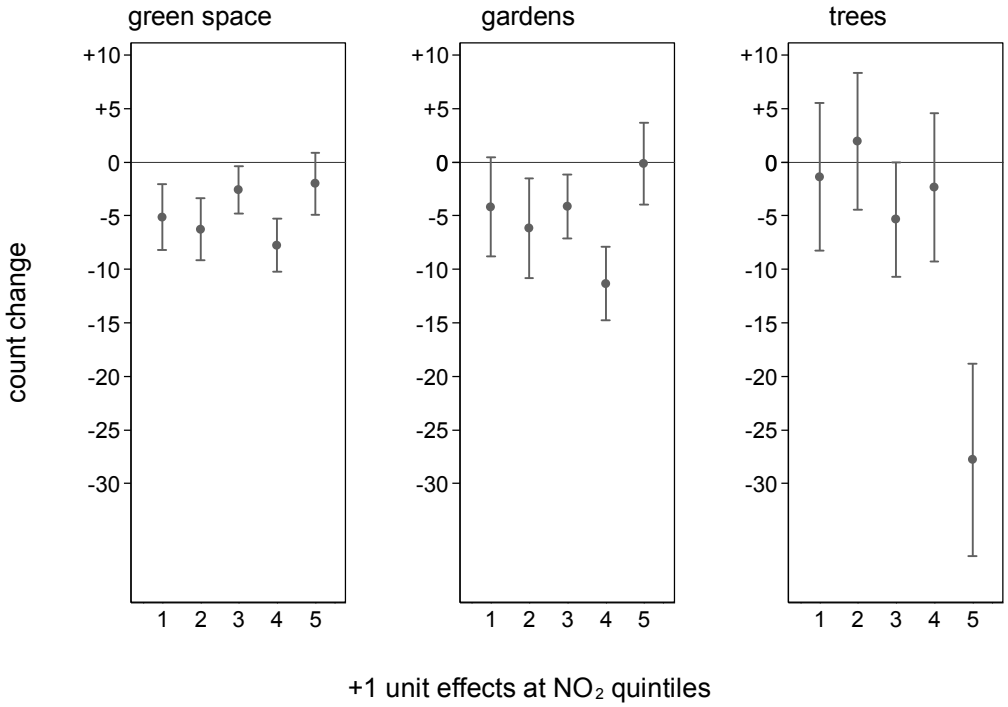
[a] Adjusted for deprivation component variables, government office region; all two way natural environment by pollutant quintile interactions; the NO2/PM2.5 by SO2 two way interaction; all two way interactions and the three way interaction between natural environments; all two way pollutant quintile by deprivation component interactions; all two way natural environment by deprivation component interactions. [b] +24.1%. [c] +15.9%. [d] +298.5

trees/km^2. [e] The 1st (least polluted) quintile is the reference for all comparisons; C.I. and p values Bonferroni adjusted for 4 comparisons. Fit statistics: **NO2/SO2** (Log pseudolikelihood = -211361.18, Wald (df=87) = 10508.74 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.023, Cox-Snell/ML = 0.314, Cragg-Uhler/Nagelkerke = 0.314; BIC (df=89) = 423628.67); **PM2.5/SO2** (Log pseudolikelihood = -211324.37, Wald (df=87) = 10448.67 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.023, Cox-Snell/ML = 0.316, Cragg-Uhler/Nagelkerke = 0.316; BIC (df=89) = 423555.05)

Figure 1. NO2/SO2 model with interaction terms. Marginal effects of natural environments at NO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase

B) + 1 S.D. increase



B) + 1 S.D. increase

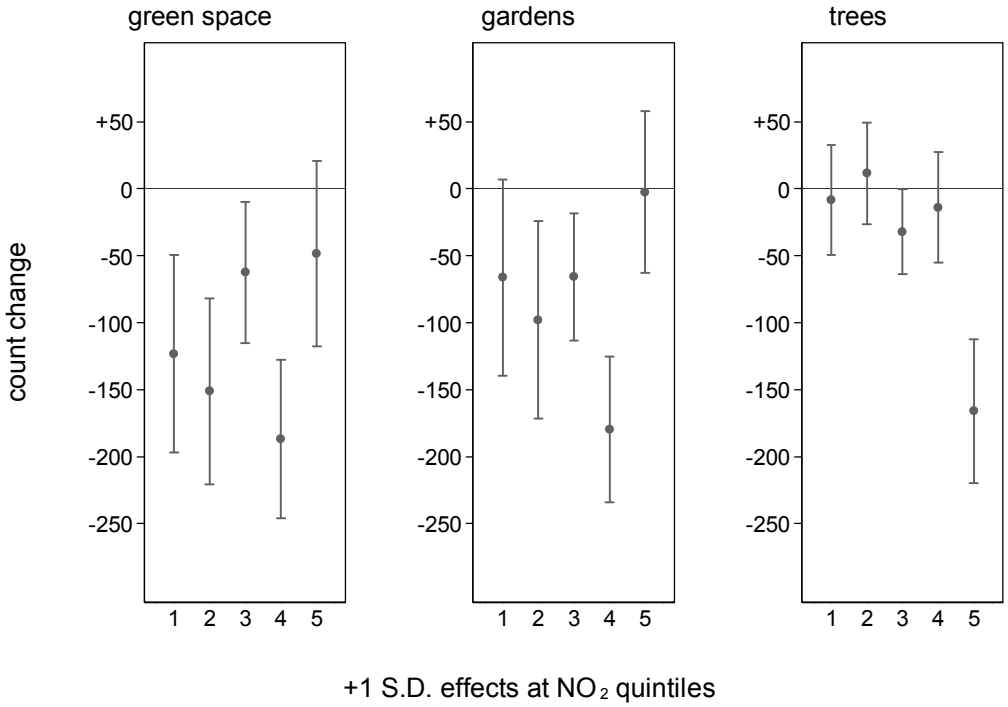
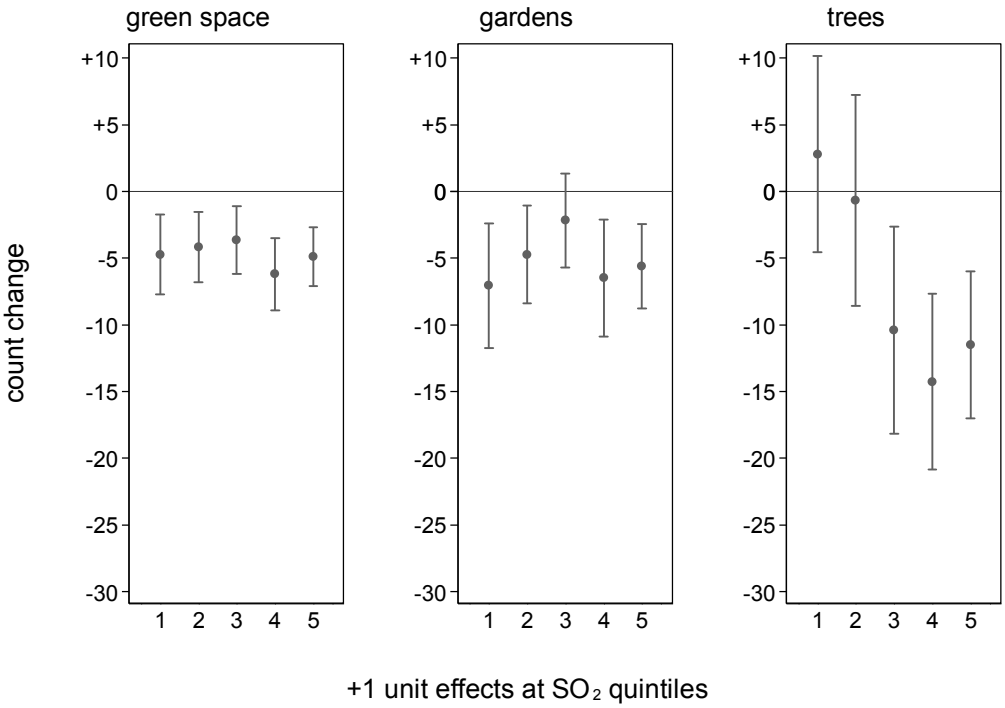


Figure 2. NO2/SO2 model with interaction terms. Marginal effects of natural environments at SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

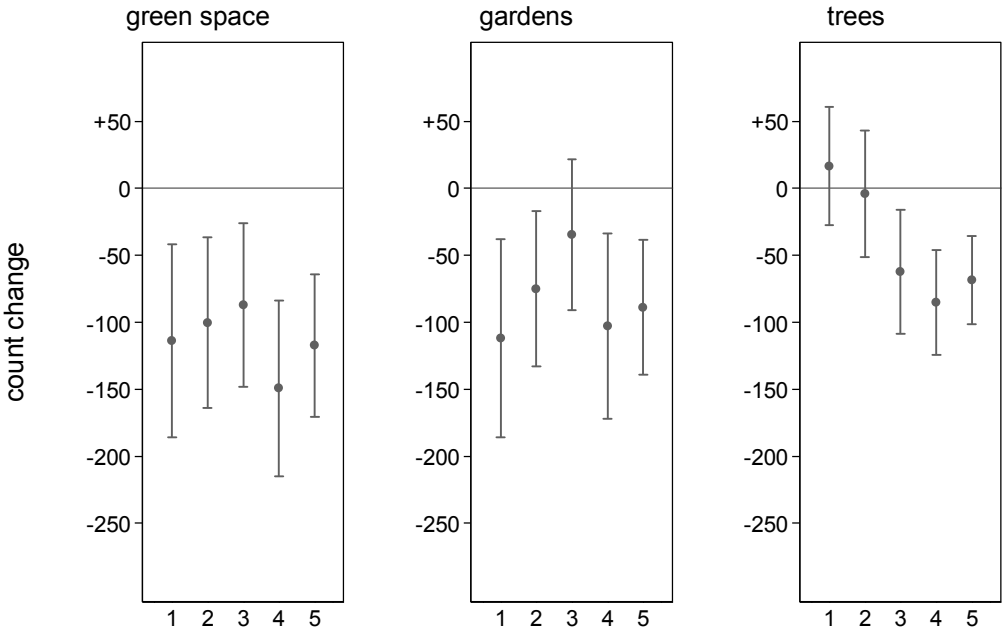
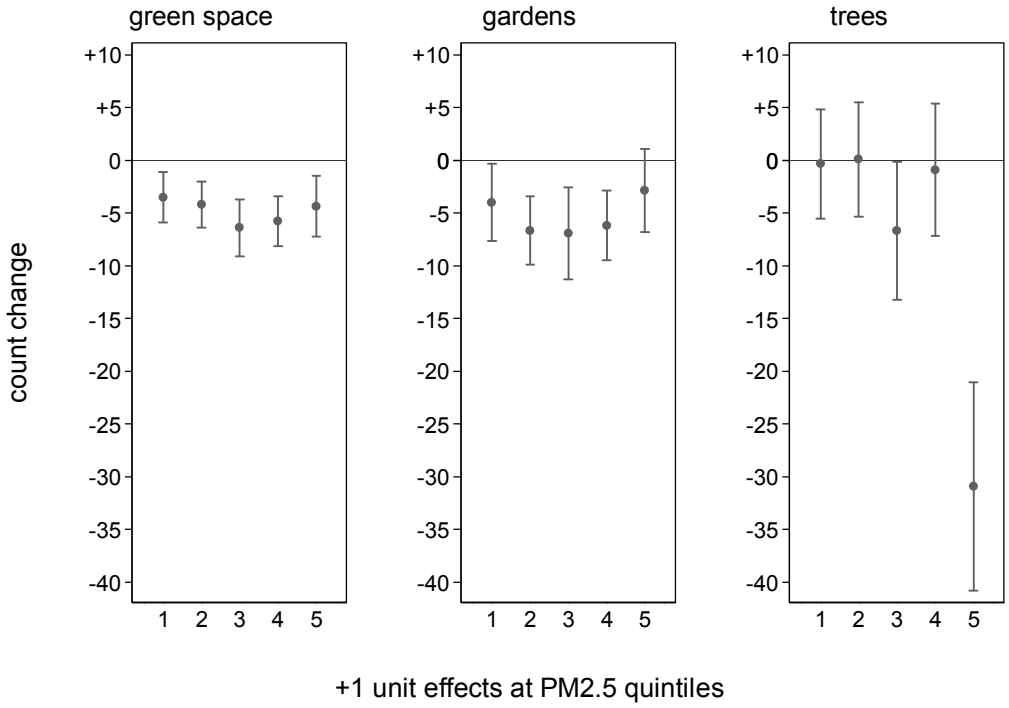


Figure 3. PM2.5/SO2 model with interaction terms. Marginal effects of natural environments at PM2.5 quintiles on geometric mean of asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

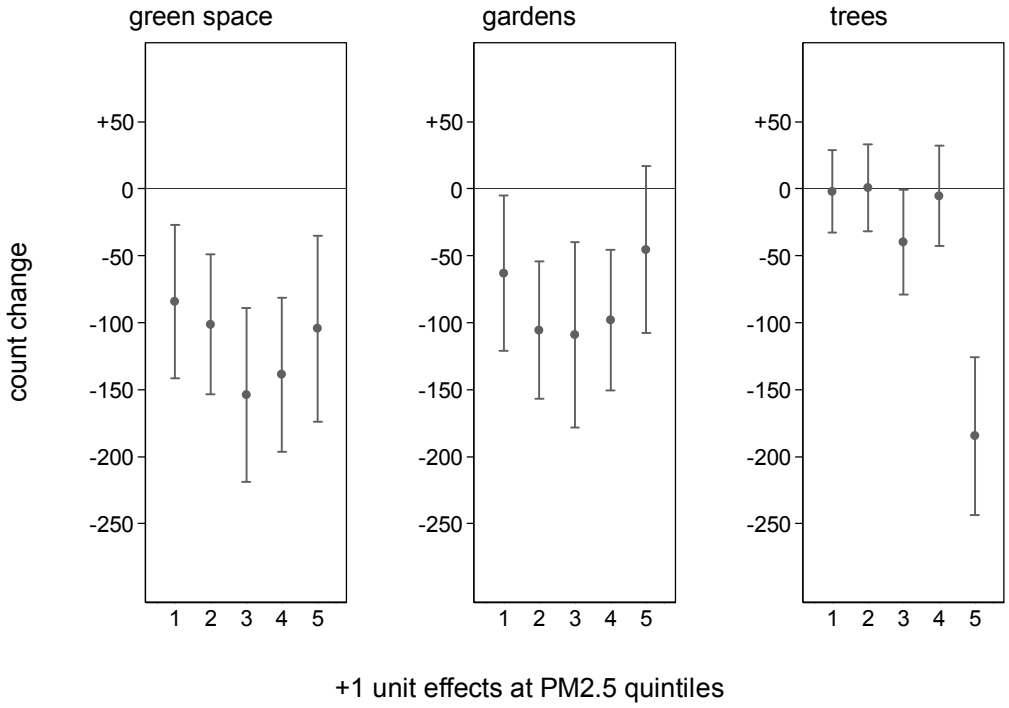
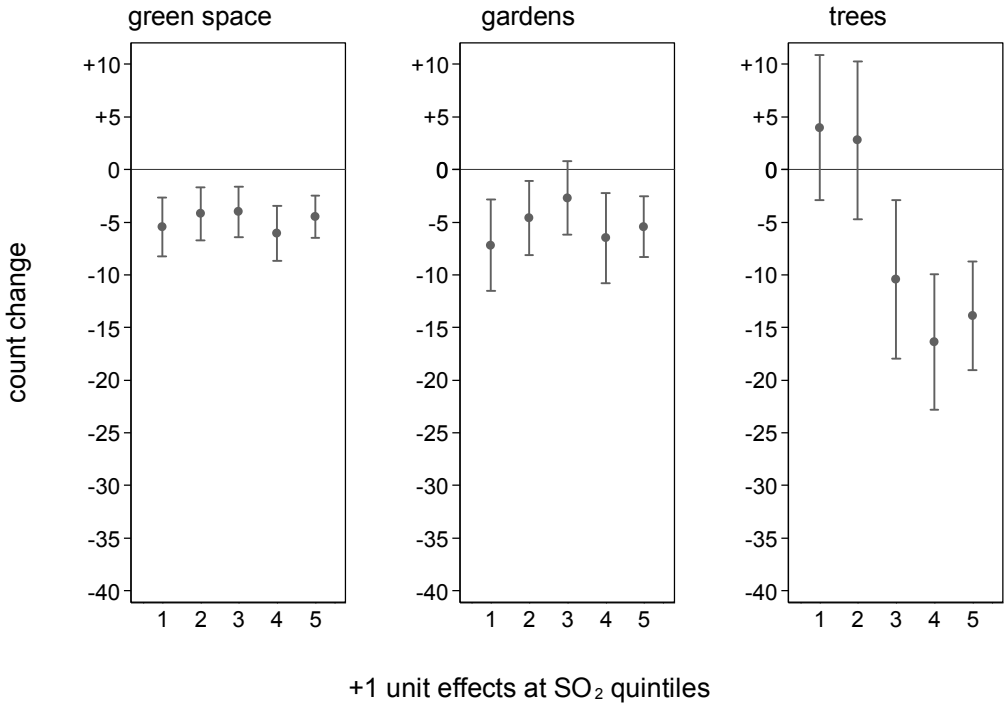
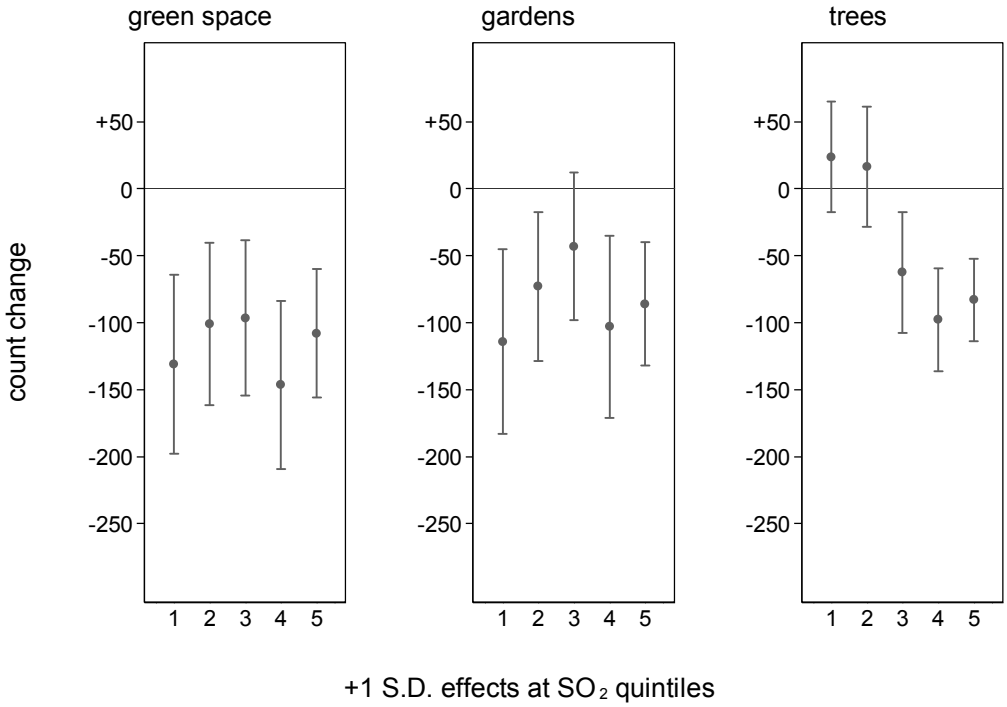


Figure 4. PM2.5/SO2 model with interaction terms. Marginal effects of natural environments at SO2 quintiles on geometric mean of asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase



largely consistent with those observed in the sensitivity analyses between the natural environments and the penetrating pollutants (Figure A5-A8).

In the penetrating NO2/SO2 model, green space and gardens were associated with significantly reduced asthma rate at all NO2 quintiles except at the 5th (most polluted) quintile, where their associations were non-significant (Figure A5). However, in contrast to the main model, the differences in effects of green space between the 5th and 1st-3rd quintiles were significant (Table A31); and differences in effects of gardens between the 5th and 1st-3rd quintiles were significant or marginally significant (Table A32). Trees were associated with significantly reduced asthma rate at the 3rd-5th NO2 quintiles (Figure A5) and there were significant differences in effects between the 5th and 1st-3rd, and between the 4th and 1st-2nd quintiles (Table A33). As in the main model, green space was associated with reduced asthma rate at all SO2 quintiles (Figure A6) and there was no evidence of trend (Table A34). Gardens were associated with reduced asthma rate at the 3rd-5th SO2 quintiles, and trees at the 2nd-5th quintiles (Figure A6) though there were no significant differences in effects (Table A35, A36).

In the penetrating PM2.5/SO2 model, green space was associated with reduced asthma rate at the 1st-4th PM2.5 quintile (Figure A7), and differences in effects between the 5th and the 2nd/4th quintiles were significant (Table A37). Gardens were associated with reduced asthma rate at the 1st, 2nd and 4th PM2.5 quintiles (Figure A7) and the difference in effects between the 5th and 2nd quintiles was significant (Table A38). Trees were associated with reduced hospitalisations at the 4th/5th PM2.5 quintiles (Figure A7), and differences in effect between the 5th and 1st-3rd, and between the 4th and 1st/2nd quintiles were significant or marginally significant (Table A39). Green space and gardens were associated with reduced asthma rate at all SO2 quintiles (Figure A8), with no evidence of trend across the quintiles (Table A40, A41), whilst trees were associated with reduced asthma rate at the 2nd-5th SO2 quintiles, and all contrasts with the 1st quintile were significant (Table A42).

4 **Discussion**

This is the first large scale epidemiological analysis to relate residential area natural environments to asthma in England. Regional studies are important in this field; since vegetation varies geographically, the net effects of the multiple mechanisms by which exposure to natural environments may impact on asthma, may not be easily inferred from one region to another. This cross-sectional study found that the rate of emergency hospitalisation for asthma in urban residential areas of England was significantly related to land used for green space and for gardens, and also to tree density. On average, these natural environments were associated with reduced hospitalisation. However, this association varied by pollutant exposure.

Generalising across the findings from estimates which controlled on background concentrations of pollutants, and also controlled on the penetration of housing by background concentrations of pollutants, this study found that increases in tree density were associated with greater reductions in asthma hospitalisation when NO2, PM2.5 and SO2 were higher, (and had no benefit when they were very low). In contrast, there was some (limited) evidence that increases in green space and gardens were associated with greater reductions in asthma hospitalisation when NO2 and PM2.5 exposure were lower. Interestingly, across all levels of air pollutant exposure, there was little difference in how asthma emergency rates were associated with residential area green space, which tends to be publicly accessible, and gardens, which tend to be privately owned.

This study design cannot indicate the potential mechanisms that may be involved in the associations between natural environments and asthma, and how they are changed by specific pollutant

exposures. However, these findings raise the possibility that whilst urban green space and gardens have generally beneficial associations with asthma hospitalisation, their production of pollen might reduce any benefit when pollutant exposures are very high. This could be due to synergistic effects of pollutants and pollens on asthma exacerbation (Amato et al. 2010), and/or the effects of air pollutants on the bioavailability of pollen allergens (Ghiani et al. 2012; Chassard et al. 2015; Zhao et al. 2015; Namork et al. 2006). Trees can also produce allergenic pollen, but the results do not suggest that these mechanisms are affecting the relationship between trees and asthma exacerbation. Rather, the findings suggest that the mechanisms dominating the relationship between trees and asthma are pollutant removal and dispersion. A review of measured differences in particulate matter concentration upwind and downwind of urban street trees and hedges suggested a reduction of 24% is typical in these settings (McDonald et al. 2016). Removal rates of many pollutants by trees are a linear function of ambient concentrations, so particulate deposition rates, for example, are higher when concentrations are higher. This would explain the greater reductions in asthma hospitalisations which are associated with increases in tree density in more polluted areas. The fact that shorter vegetation traps particles through dry deposition far less efficiently than trees (Fowler et al. 2004; Freer-Smith et al. 2005), combined with possible interaction of pollutants and grass pollen, might explain why our findings suggest greater reductions in asthma hospitalisation are associated with increases in green space in less polluted areas.

4.1 Strengths and Weaknesses

A major strength of this analysis is the size and breadth of the data collected. We used a 15-year long cross-section of 660,505 asthma emergency hospitalisations from urban areas of England, which resulted in a statistically powerful sample. By focussing on severe asthma events, we reduced the likelihood of outcome misclassification, especially when self-reported asthma status is prone to include wheezing during childhood (Scott et al. 2011) and COPD in adulthood (Abramson et al. 2014). Our area-level measures of gardens and tree cover are more precise indicators of exposure to the natural environment than remotely sensed measures, such as the Normalised Difference Vegetation Index which has been used in most previous research. The natural environment measures also show how subtypes of green space may have important associations with specific health outcomes, in addition to general health found previously (Wheeler et al. 2015). Importantly, this is the first study to consider how the association between the natural environment and asthma varies with coexisting air pollution. Whilst we considered traffic related air pollutants (NO2 and PM2.5), affecting a large proportion of urban populations, we also considered SO2 (mainly produced from industrial processes), and affecting smaller pockets of urban and rural populations. Additionally we investigated whether the associations differ by indoor penetration rates, addressing a methodological weakness in previous work.

The environmental variables used in this work are assumed to be indicative of group exposures to natural environments and air pollution. They have analogues at the individual level, but these are not easily operationalised and measured. Whilst ubiquitous background air pollution is commonly operationalised as an affliction of a population in the aggregate, rather than of its individuals, and whilst ecologic (population level) effects are the central concern for policy makers, an ecological study design is prone to misclassification of an individual's true exposure due to area aggregation, and therefore this study is not appropriate to make causal inferences. Furthermore, we have not examined the extent to which the results are sensitive to size of the area used for aggregation (i.e. LSOA) and caution is warranted if interpreting the results on a different spatial scale. Despite accounting for the indoor penetration of background outdoor air pollutants, exposure to pollutants from indoor sources has not been accounted for in this work. Our analysis of an extended period

cross-section provides 'static' measures of what are in reality dynamic processes, and the approach does not allow us to see any seasonal or secular trends in how asthma emergencies relate to interaction effects between natural environment and air pollutant exposures. Our use of deprivation and natural environment measures collected at points within the period, rather than averages across the period, means we do not account for within-area change in these factors, but any bias resulting from this will be extremely slight since within-area differences over the period will be negligible in comparison to between area differences.

4.2 Potential Policy Implications

The differential effects of green space and trees at both very high and very low pollutant levels have implications for urban planning policy which aims to leverage health co-benefits from environmental improvements. Our findings support other work (Rao et al. 2014) in suggesting that the respiratory health of populations in highly polluted urban areas can be improved by the expansion of tree cover. However, our work calls into question whether similar improvement is likely to follow from the expansion of open green space such as pasture, or of gardens, in these highly polluted areas. Our results further suggest the possibility that the respiratory health of populations in urban areas with very low air pollution can, in contrast to highly polluted areas, be improved by the expansion of gardens and green spaces; and that this may be more beneficial than the expansion of tree coverage in these areas. However, we acknowledge that ecological analyses of the type presented in this work are fundamentally exploratory, and therefore that these suggestions are speculative. Further evidence is needed to inform planning policy, ideally from longitudinal individual level studies.

5. **Acknowledgements**

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Appendix. Supplementary Data.

Part 1 of this Appendix presents further data on the variables used in this study. Part 2 of this Appendix presents a tabulated version of the results (presented as plots in Figure 1-4) of the marginal effects, derived from the models with interaction terms, of natural environments at pollutant quintiles. Pairwise Wald tests of equivalence of marginal effects of natural environments conditional on pollutant quintiles were carried out and results are also presented. Part 3 of this Appendix presents results of the age-restricted sensitivity analysis, where the NO2/SO2 and PM2.5/SO2 models with interaction terms excluded emergency asthma hospitalisations amongst children (under 15 years old) and the very elderly (over 79 years old). Part 4 of this Appendix presents relevant descriptive statistics and the results from the penetrating pollutants sensitivity analysis.

Part 1. Data on the variables used in this study.

Pearson correlation coefficients between variables used in this study are presented in Table A1; (pollutant measures here are the interval scales from which quintiles were derived). Cross-tabulations of the pollutant quintile categories, showing the extent to which areas in the highest category for one pollutant were also in the highest category for another pollutant, for example, are presented in Table A2-A4. Descriptive statistics on the asthma rate disaggregated by pollutant quintiles are summarised in Table A5, which shows that whilst the asthma rate was highest in the areas most polluted by PM2.5, there was not a clear trend of asthma increasing by pollutant quintile, since there was a higher rate in quintiles 1 and 2, than in quintiles 3 and 4; in contrast, the asthma rate did increase by NO2 and SO2 pollutant quintiles.

Table A1. Pearson correlation coefficients between variables used in this study

	greenspace	gardens	trees	NO2	SO2	PM2.5	income deprivation	employment deprivation	education deprivation	services deprivation
gardens	-0.68									
trees	0.11	0.13								
NO2	-0.36	-0.01	0.05							
SO2	-0.01	-0.05	-0.07	0.21						
PM2.5	-0.31	0.07	0.08	0.82	0.01					
income deprivation	-0.19	-0.16	-0.22	0.31	0.19	0.16				
employment deprivation	-0.12	-0.18	-0.23	0.16	0.27	-0.06	0.87			
education deprivation	-0.04	-0.10	-0.26	0.01	0.32	-0.09	0.76	0.75		
services deprivation	-0.02	-0.15	0.07	0.43	-0.23	0.48	0.19	0.03	-0.10	
crime deprivation	-0.18	-0.14	-0.12	0.37	0.25	0.21	0.58	0.57	0.50	0.08

Table A2. Cross-tabulation of NO2 and SO2 pollutant concentration quintiles

		Quintiles of SO2					
		1[a]	**2**	**3**	**4**	**5**[b]	**Total**
Quintiles of NO2	**1**[a]	2,749	1,011	794	438	299	5,291
	2	1,087	1,077	1,129	970	1,031	5,294
	3	547	863	1,088	1,252	1,538	5,288
	4	474	660	1,023	1,632	1,502	5,291
	5[b]	434	1,680	1,257	999	921	5,291
	Total	5,291	5,291	5,291	5,291	5,291	26,455

[a] Least polluted quintile. [b] Most polluted quintile.

Table A3. Cross-tabulation of NO2 and PM2.5 pollutant concentration quintiles

		Quintiles of PM2.5					
		1[a]	**2**	**3**	**4**	**5**[b]	**Total**
Quintiles of NO2	**1**[a]	2,768	1,436	1,082	5	0	5,291
	2	1,256	1,316	1,857	865	0	5,294
	3	1,026	1,143	1,180	1,925	14	5,288
	4	240	1,300	736	2,076	939	5,291
	5[b]	1	96	436	420	4,338	5,291
	Total	5,291	5,291	5,291	5,291	5,291	26,455

[a] Least polluted quintile. [b] Most polluted quintile.

Table A4. Cross-tabulation of SO2 and PM2.5 pollutant concentration quintiles

		Quintiles of PM2.5					
		1[a]	**2**	**3**	**4**	**5**[b]	**Total**
Quintiles of SO2	**1**[a]	1,558	1,135	1,194	679	725	5,291
	2	463	489	1,185	1,282	1,872	5,291
	3	1,289	621	880	1,170	1,331	5,291
	4	1,208	1,351	891	1,127	714	5,291
	5[b]	773	1,695	1,141	1,033	649	5,291
	Total	5,291	5,291	5,291	5,291	5,291	26,455

[a] Least polluted quintile. [b] Most polluted quintile.

Table A5. Asthma rate disaggregated by pollutant quintiles

	Asthma rate by NO2 µg/m³ quintiles		**Asthma rate by SO2 µg/m³ quintiles**		**Asthma rate by PM2.5 µg/m³ quintiles**	
	Mean	**S.D.**	**Mean**	**S.D.**	**Mean**	**S.D.**
1st quintile[a]	1401.7	863.3	1388.1	833.5	1668.0	1003.3
2nd quintile	1492.9	956.7	1452.9	889.5	1706.2	1076.1
3rd quintile	1612.2	971.6	1736.2	1104.4	1554.9	1037.1
4th quintile	1777.7	1144.4	1865.7	1269.9	1487.8	969.3
5th quintile[b]	1949.3	1174.2	1790.9	993.4	1816.8	1113.6

[a] Least polluted quintile. [b] Most polluted quintile.

Part 2. Tabulated results from the models with interaction terms.

The marginal effects of 1 unit increases in natural environments at each NO2 and SO2 pollutant quintile, derived from the NO2/SO2 model with interaction terms, are presented in Table A6; effects of 1 S.D. increases in natural environments at each NO2 and SO2 pollutant quintile, derived from the NO2/SO2 model with interaction terms, are presented in Table A7; effects of 1 unit increases in natural environments at each PM2.5 and SO2 pollutant quintile, derived from the PM2.5/SO2 model with interaction terms, are presented in Table A8; effects of 1 S.D. increases in natural environments at each PM2.5 and SO2 pollutant quintile, derived from the PM2.5/SO2 model with interaction terms, are presented in Table A9. Pairwise Wald tests of equivalence of these marginal effects of natural environments conditional on pollutant quintiles from the NO2/SO2 model with interaction terms and the PM2.5/SO2 model with interaction terms are presented in Tables A10 - A21, with contrasts from the +1 unit models, and with unadjusted p values and p values with Bonferroni adjustment for the ten comparisons displayed.

Table A6. NO2/SO2 model with interaction terms. Marginal effects of unit increases in natural environments at NO2 and SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

		Change to asthma rate (95% CI)		
		Green space + 1%	**Gardens + 1%**	**Tree density +50/km^2**
NO2	**1st quintile**[a]	-5.13 (-8.19, -2.06)	-4.18 (-8.81, +0.45)	-1.39 (-8.28, +5.5)
	2nd quintile	-6.29 (-9.18, -3.39)	-6.18 (-10.84, -1.52)	+1.94 (-4.41, +8.3)
	3rd quintile	-2.6 (-4.78, -0.41)	-4.15 (-7.15, -1.15)	-5.35 (-10.68, -0.03)
	4th quintile	-7.77 (-10.23, -5.3)	-11.34 (-14.77, -7.91)	-2.33 (-9.26, +4.6)
	5th quintile[b]	-2.01 (-4.9, +0.87)	-0.15 (-3.97, +3.66)	-27.79 (-36.79, -18.8)
SO2	**1st quintile**[a]	-4.73 (-7.73, -1.73)	-7.07 (-11.74, -2.4)	+2.79 (-4.57, +10.16)
	2nd quintile	-4.17 (-6.82, -1.52)	-4.73 (-8.4, -1.05)	-0.67 (-8.56, +7.23)
	3rd quintile	-3.62 (-6.16, -1.09)	-2.18 (-5.73, +1.36)	-10.4 (-18.16, -2.65)
	4th quintile	-6.21 (-8.93, -3.48)	-6.49 (-10.86, -2.12)	-14.26 (-20.83, -7.69)
	5th quintile[b]	-4.88 (-7.09, -2.67)	-5.6 (-8.78, -2.43)	-11.49 (-16.99, -5.99)

[a] Least polluted quintile. [b] Most polluted quintile.

Table A7. NO2/SO2 model with interaction terms. Marginal effects of S.D. increases in natural environments at NO2 and SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

		Change to asthma rate (95% CI)		
		Green space + 1 S.D.[a]	**Gardens + 1 S.D.**[b]	**Tree density + 1 S.D.**[c]
NO2	**1st quintile**[d]	-123.3 (-197.1, -49.5)	-66.32 (-139.75, +7.11)	-8.29 (-49.43, +32.85)
	2nd quintile	-151.21 (-220.78, -81.63)	-97.94 (-171.8, -24.07)	+11.6 (-26.36, +49.56)
	3rd quintile	-62.46 (-115.09, -9.84)	-65.82 (-113.38, -18.26)	-31.97 (-63.77, -0.17)
	4th quintile	-186.79 (-246.09, -127.49)	-179.83 (-234.21, -125.45)	-13.93 (-55.3, +27.45)
	5th quintile[e]	-48.45 (-117.85, +20.95)	-2.43 (-62.9, +58.04)	-165.95 (-219.68, -112.23)

SO2	**1st quintile**[d]	-113.79 (-185.98, -41.6)	-112.04 (-186.08, -37.99)	+16.67 (-27.29, +60.63)
	2nd quintile	-100.27 (-164.06, -36.49)	-74.93 (-133.14, -16.72)	-3.98 (-51.13, +43.16)
	3rd quintile	-87.19 (-148.24, -26.14)	-34.61 (-90.79, +21.56)	-62.12 (-108.44, -15.8)
	4th quintile	-149.29 (-214.85, -83.73)	-102.84 (-172.14, -33.53)	-85.15 (-124.39, -45.91)
	5th quintile[e]	-117.3 (-170.44, -64.15)	-88.84 (-139.2, -38.48)	-68.61 (-101.44, -35.78)

[a] +24.1%. [b] +15.9%. [c] +298.5 trees/km^2. [d] Least polluted quintile. [e] Most polluted quintile.

Table A8. PM2.5/SO2 model with interaction terms. Marginal effects of unit increases in natural environments at PM2.5 and SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

		Change to asthma rate (95% CI)		
		Green space + 1%	**Gardens + 1%**	**Tree density +50/km^2**
PM2.5	**1st quintile** [a]	-3.5 (-5.88, -1.12)	-3.98 (-7.63, -0.33)	-0.33 (-5.51, +4.84)
	2nd quintile	-4.21 (-6.38, -2.04)	-6.65 (-9.88, -3.43)	+0.09 (-5.34, +5.53)
	3rd quintile	-6.4 (-9.09, -3.71)	-6.89 (-11.26, -2.52)	-6.68 (-13.2, -0.16)
	4th quintile	-5.77 (-8.16, -3.38)	-6.17 (-9.48, -2.86)	-0.9 (-7.17, +5.38)
	5th quintile [b]	-4.34 (-7.23, -1.46)	-2.87 (-6.79, +1.06)	-30.94 (-40.81, -21.06)
SO2	**1st quintile** [a]	-5.44 (-8.22, -2.66)	-7.2 (-11.54, -2.85)	+3.98 (-2.91, +10.88)
	2nd quintile	-4.2 (-6.72, -1.68)	-4.61 (-8.11, -1.1)	+2.78 (-4.73, +10.29)
	3rd quintile	-4.01 (-6.43, -1.6)	-2.71 (-6.19, +0.77)	-10.44 (-17.99, -2.89)
	4th quintile	-6.09 (-8.7, -3.48)	-6.5 (-10.78, -2.22)	-16.37 (-22.82, -9.92)
	5th quintile [b]	-4.48 (-6.48, -2.49)	-5.43 (-8.33, -2.52)	-13.88 (-19.04, -8.72)

[a] Least polluted quintile. [b] Most polluted quintile.

Table A9. PM2.5/SO2 model with interaction terms. Marginal effects of S.D. increases in natural environments at PM2.5 and SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

		Change to asthma rate (95% CI)		
		Green space + 1 S.D.[a]	**Gardens + 1 S.D.**[b]	**Tree density + 1 S.D.**[c]
PM2.5	**1st quintile** [d]	-84.22 (-141.4, -27.03)	-63.14 (-121.03, -5.26)	-1.99 (-32.9, +28.93)
	2nd quintile	-101.21 (-153.4, -49.01)	-105.5 (-156.7, -54.31)	+0.56 (-31.88, +33.01)
	3rd quintile	-153.93 (-218.68, -89.18)	-109.24 (-178.47, -40.02)	-39.88 (-78.82, -0.94)
	4th quintile	-138.73 (-196.18, -81.29)	-97.87 (-150.37, -45.37)	-5.36 (-42.82, +32.1)
	5th quintile [e]	-104.5 (-173.85, -35.15)	-45.46 (-107.7, +16.78)	-184.71 (-243.65, -125.76)
SO2	**1st quintile** [d]	-130.88 (-197.66, -64.1)	-114.12 (-183.04, -45.21)	+23.78 (-17.4, +64.95)
	2nd quintile	-101.04 (-161.59, -40.49)	-73.02 (-128.58, -17.46)	+16.58 (-28.26, +61.42)
	3rd quintile	-96.56 (-154.64, -38.49)	-42.98 (-98.22, +12.26)	-62.34 (-107.39, -17.28)
	4th quintile	-146.39 (-209.19, -83.59)	-103.04 (-170.89, -35.19)	-97.74 (-136.26, -59.23)
	5th quintile [e]	-107.87 (-155.85, -59.89)	-86.03 (-132.11, -39.95)	-82.89 (-113.7, -52.08)

[a] +24.1%. [b] +15.9%. [c] +298.5 trees/km^2. [d] Least polluted quintile. [e] Most polluted quintile.

Table A10. NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on NO2 quintile

NO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-1.16	1.417	-0.82	0.413	1.000
3 vs 1	+2.529	1.387	1.82	0.068	0.682
4 vs 1	-2.639	1.469	-1.80	0.072	0.724
5 vs 1	+3.112	1.686	1.85	0.065	0.649
3 vs 2	+3.689	1.295	2.85	0.004	0.044
4 vs 2	-1.479	1.391	-1.06	0.288	1.000
5 vs 2	+4.272	1.623	2.63	0.008	0.085
4 vs 3	-5.168	1.193	-4.33	<0.001	<0.001
5 vs 3	+0.583	1.395	0.42	0.676	1.000
5 vs 4	+5.751	1.455	3.95	<0.001	0.001

Table A11. NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on NO2 quintile

NO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-1.994	2.261	-0.88	0.378	1.000
3 vs 1	+0.031	2.093	0.02	0.988	1.000
4 vs 1	-7.16	2.222	-3.22	0.001	0.013
5 vs 1	+4.03	2.41	1.67	0.094	0.945
3 vs 2	+2.025	2.05	0.99	0.323	1.000
4 vs 2	-5.166	2.199	-2.35	0.019	0.188
5 vs 2	+6.024	2.38	2.53	0.011	0.114
4 vs 3	-7.191	1.658	-4.34	<0.001	<0.001
5 vs 3	+3.998	1.843	2.17	0.030	0.301
5 vs 4	+11.189	1.918	5.83	<0.001	<0.001

Table A12. NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on NO2 quintile

NO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+3.332	3.203	1.04	0.298	1.000
3 vs 1	-3.966	3.202	-1.24	0.216	1.000
4 vs 1	-.943	3.77	-0.25	0.802	1.000
5 vs 1	-26.406	4.597	-5.74	<0.001	<0.001
3 vs 2	-7.298	3.016	-2.42	0.016	0.155
4 vs 2	-4.276	3.548	-1.20	0.228	1.000
5 vs 2	-29.738	4.432	-6.71	<0.001	<0.001

4 vs 3	+3.022	3.224	0.94	0.349	1.000
5 vs 3	-22.44	4.103	-5.47	<0.001	<0.001
5 vs 4	-25.463	4.367	-5.83	<0.001	<0.001

Table A13. NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.562	1.454	0.39	0.699	1.000
3 vs 1	+1.106	1.457	0.76	0.448	1.000
4 vs 1	-1.476	1.562	-0.94	0.345	1.000
5 vs 1	-0.146	1.459	-0.10	0.920	1.000
3 vs 2	+0.544	1.306	0.42	0.677	1.000
4 vs 2	-2.038	1.413	-1.44	0.149	1.000
5 vs 2	-0.708	1.327	-0.53	0.594	1.000
4 vs 3	-2.582	1.338	-1.93	0.054	0.537
5 vs 3	-1.252	1.225	-1.02	0.307	1.000
5 vs 4	+1.33	1.171	1.14	0.256	1.000

Table A14. NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+2.341	2.216	1.06	0.291	1.000
3 vs 1	+4.883	2.209	2.21	0.027	0.271
4 vs 1	+0.58	2.562	0.23	0.821	1.000
5 vs 1	+1.463	2.241	0.65	0.514	1.000
3 vs 2	+2.543	1.855	1.37	0.170	1.000
4 vs 2	-1.76	2.191	-0.80	0.422	1.000
5 vs 2	-0.877	1.913	-0.46	0.647	1.000
4 vs 3	-4.303	2.08	-2.07	0.039	0.386
5 vs 3	-3.42	1.785	-1.92	0.055	0.554
5 vs 4	+0.883	1.786	0.49	0.621	1.000

Table A15. NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-3.459	3.664	-0.94	0.345	1.000

3 vs 1	-13.197	4.01	-3.29	0.001	0.010
4 vs 1	-17.055	3.801	-4.49	<0.001	<0.001
5 vs 1	-14.283	3.624	-3.94	<0.001	0.001
3 vs 2	-9.737	4.195	-2.32	0.020	0.203
4 vs 2	-13.595	4.009	-3.39	0.001	0.007
5 vs 2	-10.824	3.76	-2.88	0.004	0.040
4 vs 3	-3.858	3.852	-1.00	0.317	1.000
5 vs 3	-1.087	3.609	-0.30	0.763	1.000
5 vs 4	2.771	3.019	0.92	0.359	1.000

Table A16. PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on PM2.5 quintile

PM2.5 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-0.706	1.088	-0.65	0.516	1.000
3 vs 1	-2.898	1.234	-2.35	0.019	0.188
4 vs 1	-2.266	1.248	-1.82	0.069	0.693
5 vs 1	-0.843	1.487	-0.57	0.571	1.000
3 vs 2	-2.192	1.205	-1.82	0.069	0.690
4 vs 2	-1.56	1.174	-1.33	0.184	1.000
5 vs 2	-0.137	1.425	-0.10	0.924	1.000
4 vs 3	+0.632	1.312	0.48	0.630	1.000
5 vs 3	+2.055	1.528	1.35	0.179	1.000
5 vs 4	+1.423	1.404	1.01	0.311	1.000

Table A17. PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on PM2.5 quintile

PM2.5 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-2.672	1.766	-1.51	0.130	1.000
3 vs 1	-2.908	2.044	-1.42	0.155	1.000
4 vs 1	-2.19	1.878	-1.17	0.244	1.000
5 vs 1	+1.115	2.142	0.52	0.603	1.000
3 vs 2	-0.236	1.965	-0.12	0.904	1.000
4 vs 2	+0.481	1.728	0.28	0.781	1.000
5 vs 2	+3.787	2.002	1.89	0.059	0.585
4 vs 3	+0.717	2.063	0.35	0.728	1.000
5 vs 3	+4.023	2.226	1.81	0.071	0.708
5 vs 4	+3.306	1.899	1.74	0.082	0.817

Table A18. PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on PM2.5 quintile

PM2.5 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.427	2.662	0.16	0.872	1.000
3 vs 1	-6.346	3.114	-2.04	0.042	0.415
4 vs 1	-0.564	3.022	-0.19	0.852	1.000
5 vs 1	-30.603	4.431	-6.91	<0.001	<0.001
3 vs 2	-6.774	3.086	-2.19	0.028	0.282
4 vs 2	-0.992	3.039	-0.33	0.744	1.000
5 vs 2	-31.031	4.492	-6.91	<0.001	<0.001
4 vs 3	+5.782	3.348	1.73	0.084	0.842
5 vs 3	-24.257	4.72	-5.14	<0.001	<0.001
5 vs 4	-30.039	4.527	-6.64	<0.001	<0.001

Table A19. PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+1.241	1.371	0.90	0.366	1.000
3 vs 1	+1.427	1.353	1.05	0.292	1.000
4 vs 1	-0.645	1.389	-0.46	0.642	1.000
5 vs 1	+0.956	1.253	0.76	0.445	1.000
3 vs 2	+0.186	1.229	0.15	0.880	1.000
4 vs 2	-1.885	1.322	-1.43	0.154	1.000
5 vs 2	-0.284	1.207	-0.24	0.814	1.000
4 vs 3	-2.071	1.274	-1.63	0.104	1.000
5 vs 3	-0.47	1.151	-0.41	0.683	1.000
5 vs 4	+1.601	1.132	1.42	0.157	1.000

Table A20. PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+2.593	2.1	1.23	0.217	1.000
3 vs 1	+4.487	2.107	2.13	0.033	0.332
4 vs 1	+0.699	2.322	0.30	0.763	1.000
5 vs 1	+1.772	1.958	0.90	0.366	1.000
3 vs 2	+1.895	1.791	1.06	0.290	1.000
4 vs 2	-1.893	2.077	-0.91	0.362	1.000
5 vs 2	-0.821	1.762	-0.47	0.641	1.000

4 vs 3	-3.788	2.039	-1.86	0.063	0.632
5 vs 3	-2.715	1.72	-1.58	0.114	1.000
5 vs 4	+1.073	1.809	0.59	0.553	1.000

Table A21. PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on SO2 quintile

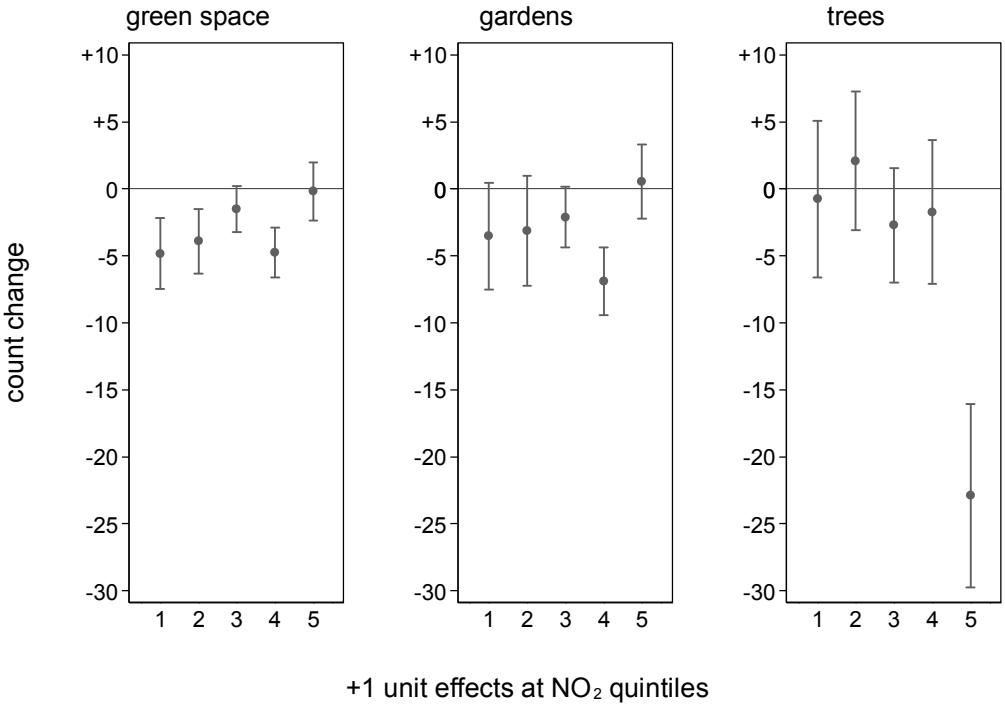
SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-1.205	3.524	-0.34	0.732	1.000
3 vs 1	-14.423	3.93	-3.67	<0.001	0.002
4 vs 1	-20.353	3.539	-5.75	<0.001	<0.001
5 vs 1	-17.865	3.24	-5.51	<0.001	<0.001
3 vs 2	-13.218	4.129	-3.20	0.001	0.014
4 vs 2	-19.149	3.839	-4.99	<0.001	<0.001
5 vs 2	-16.661	3.497	-4.76	<0.001	<0.001
4 vs 3	-5.931	3.757	-1.58	0.114	1.000
5 vs 3	-3.443	3.518	-0.98	0.328	1.000
5 vs 4	-1.205	3.524	-0.34	0.732	1.000

Part 3. Age restricted sensitivity analysis

When only asthma hospitalisations from those aged 15-79 years old were included, the mean asthma rate (i.e. period mean per 100,000 ESP, as for the main analysis - see 2.2) was 1012 (S.D. = 797.7). Figure A1 and A2 present plots of natural environment effects at quintiles of NO2 and SO2, respectively, derived from the NO2/SO2 model with interaction terms for the age restricted sensitivity analysis; Figure A3 and A4 present plots of natural environment effects at quintiles of PM2.5 and SO2, respectively, derived from the PM2.5/SO2 model with interaction terms for the age restricted sensitivity analysis.

Figure A1. NO2/SO2 model with interaction terms for age restricted sensitivity analysis. Marginal effects of natural environments at NO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

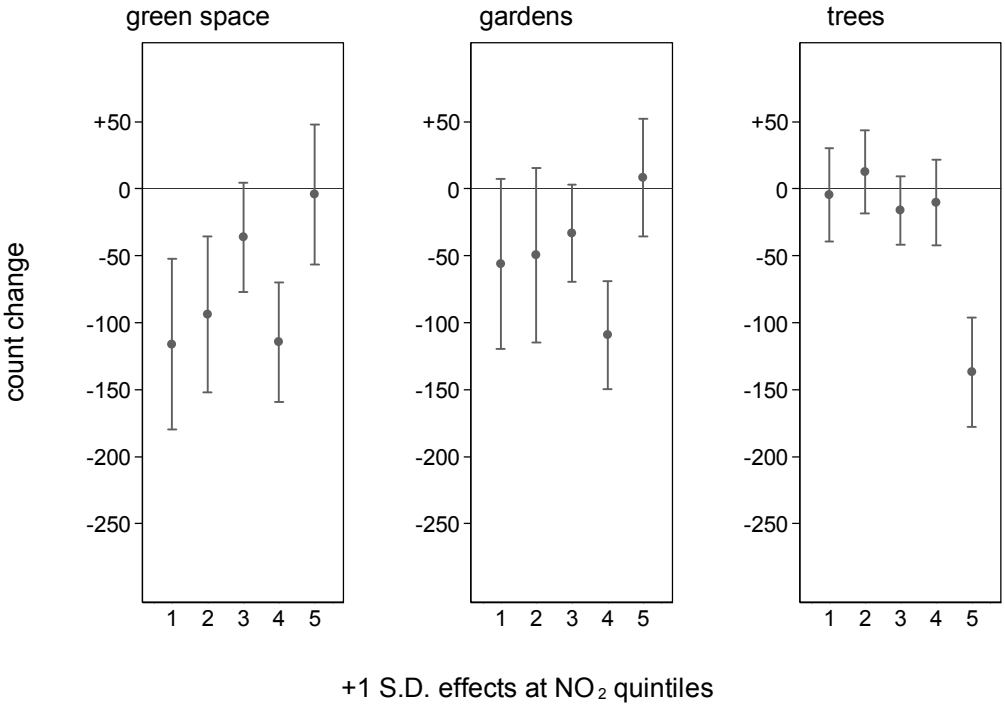
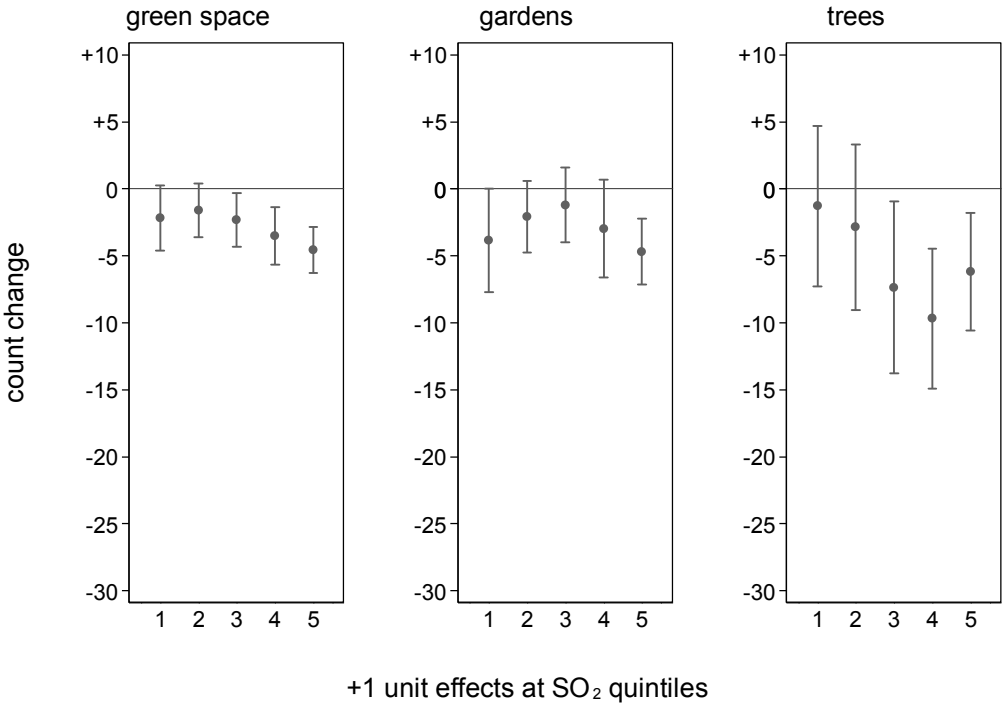


Figure A2. NO2/SO2 model with interaction terms for age restricted sensitivity analysis. Marginal effects of natural environments at SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

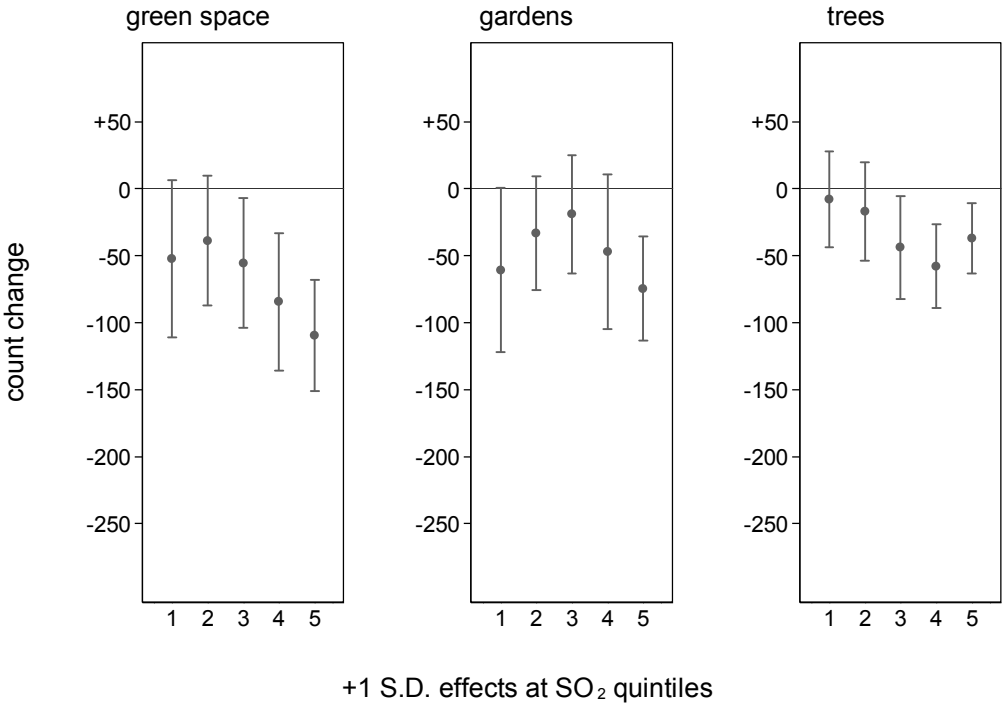
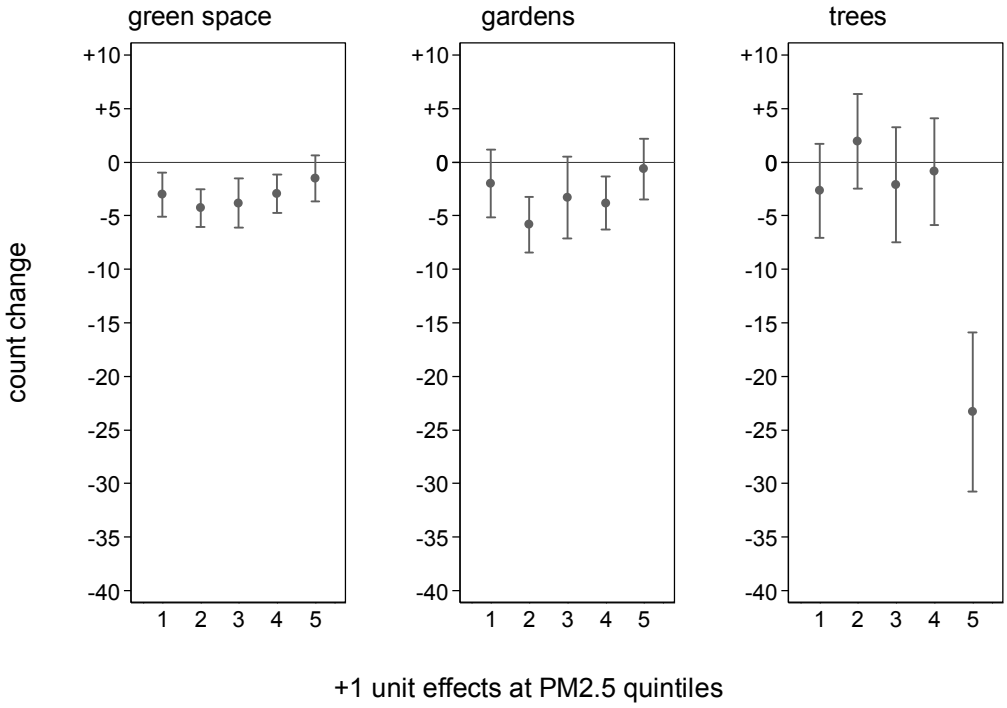


Figure A3. PM2.5/SO2 model with interaction terms for age restricted sensitivity analysis. Marginal effects of natural environments at PM2.5 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

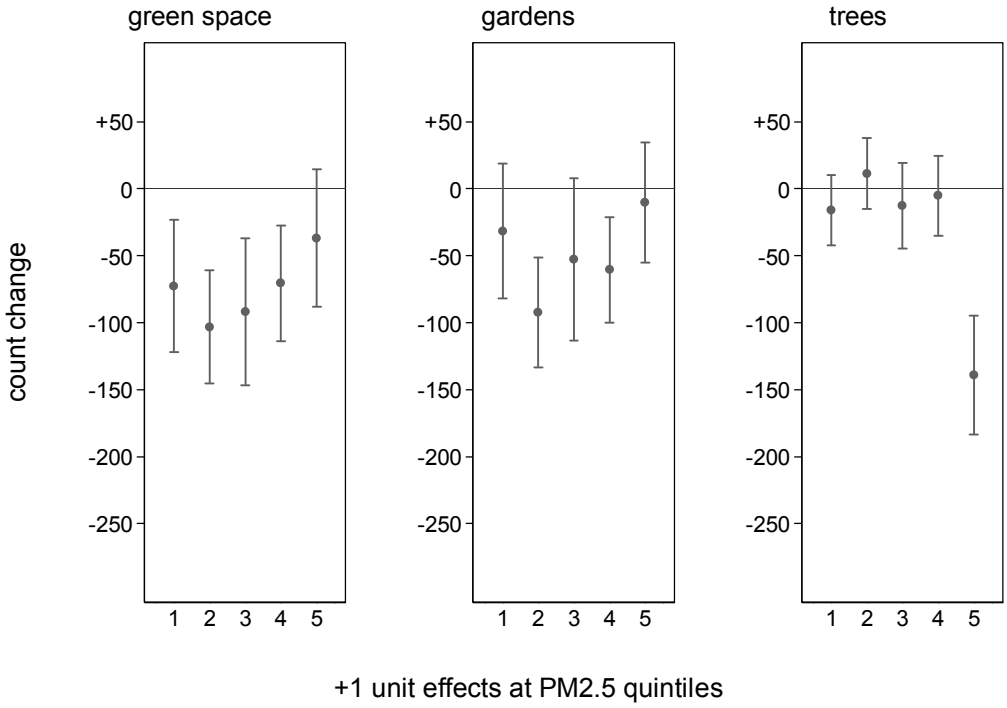
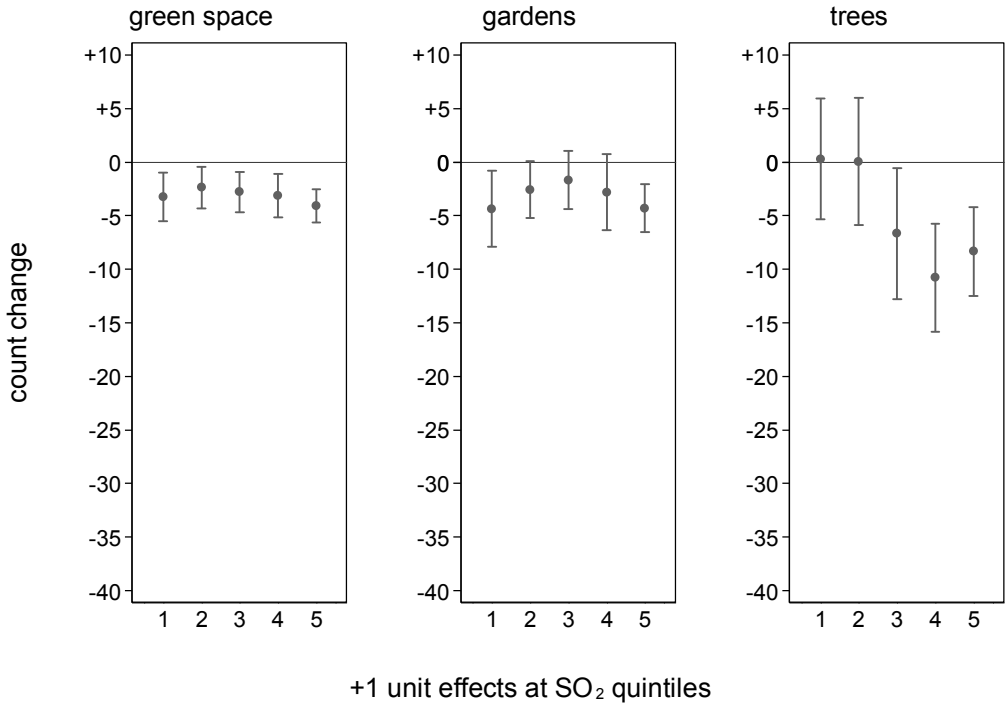
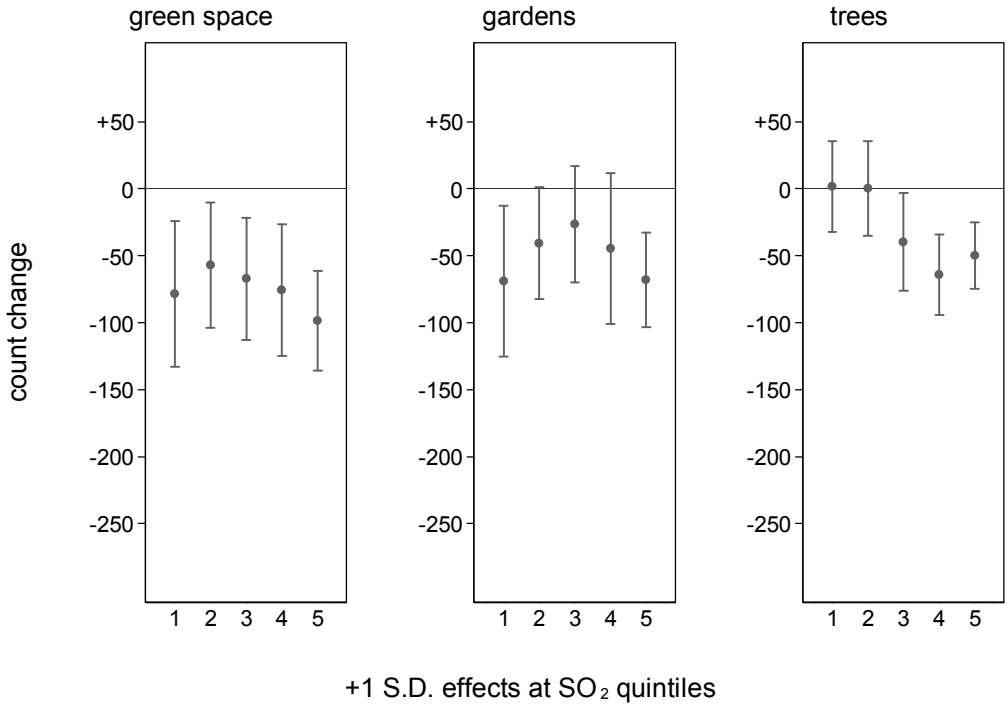


Figure A4. PM2.5/SO2 model with interaction terms for age restricted sensitivity analysis. Marginal effects of natural environments at SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase



Part 4. Penetrating pollutants sensitivity analysis

The estimation sample used in the penetrating pollutants sensitivity analysis comprised 26,139 of the urban LSOAs used in the main analysis; 316 urban LSOAs were missing data on penetrating pollutants. The mean of the asthma rate for this sample was 1645.4 (S.D. = 1047.7). Table A22 presents descriptive data on the mean penetrating pollutant concentrations disaggregated by penetrating pollutant quintiles. Table A23-A25 present cross-tabulations of penetrating pollutant quintiles. Table A26-A28 present cross-tabulations of quintiles of NO2 by quintiles of penetrating NO2; quintiles of SO2 by quintiles of penetrating SO2; and quintiles of PM2.5 by quintiles of penetrating PM2.5. Table A29 presents descriptive data on the mean asthma rate disaggregated by penetrating pollutant quintiles. Table A30 presents mean marginal effects from the penetrating pollutant quintile versions of the NO2/SO2 and PM2.5/SO2 models with interaction terms. Figure A5 and A6 present plots of natural environment effects at quintiles of penetrating NO2 and SO2, respectively, derived from the penetrating pollutant version of the NO2/SO2 model with interaction terms; Figure A7 and A8 present plots of natural environment effects at quintiles of penetrating PM2.5 and SO2, respectively, derived from the penetrating pollutant version of the PM2.5/SO2 model with interaction terms. Table A31-A42 present pairwise Wald tests of equivalence of these marginal effects of natural environments conditional on penetrating pollutant quintiles from the penetrating NO2/SO2 model with interaction terms and the penetrating PM2.5/SO2 model with interaction terms, with contrasts from the +1 unit models, and with unadjusted p values and p values with Bonferroni adjustment for the ten comparisons displayed.

Table A22. Descriptive data on penetrating pollutant concentrations in the penetrating pollutant quintile categories

	Penetrating NO2 μg/m^3				**Penetrating SO2 μg/m^3**				**Penetrating PM2.5 μg/m^3**			
	Mean	**S.D.**	**min**	**max**	**Mean**	**S.D.**	**min**	**max**	**Mean**	**S.D.**	**min**	**max**
1st quintile[a]	5.31	0.83	2.26	6.37	0.07	0.01	0.02	0.09	5.45	0.44	3.64	6.01
2nd quintile	7.07	0.39	6.37	7.71	0.10	0.01	0.09	0.11	6.36	0.19	6.01	6.66
3rd quintile	8.32	0.35	7.71	8.95	0.13	0.01	0.11	0.14	6.93	0.15	6.66	7.19
4th quintile	9.68	0.44	8.95	10.48	0.16	0.01	0.14	0.18	7.47	0.16	7.19	7.76
5th quintile[b]	12.13	1.72	10.48	27.72	0.24	0.06	0.18	0.77	8.34	0.56	7.76	12.42

[a] Least polluted quintile. [b] Most polluted quintile.

Table A23. Cross-tabulation of penetrating NO2 and penetrating SO2 pollutant concentration quintiles

		Quintiles of penetrating SO2					
		1[a]	**2**	**3**	**4**	**5**[b]	**Total**
Quintiles of penetrating NO2	**1**[a]	2,283	1,238	835	602	270	5,228
	2	993	1,139	1,124	1,082	890	5,228
	3	610	1,007	1,141	1,172	1,298	5,228
	4	684	860	1,061	1,197	1,426	5,228
	5[b]	658	984	1,067	1,175	1,343	5,227
	Total	5,228	5,228	5,228	5,228	5,227	26,139

[a] Least polluted quintile. [b] Most polluted quintile.

Table A24. Cross-tabulation of penetrating NO2 and penetrating PM2.5 pollutant concentration quintiles

		Quintiles of penetrating PM2.5					
		1[a]	**2**	**3**	**4**	**5**[b]	**Total**
Quintiles of penetrating NO2	**1**[a]	2,774	1,631	747	75	1	5,228
	2	1,387	1,395	1,631	775	40	5,228
	3	921	1,115	1,467	1,478	247	5,228
	4	146	1,015	893	2,029	1,145	5,228
	5[b]	0	72	490	871	3,794	5,227
	Total	5,228	5,228	5,228	5,228	5,227	26,139

[a] Least polluted quintile. [b] Most polluted quintile.

Table A25. Cross-tabulation of penetrating SO2 and penetrating PM2.5 pollutant concentration quintiles

		Quintiles of penetrating PM2.5					
		1[a]	**2**	**3**	**4**	**5**[b]	**Total**
Quintiles of penetrating SO2	**1**[a]	1,644	1,300	897	934	453	5,228
	2	1,089	947	1,121	914	1,157	5,228
	3	1,104	808	924	1,095	1,297	5,228
	4	952	1,033	1,029	1,055	1,159	5,228
	5[b]	439	1,140	1,257	1,230	1,161	5,227
	Total	5,228	5,228	5,228	5,228	5,227	26,139

[a] Least polluted quintile. [b] Most polluted quintile.

Table A26. Cross-tabulation of quintiles of NO2 by quintiles of penetrating NO2

		Quintiles of NO2					
		1[a]	**2**	**3**	**4**	**5**[b]	**Total**
Quintiles of penetrating NO2	**1**[1]	4,297	843	85	3	0	5,228
	2	963	2,813	1,185	266	1	5,228
	3	27	1,543	2,263	1,220	175	5,228
	4	1	87	1,679	2,288	1,173	5,228
	5[2]	0	0	60	1,497	3,670	5,227
	missing	3	8	16	17	272	316
	Total	5,291	5,294	5,288	5,291	5,291	26,455

[a] Least polluted quintile. [b] Most polluted quintile.

Table A27. Cross-tabulation of quintiles of SO2 by quintiles of penetrating SO2

		Quintiles of SO2

		1[a]	2	3	4	5[b]	Total
Quintiles of penetrating SO2	**1**[a]	2,752	1,459	783	226	8	5,228
	2	1,684	1,375	1,101	771	297	5,228
	3	688	1,558	1,449	949	584	5,228
	4	126	644	1,536	1,864	1,058	5,228
	5[b]	9	91	330	1,462	3,335	5,227
	missing	32	164	92	19	9	316
	Total	5,291	5,291	5,291	5,291	5,291	26,455

[a] Least polluted quintile. [b] Most polluted quintile.

Table A28. Cross-tabulation of quintiles of PM2.5 by quintiles of penetrating PM2.5

		Quintiles of PM2.5					
		1[a]	2	3	4	5[b]	Total
Quintiles of penetrating PM2.5	**1**[a]	4,091	948	169	18	2	5,228
	2	1,145	2,350	1,191	531	11	5,228
	3	49	1,733	2,021	1,096	329	5,228
	4	1	241	1,694	1,982	1,310	5,228
	5[b]	0	14	209	1,640	3,364	5,227
	missing	5	5	7	24	275	316
	Total	5,291	5,291	5,291	5,291	5,291	26,455

[a] Least polluted quintile. [b] Most polluted quintile.

Table A29. Asthma rate disaggregated by penetrating pollutant quintiles

	Asthma outcome by penetrating NO2 µg/m^3 quintiles		Asthma outcome by penetrating SO2 µg/m^3 quintiles		Asthma outcome by penetrating PM2.5 µg/m^3 quintiles	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
1st quintile[a]	1503.3	930.5	1742.4	1066.6	1838.3	1097.9
2nd quintile	1580.9	1042.0	1762.2	1141.3	1715.7	1070.7
3rd quintile	1686.3	1059.1	1627.4	1060.7	1577.3	1036.6
4th quintile	1703.9	1103.4	1593.0	1005.7	1523.8	1000.5
5th quintile[b]	1757.8	1075.3	1507.1	931.3	1577.1	997.9

[a] Least polluted quintile. [b] Most polluted quintile.

Table A30. Results of the penetrating pollutant versions of the models with interaction terms,[a] mean marginal effects with other variables held as observed (*n* = 26,139). Note that natural environment effects are presented both for a scale point increase and for an estimation sample S.D. increase.

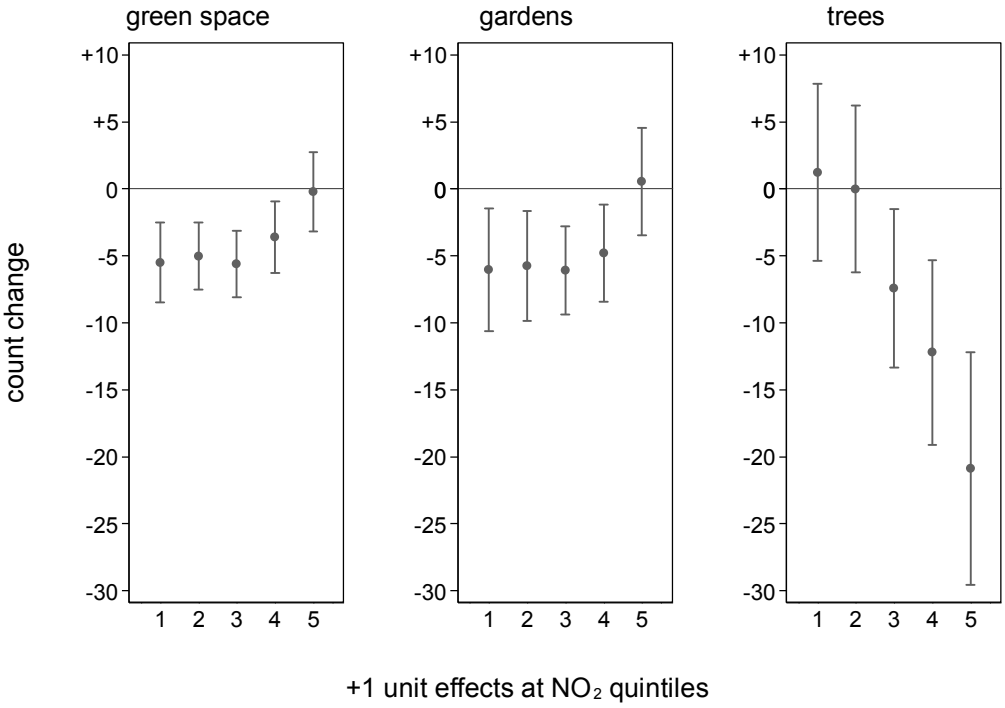
Predictors of interest		**NO2/SO2 model with interaction terms** **Mean change to asthma rate, p value, (95% CI)**	**PM2.5/SO2 model with interaction terms** **Mean change to asthma rate, p value, (95% CI)**
Greenspace	**+1 %**	-3.93, p<0.001, (-4.95, -2.92)	-4.54, p<0.001, (-5.54, -3.54)
Gardens	**+1 %**	-4.32, p<0.001, (-5.73, -2.91)	-5.01, p<0.001, (-6.42, -3.6)
Trees	**+50/km^2**	-8.03, p<0.001, (-10.54, -5.51)	-7.18, p<0.001, (-9.64, -4.72)
Greenspace	***+1 S.D.***[b]	*-94.57, p<0.001, (-119.02, -70.12)*	-109.14, p<0.001, (-133.2, -85.05)
Gardens	***+1 S.D.***[c]	*-68.53, p<0.001, (-90.91, -46.15)*	-79.43, p<0.001, (-101.73, -57.13)
Trees	***+1 S.D.***[d]	*-47.92, p<0.001, (-62.92, -32.92)*	-42.86, p<0.001, (-57.57, -28.15)
NO2[e]	**2nd quintile**	+51.39, p=0.181, (-12.68, +115.45)	
	3rd quintile	+101.54, p<0.001, (+38.66, +164.41)	
	4th quintile	+137.98, p<0.001, (+72.16, +203.8)	
	5th quintile	+172.03, p<0.001, (+93.77, +250.29)	
PM2.5[e]	**2nd quintile**		+87.1, p<0.001, (+33.39, +140.82)
	3rd quintile		+119.29, p<0.001, (+58.58, +180)
	4th quintile		+163.13, p<0.001, (+95.37, +230.89)
	5th quintile		+201.03, p<0.001, (+115.08, +286.98)
SO2[e]	**2nd quintile**	-29.95, p=0.880, (-90.95, 31.04)	+9.69, p=1.000, (-43.1, 62.47)
	3rd quintile	-114.09, p<0.001, (-174.89, -53.3)	-69.26, p=0.008, (-125.09, -13.43)
	4th quintile	-144.19, p<0.001, (-208.47, -79.92)	-103.47, p<0.001, (-161.24, -45.7)
	5th quintile	-219.65, p<0.001, (-289.71, -149.59)	-177.16, p<0.001, (-240.43, -113.89)

[a] Adjusted for deprivation component variables; government office region; all two way natural environment by pollutant quintile interactions; the NO2/PM2.5 by SO2 two way interaction; all two way interactions and the three way interaction between natural environments; all two way pollutant quintile by deprivation component interactions; all two way natural environment by deprivation component interactions. [b] +24.1%. [c] +15.9%. [d] +298.5 trees/km^2. [e] The 1st (least polluted) quintile is the reference for all comparisons; C.I. and p values Bonferroni adjusted for 4 comparisons. Fit statistics: **NO2/SO2** (Log pseudolikelihood = -208919.25, Wald (df=87) = 10142.07 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.022, Cox-Snell/ML = 0.308, Cragg-

Uhler/Nagelkerke = 0.308; BIC (df=89) = 418743.74); **PM2.5/SO2** (Log pseudolikelihood = -208870.72, Wald (df=87) = 10280.3 (p<0.001); Pseudo-R2 - McFadden (adjusted) = 0.022, Cox-Snell/ML = 0.31, Cragg-Uhler/Nagelkerke = 0.31; BIC (df=89) = 418646.67)

Figure A5. NO2/SO2 model with interaction terms. Marginal effects of natural environments at penetrating NO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. point increase

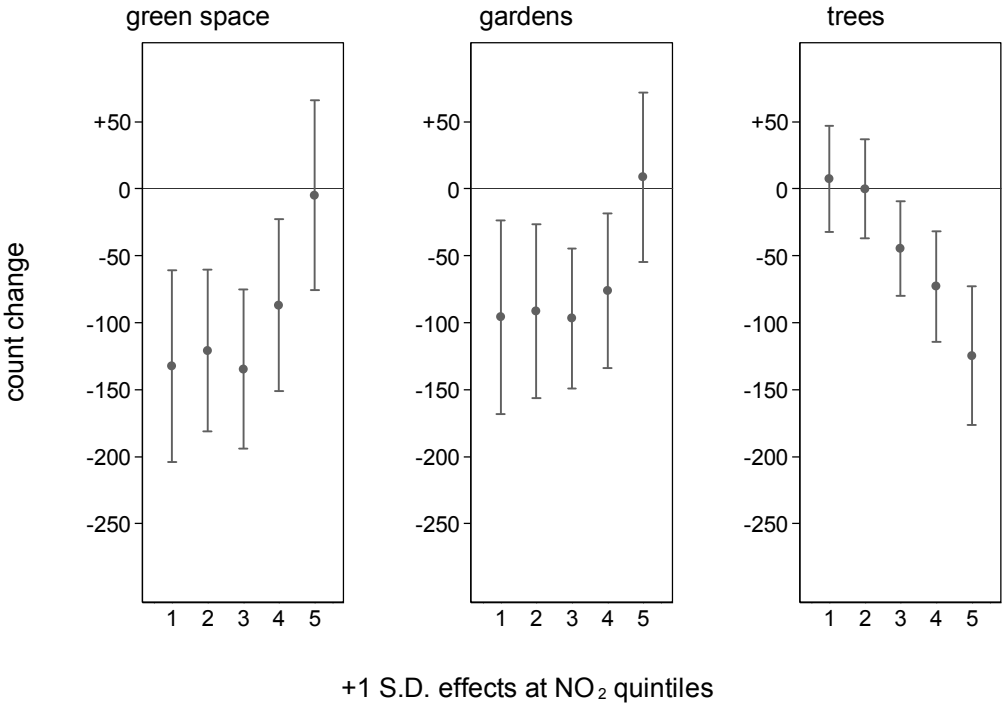
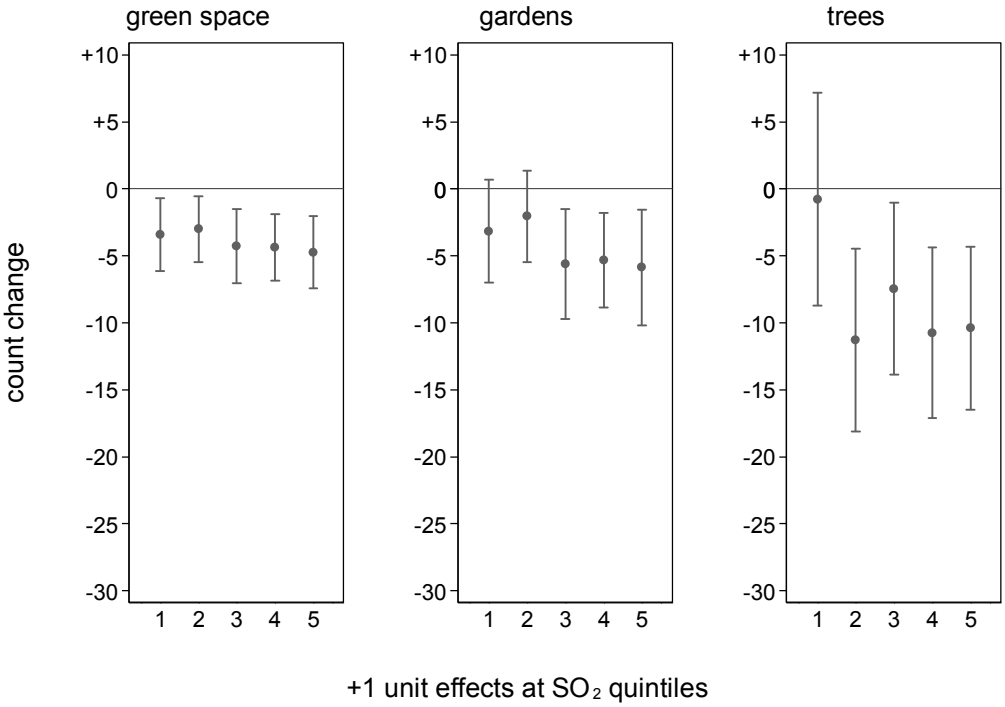


Figure A6. NO2/SO2 model with interaction terms. Marginal effects of natural environments at penetrating SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

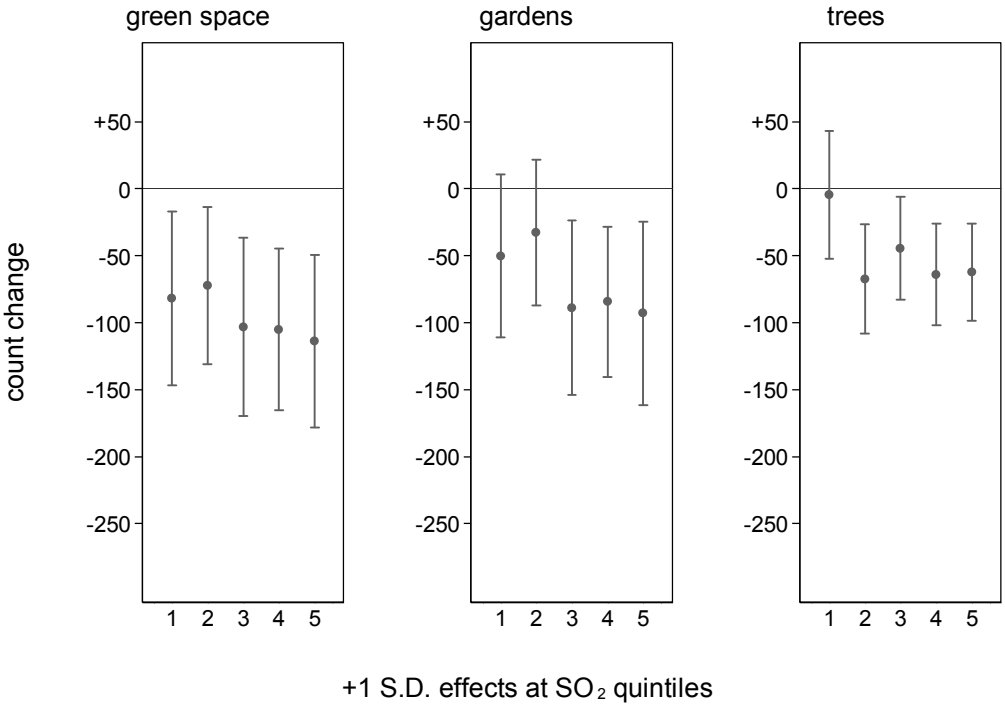
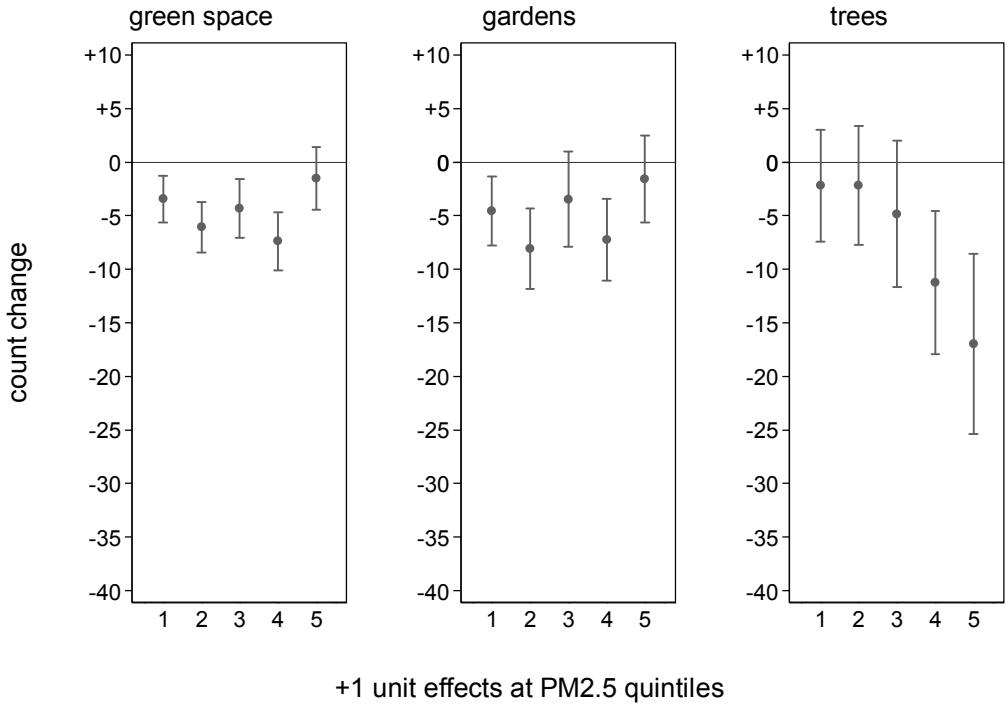


Figure A7. PM2.5/SO2 model with interaction terms. Marginal effects of natural environments at penetrating PM2.5 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

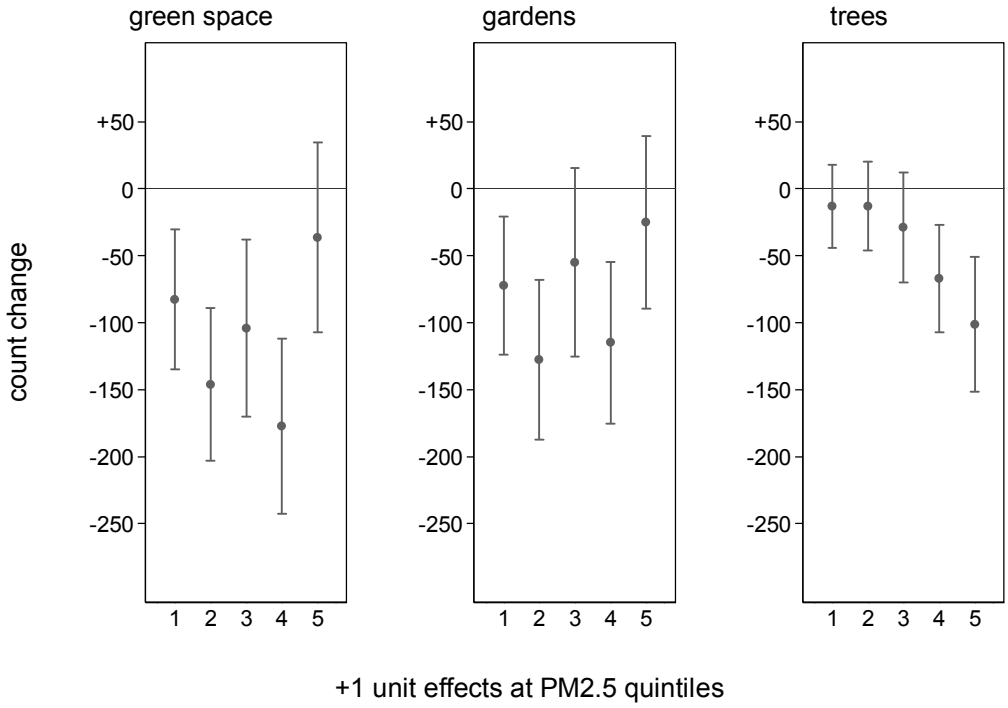
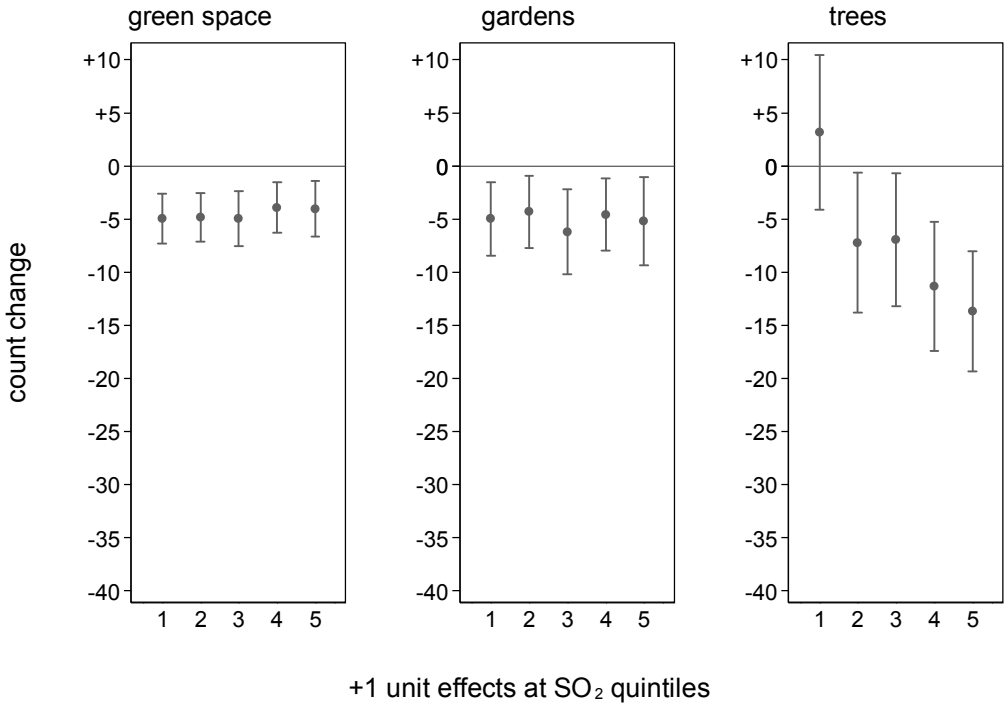


Figure A8. PM2.5/SO2 model with interaction terms. Marginal effects of natural environments at penetrating SO2 quintiles on asthma rate (95 % CI, Bonferroni adjusted for the 5 quintile comparisons).

A) + 1 scale point increase



B) + 1 S.D. increase

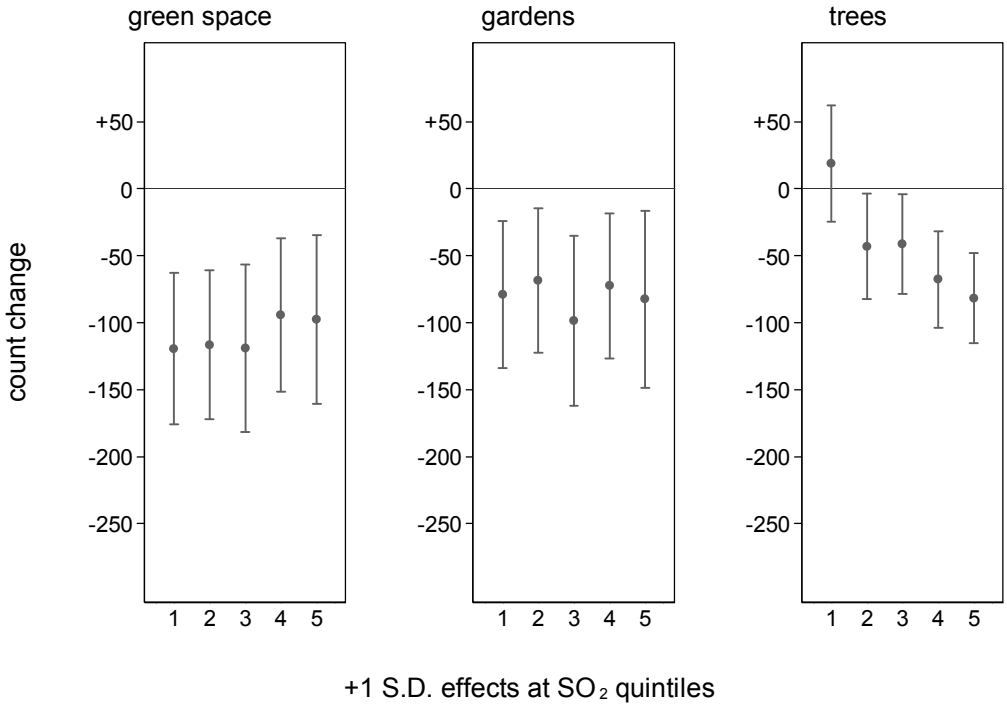


Table A31. Penetrating NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on penetrating NO2 quintile

NO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.477	1.325	0.36	0.719	1.000
3 vs 1	-0.099	1.438	-0.07	0.945	1.000
4 vs 1	+1.885	1.533	1.23	0.219	1.000
5 vs 1	+5.294	1.735	3.05	0.002	0.023
3 vs 2	-0.575	1.267	-0.45	0.650	1.000
4 vs 2	+1.408	1.345	1.05	0.295	1.000
5 vs 2	+4.818	1.513	3.19	0.001	0.014
4 vs 3	+1.984	1.341	1.48	0.139	1.000
5 vs 3	+5.393	1.479	3.65	<0.001	0.003
5 vs 4	+3.409	1.474	2.31	0.021	0.207

Table A32. Penetrating NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on penetrating NO2 quintile

NO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.281	2.105	0.13	0.894	1.000
3 vs 1	-0.06	2.122	-0.03	0.978	1.000
4 vs 1	+1.24	2.301	0.54	0.590	1.000
5 vs 1	+6.596	2.539	2.60	0.009	0.094
3 vs 2	-0.341	1.925	-0.18	0.859	1.000
4 vs 2	+0.959	2.086	0.46	0.646	1.000
5 vs 2	+6.315	2.284	2.77	0.006	0.057
4 vs 3	+1.299	1.829	0.71	0.478	1.000
5 vs 3	+6.656	1.986	3.35	0.001	0.008
5 vs 4	+5.356	1.983	2.70	0.007	0.069

Table A33. Penetrating NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on penetrating NO2 quintile

NO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-1.249	3.179	-0.39	0.694	1.000
3 vs 1	-8.684	3.365	-2.58	0.010	0.099
4 vs 1	-13.445	3.715	-3.62	<0.001	0.003
5 vs 1	-22.11	4.471	-4.95	<0.001	<0.001
3 vs 2	-7.435	3.215	-2.31	0.021	0.207
4 vs 2	-12.196	3.545	-3.44	0.001	0.006
5 vs 2	-20.861	4.262	-4.89	<0.001	<0.001

4 vs 3	-4.761	3.263	-1.46	0.145	1.000
5 vs 3	-13.426	4.013	-3.35	0.001	0.008
5 vs 4	-8.665	4.1	-2.11	0.035	0.346

Table A34. Penetrating NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on penetrating SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.407	1.289	0.32	0.752	1.000
3 vs 1	-0.881	1.52	-0.58	0.562	1.000
4 vs 1	-0.959	1.422	-0.67	0.500	1.000
5 vs 1	-1.328	1.487	-0.89	0.372	1.000
3 vs 2	-1.288	1.381	-0.93	0.351	1.000
4 vs 2	-1.366	1.29	-1.06	0.290	1.000
5 vs 2	-1.735	1.341	-1.29	0.196	1.000
4 vs 3	-0.078	1.357	-0.06	0.954	1.000
5 vs 3	-0.447	1.391	-0.32	0.748	1.000
5 vs 4	-0.369	1.281	-0.29	0.773	1.000

Table A35. Penetrating NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on penetrating SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+1.117	1.869	0.60	0.550	1.000
3 vs 1	-2.442	2.269	-1.08	0.282	1.000
4 vs 1	-2.148	2.047	-1.05	0.294	1.000
5 vs 1	-2.689	2.303	-1.17	0.243	1.000
3 vs 2	-3.56	2.035	-1.75	0.080	0.802
4 vs 2	-3.266	1.851	-1.76	0.078	0.776
5 vs 2	-3.807	2.085	-1.83	0.068	0.679
4 vs 3	+0.294	2.001	0.15	0.883	1.000
5 vs 3	-0.247	2.184	-0.11	0.910	1.000
5 vs 4	-0.541	2.005	-0.27	0.787	1.000

Table A36. Penetrating NO2/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on penetrating SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-10.523	3.816	-2.76	0.006	0.058

3 vs 1	-6.685	3.931	-1.70	0.089	0.890
4 vs 1	-9.982	4.019	-2.48	0.013	0.130
5 vs 1	-9.631	4.111	-2.34	0.019	0.191
3 vs 2	+3.838	3.467	1.11	0.268	1.000
4 vs 2	+0.541	3.516	0.15	0.878	1.000
5 vs 2	+0.891	3.532	0.25	0.801	1.000
4 vs 3	-3.296	3.26	-1.01	0.312	1.000
5 vs 3	-2.946	3.226	-0.91	0.361	1.000
5 vs 4	+0.35	3.109	0.11	0.910	1.000

Table A37. Penetrating PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on penetrating PM2.5 quintile

PM2.5 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-2.643	1.08	-2.45	0.014	0.144
3 vs 1	-0.89	1.243	-0.72	0.474	1.000
4 vs 1	-3.935	1.311	-3.00	0.003	0.027
5 vs 1	+1.92	1.472	1.30	0.192	1.000
3 vs 2	+1.752	1.306	1.34	0.180	1.000
4 vs 2	-1.292	1.346	-0.96	0.337	1.000
5 vs 2	+4.562	1.496	3.05	0.002	0.023
4 vs 3	-3.045	1.43	-2.13	0.033	0.332
5 vs 3	+2.81	1.516	1.85	0.064	0.638
5 vs 4	+5.855	1.485	3.94	<0.001	0.001

Table A38. Penetrating PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on penetrating PM2.5 quintile

PM2.5 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-3.502	1.762	-1.99	0.047	0.469
3 vs 1	+1.1	1.972	0.56	0.577	1.000
4 vs 1	-2.686	1.949	-1.38	0.168	1.000
5 vs 1	+2.977	2.132	1.40	0.162	1.000
3 vs 2	+4.601	2.173	2.12	0.034	0.342
4 vs 2	+0.816	2.076	0.39	0.694	1.000
5 vs 2	+6.479	2.231	2.90	0.004	0.037
4 vs 3	-3.785	2.236	-1.69	0.091	0.906
5 vs 3	+1.878	2.304	0.81	0.415	1.000
5 vs 4	+5.663	2.041	2.77	0.006	0.055

Table A39. Penetrating PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on penetrating PM2.5 quintile

PM2.5 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.01	2.791	0.00	0.997	1.000
3 vs 1	-2.644	3.245	-0.81	0.415	1.000
4 vs 1	-9.036	3.237	-2.79	0.005	0.053
5 vs 1	-14.757	3.934	-3.75	<0.001	0.002
3 vs 2	-2.653	3.242	-0.82	0.413	1.000
4 vs 2	-9.046	3.102	-2.92	0.004	0.035
5 vs 2	-14.767	3.824	-3.86	<0.001	0.001
4 vs 3	-6.392	3.553	-1.80	0.072	0.720
5 vs 3	-12.114	4.138	-2.93	0.003	0.034
5 vs 4	-5.722	3.909	-1.46	0.143	1.000

Table A40. Penetrating PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of green space conditional on penetrating SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.118	1.176	0.10	0.920	1.000
3 vs 1	+0.009	1.31	0.01	0.995	1.000
4 vs 1	+1.043	1.236	0.84	0.399	1.000
5 vs 1	+0.908	1.309	0.69	0.488	1.000
3 vs 2	-0.109	1.269	-0.09	0.932	1.000
4 vs 2	+0.925	1.205	0.77	0.443	1.000
5 vs 2	+0.791	1.269	0.62	0.533	1.000
4 vs 3	+1.034	1.29	0.80	0.423	1.000
5 vs 3	+0.9	1.348	0.67	0.505	1.000
5 vs 4	-0.134	1.258	-0.11	0.915	1.000

Table A41. Penetrating PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of gardens conditional on penetrating SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	+0.669	1.777	0.38	0.707	1.000
3 vs 1	-1.227	2.04	-0.60	0.547	1.000
4 vs 1	+0.419	1.843	0.23	0.820	1.000
5 vs 1	-0.22	2.04	-0.11	0.914	1.000
3 vs 2	-1.896	1.973	-0.96	0.337	1.000
4 vs 2	-0.25	1.806	-0.14	0.890	1.000
5 vs 2	-0.889	1.998	-0.45	0.656	1.000

4 vs 3	+1.646	1.989	0.83	0.408	1.000
5 vs 3	+1.007	2.164	0.47	0.642	1.000
5 vs 4	-0.639	1.982	-0.32	0.747	1.000

Table A42. Penetrating PM2.5/SO2 model with interaction terms: Pairwise Wald tests of equivalence of marginal effects of trees conditional on penetrating SO2 quintile

SO2 quintiles	Contrast dy/dx	S.E.	z	Unadjusted p	Bonferroni adjusted p
2 vs 1	-10.395	3.705	-2.81	0.005	0.050
3 vs 1	-10.119	3.649	-2.77	0.006	0.055
4 vs 1	-14.51	3.624	-4.00	<0.001	0.001
5 vs 1	-16.858	3.597	-4.69	<0.001	<0.001
3 vs 2	+0.276	3.354	0.08	0.934	1.000
4 vs 2	-4.115	3.327	-1.24	0.216	1.000
5 vs 2	-6.463	3.233	-2.00	0.046	0.456
4 vs 3	-4.391	3.162	-1.39	0.165	1.000
5 vs 3	-6.739	3.069	-2.20	0.028	0.281
5 vs 4	-2.348	2.977	-0.79	0.430	1.000