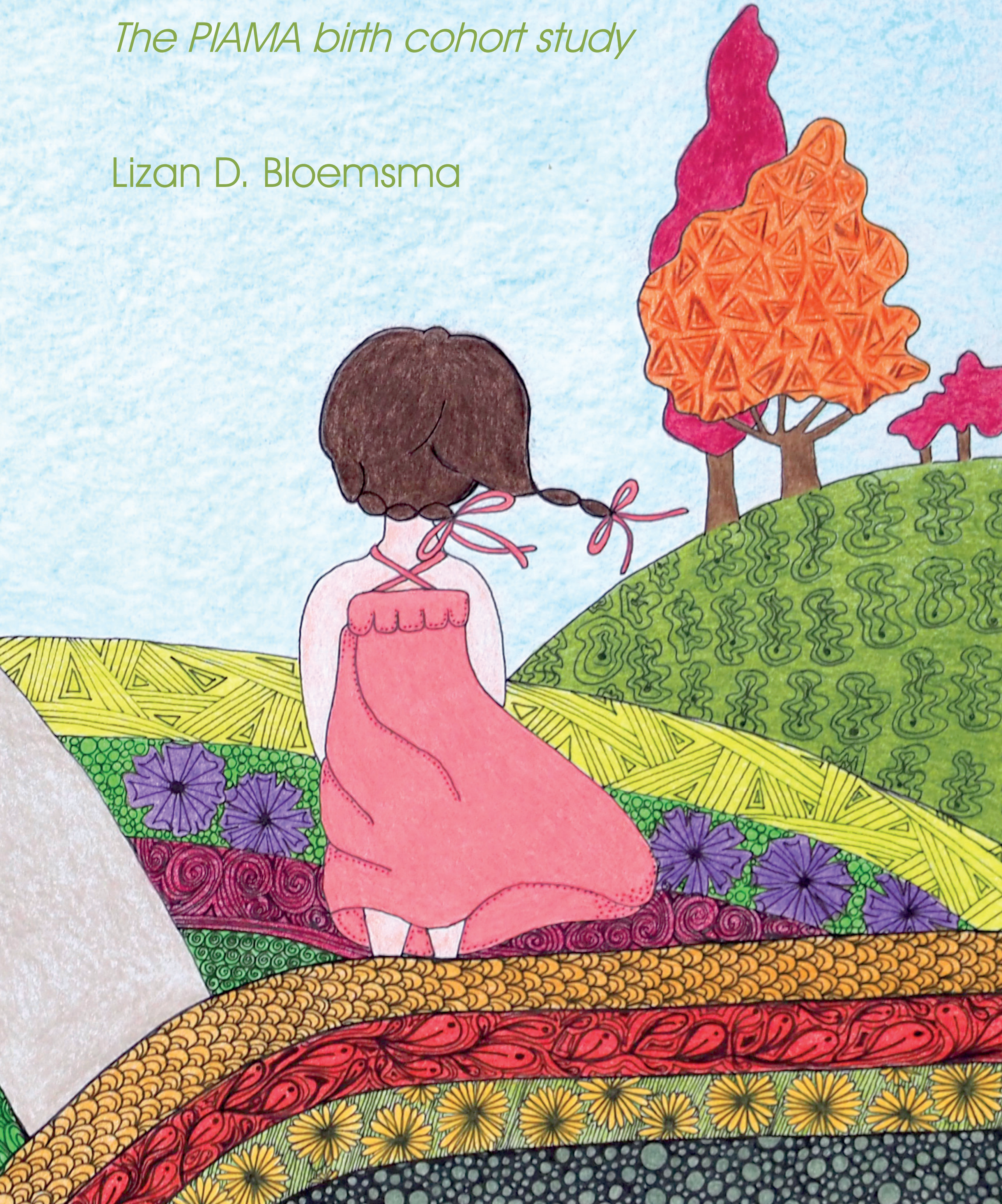
Green space, air pollution, traffic noise and children's health

The PIAMA birth cohort study

Lizan D. Bloemsma



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Printing: ProefschriftMaken || www.proefschriftmaken.nl

ISBN 978-94-6380-970-2

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Groene omgeving, luchtverontreiniging,
verkeersgeluid en de gezondheid van kinderen

De PIAMA geboortecohort studie
(met een samenvatting in het Nederlands)

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ter verkrijging van de graad van doctor aan de Universiteit Utrecht
op gezag van de rector magnificus, prof. dr. H.R.B.M. Kummeling,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen op

dinsdag 13 oktober 2020 des ochtends te 11.00 uur

door

Lizan Denise Bloemsma

geboren op 4 juli 1992
te Almere

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Chapter 1

General introduction

Background

Urbanization is one of the four demographic mega-trends, together with the growth of the global population, population ageing and international migration.[1] Globally, more people live in urban areas than in rural areas and the percentage of the world's population living in urban areas has been projected to increase from 55% in 2018 to 68% in 2050.[1] Consequently, the built environment is becoming an increasingly important determinant of the health of the world's population. Urbanization has been related to economic growth, poverty reduction and human development as cities generally offer opportunities for work and education, better sanitation, good infrastructure and health services.[1,2] However, urbanization has also brought unwanted side effects, such as increasing exposure to air pollution and noise and less availability of natural environments.[2,3] In this thesis, studies are described that investigate the health effects of green space, air pollution and traffic noise in children and adolescents living in the Netherlands.

Children are generally more susceptible than adults to environmental risks because childhood is a period of rapid growth and development. At early stages of the development of children's central nervous, reproductive, immune and digestive systems, exposure to environmental risks can lead to irreversible damage.[4] Additionally, children have less control over their environment than adults. Unlike adults, they may not recognize hazards and may be unable to make choices to protect their health.[4] Children have a larger lung surface area per unit of body weight and breathe substantially more air per unit of body weight than adults. Moreover, children tend to be more physically active outdoors and are consequently exposed to larger doses of ambient air pollution.[5,6]

Green space

Research on the beneficial health effects of green space is rapidly evolving with a considerable number of studies and reviews published in the past few years. In this thesis, we adopt the definition of green space from the United States Environmental Protection Agency [7]: "Land that is partly or completely covered with grass, trees, shrubs or other vegetation."

Exposure to higher levels of green space during pregnancy has been linked to a higher birth weight.[8] Additionally, studies found inverse relationships of exposure to green space with children's emotional and behavioral difficulties. There is also some evidence for a beneficial association of green space with mental well-being in children and depressive symptoms in adolescents.[9] Findings of studies examining relationships between green space and physical activity, obesity-related health outcomes or asthma and allergy in children have been inconsistent.[8,10]

Multiple pathways have been proposed to explain the potential health benefits of green space.[11-13] The main pathways are shown in Figure 1. Green space may affect health directly, i.e. without individuals intentionally engaging with green space, by reducing stress and reducing exposure to air pollution, noise and heat.[11] Air pollution and noise levels are generally lower in areas with green spaces, because of the absence of air pollution and noise sources (such as traffic) in green areas. Additionally, vegetation may directly remove ambient air pollutants via deposition. However, studies have shown that this potential filtering effect of vegetation is rather small.[12] Green spaces also provide opportunities for physical activity and provide settings for contacts with neighbors, which are likely to increase social cohesion within a neighborhood.[11-13] It is likely that the proposed pathways intertwine. For instance, being physically active in a green area could also reduce stress levels. The relevance of the different pathways, however, is currently unknown and very few studies have evaluated the contribution of the different pathways between green space and health outcomes in children and adolescents.[12]

Air pollution

Air pollutants are ubiquitous contaminants that continue to be steadily produced due to increasing urbanization, motorized traffic and industrialization. The pollutants with the strongest evidence for health effects are particulate matter (PM), nitrogen dioxide (NO_2), ozone (O_3) and sulfur dioxide (SO_2).[14] Globally, 93% of all children live in environments with concentrations of particulate matter with a diameter of <2.5µm ($PM_{2.5}$) above the World Health Organization (WHO) air quality guidelines.[15] While the number of premature deaths associated with unsafe water supply and sanitation is projected to decrease globally, ambient air pollution is estimated to become the leading cause of environment-related child death by 2050, unless action is taken to control ambient air pollution.[16]

Exposure to air pollution during pregnancy and childhood has been linked to increased risks of asthma development and exacerbations, increased risks of respiratory symptoms and deficits in lung function and lung function growth in children.[5,17-19] Additionally, a growing body of research provides evidence for associations between higher exposure to ambient air pollution during pregnancy and adverse birth outcomes, including preterm birth, low birth weight and small for gestational age.[15,20,21] Recent studies have indicated links between air pollution and increased blood pressure, impaired cognitive development and a higher risk of obesity in children.[22-24] However, because of the limited number of studies, evidence for associations of air pollution with these health outcomes is still insufficient. Several biological mechanisms have been proposed to explain how air pollution may negatively impact health, including: (1) pulmonary oxidative stress and systemic inflammation; (2) induction of autonomic nervous system imbalance, favoring sympathetic over parasympathetic tone; (3) access of particles or their chemical constituents to the systemic circulation.[24-26]

Traffic noise

Over the past decades, noise pollution has been recognized as an important public health issue. Road traffic is the predominant source of environmental noise. Approximately 100 million people are exposed to road traffic noise levels above 55 decibels (dB) L_{den} (day-evening-night noise level) in Europe, of which 32 million people are exposed to noise levels above 65 dB L_{den}.[27] The WHO recommends reducing noise levels produced by road traffic to below 53 dB L_{den}.[28] Railways are the second most important source of environmental noise: 19 million people are exposed to railway noise levels above 55 dB L_{den} in Europe.[27] Aircraft noise, with more than four million people exposed above 55 dB L_{den} in Europe, is the third main noise source.[27]

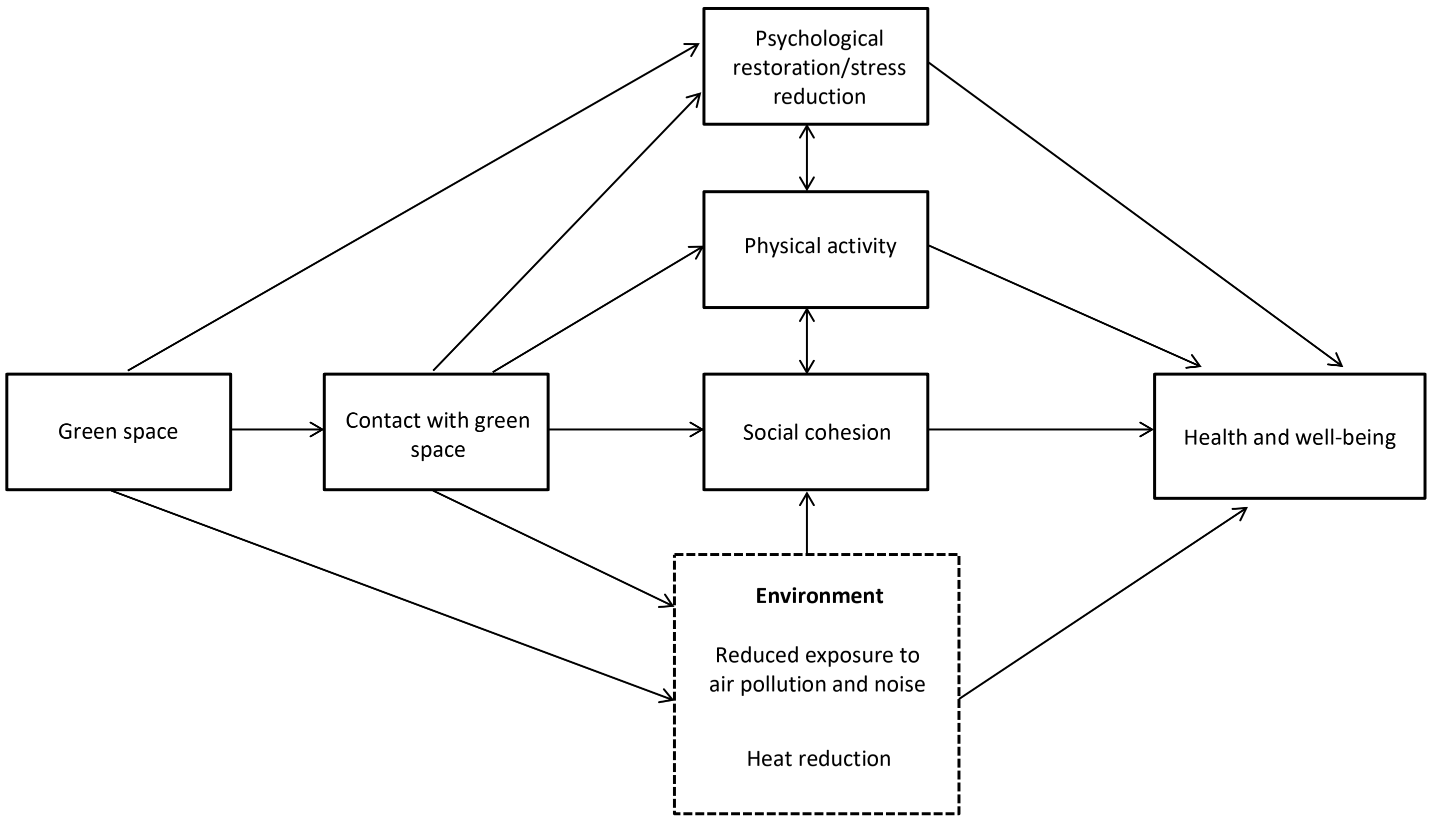

Figure 1. Main pathways through which green space can affect children's health.

Traffic noise may affect health by inducing a stress response that activates the sympathetic branch of the autonomous nervous system and the endocrine system. Noise exposure can also lead to annoyance and sleep disturbances.[29,30] Traffic noise may be associated with increased blood pressure, worse cognitive outcomes, increased hyperactivity symptoms and higher levels of stress hormones in children.[31-33] There is some evidence for a link between environmental noise and sleep disturbances in children.[34] A recent meta-analysis has shown that road traffic noise exposure during pregnancy may be associated with a lower birth weight.[35] Finally, recent studies have examined relationships between traffic noise and adiposity.[36] Other health outcomes have not been studied in relation to noise exposure in children. Therefore, more epidemiological studies are needed to establish whether traffic noise affects children's health.

Combined exposures

In daily life, people are exposed to *multiple* environmental risks (such as air pollution and noise) and environmental amenities with potentially positive health effects (such as green space). Exposures to green space, air pollution and traffic noise are generally spatially correlated since road traffic is a major source of both air pollution and noise.[37,38] Additionally, higher levels of green space are associated with lower concentrations of air pollution and lower levels of traffic noise, because of the absence of air pollution and noise sources in green areas (Figure 1). It is therefore important to distinguish the effects of green space, air pollution and traffic noise exposure and to assess potential interactions with one another in studies of long-term exposure and children's health.

In terms of public health, it is important to understand the relative contribution of these co-occurring environmental exposures to health outcomes. Because policy measures affect multiple environmental exposures, knowledge of the combined health effects of green space, air pollution and traffic noise is needed to evaluate their integrated effects in policy scenarios.

Aim and outline of this thesis

The aim of this thesis is to examine the individual and combined associations of residential exposure to green space, air pollution and traffic noise with health outcomes in children and adolescents living in the Netherlands. This aim is further specified through three objectives:

1. To investigate whether adolescents visit green spaces and for what purposes.

2. To examine associations of green space, air pollution and traffic noise with physical health.

3. To examine associations of green space, air pollution and traffic noise with stress and mental wellbeing.

Chapter 2 presents the frequency and predictors of green space visits in adolescents aged 17 years. The specific purposes of green space visits are examined, giving an indication for the relevance of the different pathways through which green space may affect health in this age group (objective 1). In **chapter 3**, associations of residential exposure to green space, air pollution and traffic noise with overweight from age three to 17 years (objective 2) are investigated. **Chapter 4** presents associations of the environmental exposures with cardiometabolic health (i.e. waist circumference, blood pressure, glycated hemoglobin (HbA1c) and cholesterol) at ages 12 and 16 years (objective 2). **Chapter 5** describes relationships of green space, air pollution and traffic noise with saliva cortisol at age 12 years (objective 3). The associations between the environmental exposures and mental wellbeing from age 11 to 20 years (objective 3) are described in **chapter 6**. The results from chapters 2-6 and their implications for public health policy and future research are discussed in the General discussion (**chapter 7**).

An overview of the outcomes studied in this thesis is provided in Figure 2.

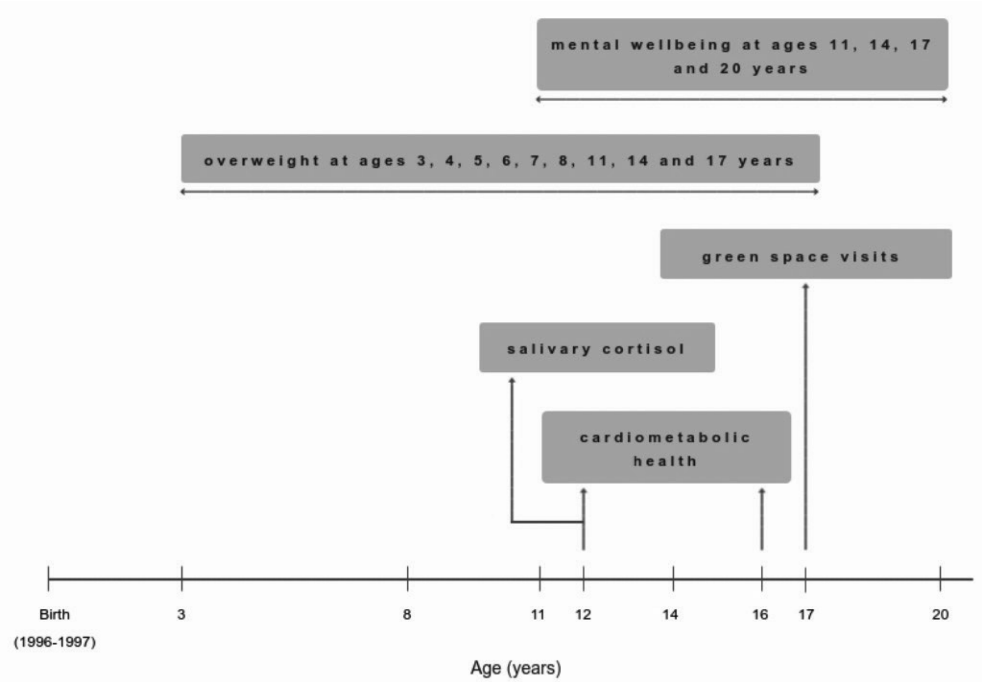

Figure 2. Overview of the outcomes studied in this thesis among children participating in the PIAMA study.

The PIAMA birth cohort study

The studies presented in this thesis are embedded in the ongoing Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study, which followed children from birth until young adulthood. Pregnant women were recruited from the general population in 1996/1997 through 52 antenatal clinics in three regions of the Netherlands

(Figure 3A): north (provinces Friesland, Groningen, Drenthe); central (provinces Utrecht, Gelderland); and west (Rotterdam and surrounding municipalities). Region north is less densely populated and has substantially lower air pollution and traffic noise levels than regions central and west. The total number of children at baseline was 3963. Questionnaires for parental completion were administered during pregnancy, at the child's ages of three months and one year and yearly thereafter until the child was eight years old. When the children were 11, 14 and 17 years old, both parents and children were invited to complete questionnaires. At the age of 20 years, only the participants (i.e. not the parents) filled in questionnaires. Medical examinations were conducted in subsamples of the population at ages four, eight, 12 and 16 years. At age 20 years, 2206 participants completed the questionnaire (73.6% of invited participants; 55.7% of the population at baseline). Figure 3B shows the places of residence of the PIAMA participants at the time of completing the 20-year questionnaires.

Information on the frequency of green space visits (chapter 2) and mental wellbeing (chapter 6) was retrieved from questionnaires completed by the adolescents. Overweight from age three until 17 years (chapter 3) was assessed from parental questionnaires. Cardiometabolic health outcomes (chapter 4) and saliva cortisol (chapter 5) have been measured during the medical examinations at ages 12 and/or 16 years.

A **B**

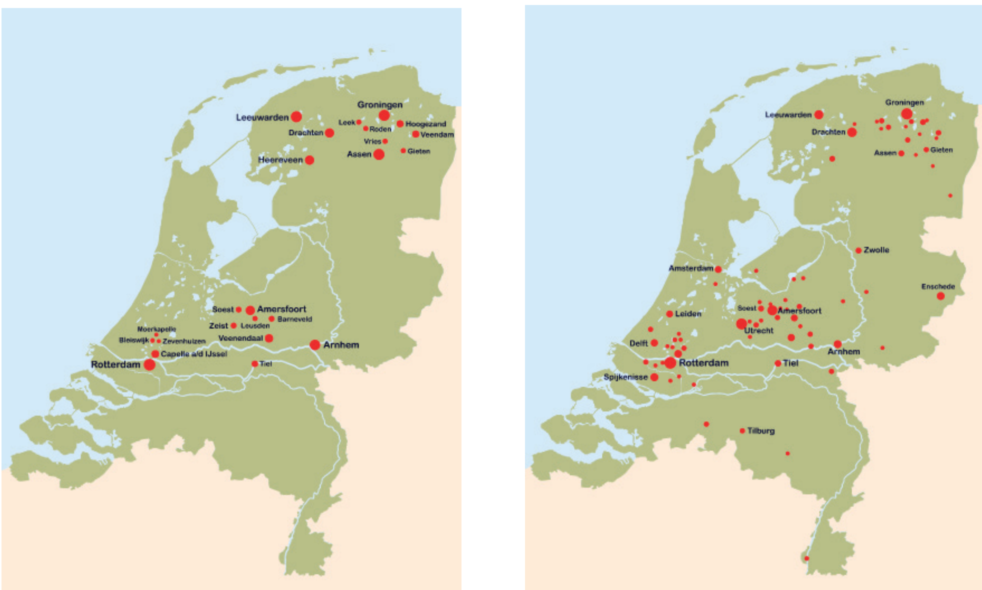

Figure 3. Locations of the antenatal clinics that recruited pregnant women in 1996/1997 (A) and places of residence of the PIAMA participants at the time of completing the 20-year questionnaires (B).

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Chapter 2

Green space visits among adolescents: frequency and predictors in the PIAMA birth cohort study

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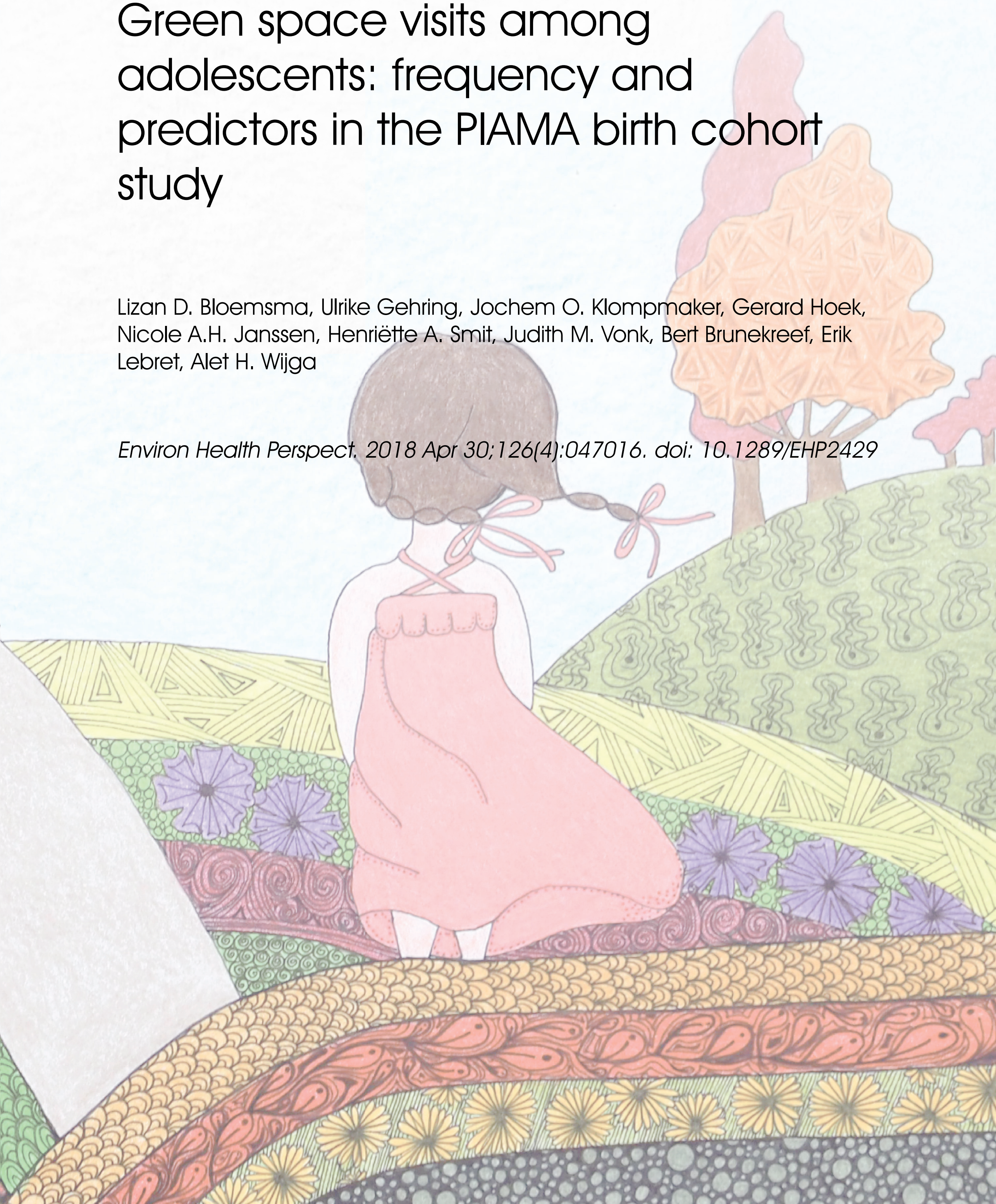
Environ Health Perspect. 2018 Apr 30;126(4):047016. doi: 10.1289/EHP2429



Abstract

Background: Green space may influence health through several pathways, for example increased physical activity, enhanced social cohesion, reduced stress and improved air quality. For green space to increase physical activity and social cohesion, spending time in green spaces is likely to be important.

Objectives: We examined whether adolescents visit green spaces and for what purposes. Furthermore, we assessed the predictors of green space visits.

Methods: In this cross-sectional study, data for 1911 participants of the Dutch PIAMA birth cohort were analyzed. At age 17, adolescents reported how often they visited green spaces for physical activities, social activities, relaxation, and to experience nature and quietness. We assessed the predictors of green space visits altogether and for different purposes by log-binomial regression.

Results: 53% of the adolescents visited green spaces at least once a week in summer, mostly for physical and social activities. Adolescents reporting that a green environment was (very) important to them visited green spaces most frequently (adj. prevalence ratio [95% confidence interval] very vs. not important 6.84 [5.10-9.17] for physical activities and 4.76 [3.72-6.09] for social activities). Boys and adolescents with highly educated fathers visited green spaces more often for physical and social activities. Adolescents who own a dog visited green spaces more often to experience nature and quietness. Green space visits were not associated with the objectively measured quantity of residential green space, i.e. the average Normalized Difference Vegetation Index and percentages of urban, agricultural and natural green space in circular buffers around the adolescents' homes.

Conclusions: Subjective variables are stronger predictors of green space visits in adolescents than the objectively measured quantity of residential green space.

Introduction

Exposure to green space may be associated with beneficial health effects, including improved pregnancy outcomes, reduced cardiovascular morbidity and mortality and improved mental health. However, only few studies examined the effects of green space on the health of adolescents (Banay et al. 2017; Dzhambov et al. 2014; Gascon et al. 2015; James et al. 2015; Nieuwenhuijsen et al. 2017).

Green space may influence health through several pathways. For example, green space may influence health by providing opportunities for physical activity, enhancing social cohesion, reducing stress, and decreasing noise levels and improving air quality (Hartig et al. 2014; Markevych et al. 2017; Nieuwenhuijsen et al. 2017). However, very few studies have examined the contribution of the different pathways between green space and morbidity (Nieuwenhuijsen et al. 2017). Reduced stress, decreased noise levels and improved air quality can beneficially affect health without individuals consciously engaging with green space (Hartig et al. 2014). In contrast, for green space to increase physical activity and social interaction, actual green space visits are likely to be important. It is therefore important to examine whether people actually spend time in green spaces and for what purposes green spaces are visited to get more insights into the contribution of different pathways.

Generally, objectively measured surrounding greenness and/or access to green space are used in epidemiological studies, assessed by land use maps or remote sensing indices such as the Normalized Difference Vegetation Index (NDVI) (Dadvand et al. 2012; Huynh et al. 2013; Markevych et al. 2014). A limitation of assessing exposure merely through the presence of green space is the lack of data on the actual green space visits by the study participants.

To our knowledge, only few studies have examined green space visits by adolescents. A study conducted in the United States found that adolescents used parks more often for physical activity when there was higher perceived park availability, park quality and park use by friends (Ries et al. 2009). A study in California showed that increasing age was associated with a decreased likelihood of being physically active in parks and that females were less often physically active in parks than males (Babey et al. 2015). However, these studies did not focus on visits to green spaces other than parks that may also affect the health of adolescents. Additionally, the studies mainly focused on physical activity, and not on any of the other proposed pathways.

In the present study, we aim to examine whether adolescents visit green spaces and for what purposes. We also aim to identify the predictors of green space visits.

Methods

Study design and population

This study used data from the Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort. Detailed descriptions of the PIAMA study have been published previously (Brunekreef et al. 2002; Wijga et al. 2014). In brief, pregnant women were recruited from the general population in three different parts of the Netherlands during their second trimester of pregnancy. Their children were born in 1996/1997 (n = 3963 at baseline) and have been followed from birth up to the age of 17 years. Questionnaires were sent to the participating parents during pregnancy, three months after the child was born, when the child was one year old, and yearly thereafter until the child was eight. When the children were 11, 14 and 17 years old, both parents and children were asked to complete a questionnaire. The study protocol has been approved by the medical ethical committees of the participating institutes and written informed consent was obtained from the parents of all participants.

The present cross-sectional study used data from the questionnaires completed by parents and adolescents at the age of 17 years. At this age, 3109 families (78.5% of 3963) were still participating in the study and received questionnaires: one questionnaire for the adolescents and one questionnaire for the parents. In total, 2096 adolescents (67.4% of 3109; 52.9% of 3963) and 1875 parents completed their questionnaire. Most of the information used in the present study was obtained from the questionnaire for the adolescents. However, information on some of the potential predictors of green space visits, such as dog ownership and parental level of education, was obtained from the parental questionnaire. Adolescents with complete information on green space visits and potential predictors thereof were included in this study. This resulted in a study population of 1911 adolescents.

Definition of green space visits as the outcome variable

The frequency of green space visits was assessed with the following question: "How often do you intentionally go to a green environment (not your own garden) for the following activities: physical activities (e.g. walking, cycling, doing sports), social activities (e.g. meeting friends, having a picnic), relaxation (e.g. reading, resting, watching people, sunbathing), and to experience nature and quietness?" Answering options were 'never', 'less than once a month', '1-3 times a month', 'once a week' and 'more than once a week'. We assumed that green spaces may be beneficial to health when they are visited regularly. Therefore, five binary outcome variables were created: Visiting green space at least once a week for (1) physical activities (yes/no); (2) social activities (yes/no); (3) relaxation (yes/no); (4) experiencing nature and quietness (yes/no); (5) any of the types of activity mentioned before (yes/no). Participants reported how often they visited green spaces in summer and in winter. Since only a small percentage of adolescents visited green spaces in winter (Figure 1), we only assessed predictors of green space visits in summer.

Definition of potential predictors

Socio-demographic characteristics. We included the child's sex and several indicators of socio-economic status (SES): maternal and paternal level of education (obtained from the 1 year questionnaire), the participant's level of education (obtained from the 17 year questionnaire), and area level SES (based on status scores of 4-digit postal code areas of 2014 from Statistics Netherlands (Knol 2012)). Status scores include the average income, the percentage of residents with a low income, the percentage of low educated residents and the percentage unemployed subjects in a postal code area. A higher status score indicates a higher neighborhood SES (Knol 2012). Maternal and paternal education were divided into three categories: primary school only or lower secondary or lower vocational education (low); intermediate vocational education or intermediate or higher secondary education (intermediate); and higher vocational education or university (high). The educational level of the adolescents was divided into two categories: lower secondary or lower vocational education, intermediate secondary or intermediate vocational education (low/ intermediate); higher secondary education, higher vocational education or university (high).

Urbanization. Data on address density as an indicator of the degree of urbanization per 4-digit postal code for 2011 were obtained from Statistics Netherlands (Centraal Bureau voor de Statistiek). Statistics Netherlands divides address density into five categories: ≥2500 addresses per km^2; 1500 to 2500 addresses per km^2; 1000 to 1500 addresses per km^2; 500 to 1000 addresses per km^2; and <500 addresses per km^2.

Dog ownership. Parents of the adolescents answered the following questions: ”Do you have a dog at home?” and if yes ”How many hours per week does your child walk the dog outside?”. Responses to the questions were used to create a variable with the following categories: does not own a dog; owns a dog and adolescent walks the dog one hour or less per week; owns a dog and adolescent walks the dog more than one hour per week. Since information on dog ownership was missing for 271 adolescents (14.2%), we created a fourth category, ‘no information available about dog ownership’, to avoid that these adolescents would be excluded from the analyses.

Perceived importance of a green environment. For each type of activity (i.e. physical activities, social activities, relaxation and to experience nature and quietness), adolescents reported whether a green environment was ’not important’, ’somewhat important ’, ’important’ or ’very important’ to them. Our questionnaire did not contain a question about the importance of a green environment for green space visits in general, i.e. for any type of activity. We therefore combined the responses to the four separate activities to create a variable with three categories for the outcome ‘visiting green space at least once a week for any type of activity’: not important, somewhat important, important.

Perceived neighborhood greenness. Adolescents were asked to classify their neighborhood as very green, green, moderately green, little green or not green. Since only a small group of adolescents reported that their neighborhood was not green, we combined the latter two categories into one: little to no green.

Quantity of residential green space. Different indicators were used to objectively assess the quantity of green space within certain distances of the adolescent’s home. To assess surrounding greenness levels, we used the NDVI, derived from Landsat 5 Thematic Mapper (TM) data at 30 m x 30 m resolution. NDVI values range from -1 to 1, with higher values indicating more greenness (Weier and Herring 2000). Negative values correspond to water and were set to zero, so that the effects of water surfaces do not negate the presence of green space (Markevych et al. 2014). Several options to handle negative NDVI values are available (Markevych et al. 2017). We could have artificially reduced the average NDVI by recoding negative values to zero, as compared to removing negative NDVI values. However, the average percentage of water in a buffer of 3000 m was only 6.29 in our study population, so we assume that this has not substantially affected our estimates of greenness exposure. We generated a map of the Netherlands by combining cloud free images of the summer of 2010. For each adolescent, surrounding greenness was assessed by calculating the average NDVI in buffers of 100 m, 300 m, 500 m, 1000 m and 3000 m around his/her home. The buffers of 100 m, 300 m and 500 m represent the quantity of green space near the adolescent's home, whereas the buffers of 1000 m and 3000 m represent the quantity of green space in a larger area around the adolescent's home. We hypothesize that green spaces close to home may have a different effect on the frequency of green space visits than green spaces in a larger area around the home.

We hypothesized that different types of green space may have different effects on green space visits. Top10NL is a detailed land-use map of the Netherlands (Kadaster 2014). In contrast to the NDVI, street greenery and private green property (such as gardens) are not included in the Top10NL. We used Top10NL of 2015 to assess the percentages of urban green, natural green and agricultural green in buffers of 100 m, 300 m, 500 m, 1000 m and 3000 m around the residential addresses. To distinguish between different types of green space, we defined all green spaces within a 'population cluster' as 'urban green space'. A population cluster is defined as a locality with at least 25, predominantly residential buildings (Vliegen et al. 2006). The remaining green spaces were classified as 'agricultural green space' (arable land, fruit or tree nurseries, orchards or grassland) and 'natural green space' (forests or heather). A total of 57% of the adolescents had no natural green space in the 300 m buffer around their homes (Table 1). Therefore, a binary variable was created: natural green space in a buffer of 300 m yes/no. Both the average NDVI and the percentages of urban, agricultural and natural green space in different buffer sizes were highly correlated (Table S1). We therefore decided to include the buffers of 300 m, 1000 m and 3000 m only in the present analyses, and did not perform analyses with the indicators of the quantity of green space in buffers of 100 m and 500 m. 'Bestand Bodemgebruik' is another land-use map of the Netherlands (Centraal Bureau voor de Statistiek 2008). It is less detailed than Top10NL (it contains fewer land-use categories), but in contrast to Top10NL, it contains a separate category for parks defined as public green spaces that are used for relaxation. With a detailed map covering all roads and paths of the Netherlands, we estimated the distance along roads (i.e. network distance) in meters from the adolescents' homes to the nearest park. A categorical variable was created: has a park within 300 m of the residential address, has a park within 300 m to 1000 m of the residential address, has no park within 1000 m of the residential address.

We included the following objectively measured indicators of the quantity of residential green space in the analyses: 1) the average NDVI in buffers of 300 m, 1000 m and 3000 m around the adolescent's home; 2) the percentage of urban, agricultural and natural green space in buffers of 300 m, 1000 m and 3000 m around the adolescent's home; 3) the distance from the home address to the nearest park. These indicators of the quantity of residential green space were determined in ArcGIS 10.2.2 (Esri, Redlands, CA, USA).

Statistical analyses

First, we investigated the shape of the unadjusted relationships between continuous predictors and visiting green space at least once a week (yes/no) by generalized additive models with integrated smoothness estimation and a log link (GAM function; The R Project for Statistical Computing 2.8.0, www.r-project.org). Since most of the associations were found to be linear or almost linear, the continuous predictors were not transformed. We used log-binomial regression models to calculate prevalence ratios (PRs) and 95% confidence intervals (95% CIs) (Spiegelman and Hertzmark 2005). We performed analyses of the unadjusted associations between each of the potential predictors and the five outcomes (visiting green space at least once a week for any type of activity, for physical activities, for social activities, for relaxation and for experiencing nature and quietness). Predictors that were associated with at least one outcome with a p-value of ≤0.10 were selected for multivariable modelling with backward variable selection. Simultaneous inclusion of the objectively measured indicators of the quantity of green space in buffers of 300 m, 1000 m and 3000 m in the same model resulted in multicollinearity problems (Variance Inflation Factor > 4.5). We therefore decided to include only buffers of 300 m and 3000 m in multivariable modelling. The Akaike Information Criterion (AIC) was used to determine for each of the five outcomes the model that best fit the data, i.e. five outcome-specific models were made (Burnham and Anderson 2002). In the end, we included all predictors that were selected into at least one of the five outcome-specific models in our final model to facilitate the comparison of models between outcomes.

Additionally, stratified analyses by level of urbanization were performed. The level of urbanization was divided into two categories: urban (≥1000 addresses per km^2) and non-urban (<1000 addresses per km^2).

Several sensitivity analyses were performed. We repeated the analysis of the predictors of green space visits in summer with the frequency of green space visits in five categories (never, less than once a month, 1-3 times a month, once a week, more than once a week) by polytomous logistic regression with ‘never’ as the reference category. We also performed sensitivity analyses without the predictor ‘perceived importance of a green environment’ to examine whether other predictors were associated with green space visits in summer when this predictor was omitted. Moreover, we assessed whether the predictors of green space visits in winter differed from the predictors of green space visits in summer. The percentage of adolescents that visited a green space at least once a week in winter for relaxation or to experience nature and quietness was too low to perform the analyses. Therefore, the sensitivity analyses were limited to the frequency of green space visits in winter for physical activities, social activities and any type of activity. Since log-binomial regression models failed to converge, we assessed the associations between the frequency of green space visits in winter and potential predictors with Poisson regression (Spiegelman and Hertzmark 2005).

The statistical analyses, except the generalized additive models with integrated smoothness estimation, were performed with SAS version 9.4.

Results

Population characteristics and frequencies of green space visits

Characteristics of the study population are presented in Table 1. In total, 41% of mothers and 46% of fathers were highly educated, 61% of the adolescents classified their neighborhood as (very) green and 78% of the adolescents had a park within 1000 m of their home. The median average NDVI in buffers of 300 m, 1000 m and 3000 m increased with increasing levels of 'perceived neighborhood greenness', whereas no such trend was observed for the median percentage of urban green space (Figure S1).

Adolescents reported visiting green spaces mostly for physical activities and social activities and less often for relaxation and to experience nature and quietness (Figure 1). A total of 53% of adolescents visited a green space at least once a week for any type of activity in summer, whereas this percentage was 26 in winter. Participants living in urban areas and participants living in non-urban areas hardly differed in how often they visited green spaces in summer (Figure 1).

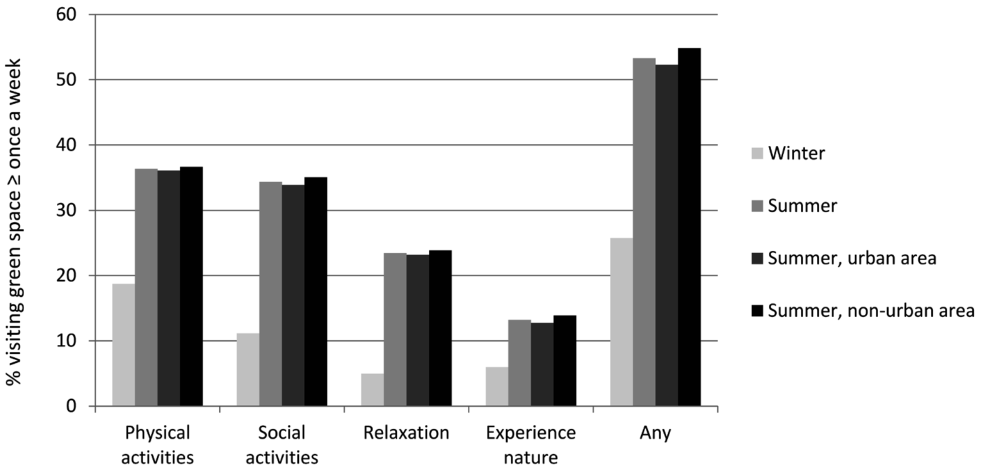


Figure 1. Percentage of adolescents visiting green spaces at least once a week according to type of activity, winter or summer season, and level of urbanization for visits during the summer. Urban area: ≥1000 addresses per km^2; non-urban area: <1000 addresses per km^2.

Predictors of green space visits

Table S2 displays the unadjusted associations between visiting green spaces at least once a week for different activities and potential predictors of green space visits. The perceived importance of a green environment is the only predictor that was strongly and consistently associated with all five outcomes. Different predictors were associated with the frequency of green space visits for different purposes. For example, adolescents who owned a dog were more likely to visit green spaces at least once a week for physical activities, relaxation and to experience nature and quietness, while boys visited green spaces more often for physical activities than girls. Table 2 shows the results from the multivariable log-binomial regression analyses. The perceived importance of a green environment remained the strongest predictor of green space visits in multivariable analyses. Adolescents who reported that a green environment was (very) important to them visited green spaces more often than adolescents for whom a green environment was not important (PR [95% CI] 6.84 [5.10-9.17] for physical activities and 4.76 [3.72-6.09] for social activities). Boys visited green spaces more often for physical and social activities than girls (PR 1.12 [95% CI 1.01 - 1.24]; PR 1.15 [95% CI 1.02 - 1.28], respectively) and adolescents who owned a dog were 1.5 - 1.7 times more likely to visit green spaces at least once a week to experience nature and quietness. Adolescents with a high level of education visited green spaces less often for social activities (PR 0.85 [95% CI 0.75 - 0.96]) and relaxation (PR 0.84 [95% CI 0.71 - 0.99]) than adolescents with a low to intermediate level of education. Participants with highly educated fathers were more likely to visit green spaces at least once a week for physical and social activities and any type of activity compared to adolescents with fathers who were less educated (PR 1.25 [95% CI 1.06 - 1.48]; PR 1.22 [95% CI 1.03 - 1.44]; PR 1.13 [95% CI 1.01 - 1.26], respectively).

Table 1. Characteristics of the study population and potential predictors of green space visits (n = 1911).

Characteristic	N (%), mean ± SD, or median (25th – 75th percentiles)
Sex	
Girl	974 (51.0)
Boy	937 (49.0)
Age in years	17.8 ± (0.3)
Maternal level of education	
Low	339 (17.7)
Intermediate	780 (40.8)
High	792 (41.4)
Paternal level of education	
Low	400 (20.9)
Intermediate	638 (33.4)
High	873 (45.7)
Educational level of adolescent	
Low/intermediate	1015 (53.1)
High	896 (46.9)
Neighborhood SES [a]	0.5 (-0.1 - 1.3)
Urbanization	
≥ 2500 addresses per km^2	153 (8.0)
1500 - 2500 addresses per km^2	638 (33.4)
1000 - 1500 addresses per km^2	378 (19.8)
500 - 1000 addresses per km^2	443 (23.2)
< 500 addresses per km^2	299 (15.7)
Owning a dog	
Does not own a dog	1198 (62.7)
Owns a dog, and walks the dog ≤ 1 hour per week	267 (14.0)
Owns a dog, and walks the dog > 1 hour per week	175 (9.2)
No information available about dog ownership	271 (14.2)

Importance of a green environment	
Not important	589 (30.8)
Somewhat important	757 (39.6)
Important	565 (29.6)
Perceived neighborhood greenness	
Very green	297 (15.5)
Green	871 (45.6)
Moderately green	643 (33.7)
Little to no green	100 (5.2)
Distance from home to the nearest park	
≤ 300m	645 (33.8)
300 – 1000m	845 (44.2)
> 1000m	421 (22.0)
Average NDVI in 300m buffer [b]	0.55 (0.48 - 0.61)
Average NDVI in 1000m buffer [b]	0.58 (0.51 - 0.65)
Average NDVI in 3000m buffer [b]	0.62 (0.56 - 0.68)
Percentage urban green in 300m buffer	9.7 (4.4 - 15.6)
Buffers that have no urban green	112 (5.9)
Percentage urban green in 1000m buffer	9.2 (5.1 - 13.9)
Buffers that have no urban green	54 (2.8)
Percentage urban green in 3000m buffer	6.0 (2.9 - 9.7)
Buffers that have no urban green	7 (0.4)
Percentage agricultural green in 300m buffer	1.1 (0.0 - 16.3)
Buffers that have no agricultural green	829 (43.4)
Percentage agricultural green in 1000m buffer	18.8 (4.9 - 39.8)
Buffers that have no agricultural green	173 (9.1)
Percentage agricultural green in 3000m buffer	39.9 (23.7 - 55.4)
Buffers that have no agricultural green	0.0 (0.0)
Percentage natural green in 300m buffer	0.0 (0.0 - 1.3)
Buffers that have no natural green	1091 (57.1)
Percentage natural green in 1000m buffer	1.8 (0.3 - 5.7)
Buffers that have no natural green	244 (12.8)
Percentage natural green in 3000m buffer	4.1 (2.1 - 10.0)
Buffers that have no natural green	0.0 (0.0)

Abbreviations: SD = standard deviation; SES = socioeconomic status; NDVI = normalized difference vegetation index.
[a] A higher score indicates a higher SES.
[b] NDVI values range from 0 to 1, with higher values indicating more greenness.

Maternal level of education, area level SES and the objectively measured quantity of green space (i.e. the average NDVI and percentages of urban, agricultural and natural green space in buffers of 300 m and 3000 m around the participants' homes and the distance to the nearest park) were not significantly associated with green space visits in multivariable analyses (data not shown). We could not add all objectively measured indicators of the quantity of green space at the same time to the models in Table 2 because of multicollinearity problems. The NDVI is the most frequently used indicator to assess exposure to greenness in epidemiological studies. We have therefore decided to only add the average NDVI in buffers of 300 m and 3000 m at the same time to the models that are displayed in Table 2. The association between the average NDVI and green space visits remained non-significant (Table S3).

When we stratified by level of urbanization, we found that the associations between adolescents living in urban areas and adolescents living in non-urban areas were generally very similar (Figure 2). However, adolescents with highly educated fathers only visited green spaces more often for physical and social activities and any type of activity when they lived in an urban area. We found no associations between paternal level of education and green space visits for social activities and any type of activity in adolescents who lived in non-urban areas.

The perceived importance of a green environment was also the strongest predictor of green space visits when the frequency of green space visits was divided into five categories (Tables S4-S8). The results of these sensitivity analyses were generally similar to those of the main analyses, except that adolescents with a higher level of education visited green spaces more often for any type of activity than adolescents with a low/intermediate level of education (odds ratio (OR) 1-3 times a month vs. never 2.57 [95% CI 1.66 - 3.98]; OR once a week vs. never 2.21 [95% CI 1.42 - 3.44]; OR more than once a week vs. never 1.60 [95% CI 1.03 - 2.50]) (Table S8). Tables S9 and S10 show the associations between the frequency of green space visits in winter and potential predictors of green space visits. The strongest predictor of the frequency of green space visits in winter was the perceived importance of a green environment, which is consistent with our results for green space visits in summer. We found some differences between the predictors of green space visits in summer and green space visits in winter. Perceived neighborhood greenness and the percentage of agricultural green space in a buffer of 3000 m around the adolescent's home were significantly associated with green space visits in winter, whereas paternal level of education was not (Table S10). Adolescents who classified their neighborhood as 'green' or 'very green' visited green spaces more often for any type of activity in winter, whereas a higher percentage of agricultural green space in a buffer of 3000 m was associated with a lower likelihood of visiting green space at least once a week for physical activities or any type of activity (Table S10). Sensitivity analyses without the predictor 'perceived importance of a green environment' yielded results similar to those of the main analyses. However, perceived neighborhood greenness was significantly associated with green space visits for physical activity only when 'perceived importance of a green environment' was omitted (Table S11). Adolescents who classified their neighborhood as 'very green' visited green spaces more often for physical activities than adolescents who classified their neighborhood as 'little to no green' (PR 1.40 [95% CI 1.00 - 1.94]). We also observed this positive trend of perceived neighborhood greenness for the other outcome variables, but these associations were non-significant.

Table 2. Predictors associated with visiting green spaces at least once a week (yes/no) from multivariable regression analysis.

Predictor	Physical activities	Social activities	Relaxation	Experiencing nature and quietness	Any type of activity
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Sex					
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	1.12 (1.01, 1.24)	1.15 (1.02, 1.28)	0.87 (0.74, 1.02)	0.86 (0.70, 1.07)	1.06 (0.99, 1.15)
Paternal level of education					
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.09 (0.91, 1.29)	1.09 (0.92, 1.29)	1.00 (0.82, 1.23)	1.08 (0.80, 1.45)	1.03 (0.92, 1.16)
High	1.25 (1.06, 1.48)	1.22 (1.03, 1.44)	0.92 (0.75, 1.14)	1.01 (0.75, 1.36)	1.13 (1.01, 1.26)
Educational level of adolescent					
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.02 (0.91, 1.14)	0.85 (0.75, 0.96)	0.84 (0.71, 0.99)	0.82 (0.65, 1.03)	0.95 (0.88, 1.04)
Owning a dog					
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	1.01 (0.86, 1.19)	1.05 (0.90, 1.23)	1.15 (0.92, 1.43)	1.47 (1.10, 1.97)	1.01 (0.90, 1.14)
Owns a dog, and walks the dog > 1 hour per week	1.07 (0.93, 1.24)	1.03 (0.85, 1.25)	1.16 (0.91, 1.47)	1.67 (1.23, 2.25)	1.05 (0.92, 1.20)
No information available about dog ownership	0.95 (0.81, 1.10)	1.17 (1.01, 1.34)	1.15 (0.93, 1.42)	1.29 (0.96, 1.73)	1.13 (1.02, 1.25)
Importance of a green environment					
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	2.53 (1.85, 3.45)	2.04 (1.59, 2.61)	1.85 (1.35, 2.52)	3.54 (1.93, 6.50)	1.82 (1.60, 2.08)
Important	4.55 (3.41, 6.09)	3.81 (3.03, 4.80)	3.48 (2.60, 4.65)	9.62 (5.48, 16.88)	2.16 (1.89, 2.46)
Very important	6.84 (5.10, 9.17)	4.76 (3.72, 6.09)	4.87 (3.53, 6.71)	18.76 (10.69, 32.92)	N/A

Abbreviations: PR = prevalence ratio; CI = confidence interval.

Results are derived from log-binomial regression analysis. The prevalence ratios are adjusted for all variables presented in this table.

Predictors that are included in at least one of the five outcome-specific models that best fit the data are presented.

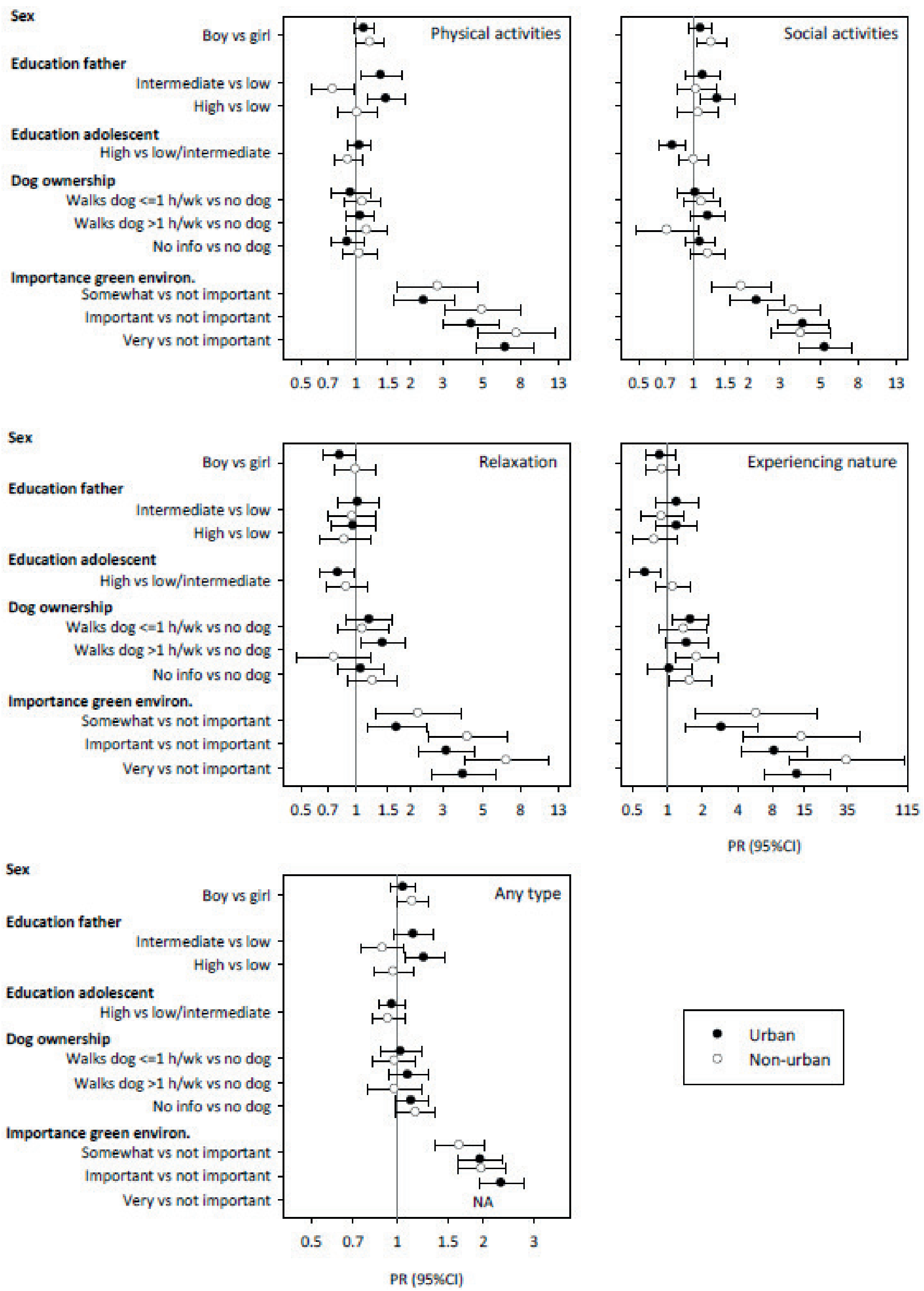


Figure 2. Predictors associated with visiting green space (yes/no) stratified by level of urbanization from multivariable log-binomial regression analysis. The prevalence ratios are adjusted for all variables presented in this figure. Note: The level of urbanization is divided into two categories: urban (≥1000 addresses per km^2) and non-urban (<1000 addresses per km^2).

Discussion

Main findings

This study found that in the Netherlands 53% of adolescents aged 17 years visited a green space at least once a week in summer. Adolescents reported visiting green space mostly for physical activities and social activities and less often for relaxation and to experience nature and quietness. The strongest predictor of green space visits in adolescents was the perceived importance of a green environment. Boys and adolescents with highly educated fathers visited green spaces more often for physical and social activities. Adolescents who own a dog visited green spaces more often to experience nature and quietness. The frequency of green space visits was not significantly associated with the objectively measured quantity of residential green space.

Comparison with other studies

Previous studies in children and adolescents have focused on the frequency and predictors of park visits. To our knowledge, this is the first study that has examined the frequency and predictors of green space visits in general (not only park visits) in adolescents. Veitch et al. examined park visits of 8-16 year old children living in disadvantaged areas of Victoria, Australia (Veitch et al. 2014). In this study, 75% of the children reported visiting parks. Among these children, 37% visited their ‘usual park’ at least once a week and 69% at least several times per month (Veitch et al. 2014). Another study found in California that 78% of adolescents aged 12-17 years reported that they visited a park in the past 30 days (Babey et al. 2015). Flowers et al. examined 2079 working age adults in the United Kingdom and found that 68% of participants visited the green space closest to their home at least a few times a month (Flowers et al. 2016).

The present study showed that adolescents who own a dog visited green spaces more often to experience nature and quietness. Our results are in line with previous research that has shown that dog walkers are frequent users of green space (Lachowycz and Jones 2013). We found that the perceived importance of a green environment was the strongest predictor of green space visits in adolescents. The frequency of green space visits was not associated with the objectively measured quantity of residential green space.

Our results are in line with a study by Flowers et al. that has shown that subjective predictors, such as nature relatedness (individual levels of connectedness with the natural world), are associated with the use of local green space in adults (Flowers et al. 2016). That study also found that the objectively measured percentage of local green spaces was not associated with the use of local green space (Flowers et al. 2016). Our findings are also consistent with a study that showed that the number of parks within a 1 mile radius around the adolescents’ homes was not associated with adolescents’ park use for physical activity (Ries et al. 2009).

In contrast, a study that examined 135 low- to middle-income children aged 8-14 years in Southern California found that children used neighborhood parks more often when parks were closer to the children’s homes (Dunton et al. 2014). The discrepancy between the current study and the study in Southern California may be due to differences in study populations: our study population was on average 17.8 years old and mainly consisted of middle and highly educated families. Furthermore, park use was measured differently in the two studies. In the Californian study, park use of participants was measured by GPS over a seven-day period while the present study used questionnaires to assess the frequency of green space visits. Our results are also not consistent with two studies that examined green space visits in adults. Giles-Corti et al. showed that the likelihood of using public open spaces increased with increasing levels of access to public open spaces in 1803 adults in Australia (Giles-Corti et al. 2005). Another study in the United States found that residents living closer to parks had a higher number of weekly park visits (Sturm and Cohen 2014).

Interpretation and implications of findings

We found that adolescents with fathers who are highly educated were more likely to visit green spaces at least once a week for physical and social activities and any type of activity. In contrast, highly educated adolescents were less likely to visit green spaces for social activities and relaxation than adolescents with a low/intermediate level of education. Maternal level of education was not associated with green space visits in adolescents. The educational level of the mother, father and adolescent may be indicators of different constructs. Paternal level of education tends to be associated with family income and standard of living, whereas the educational level of the adolescent is more likely to be an indicator of the attitudes, preferences and behaviors of his/her peer group. Maternal level of education may be an indicator of family lifestyle and health related behaviors. This may explain the discrepancy between the associations of paternal level of education, maternal level of education and the educational level of the adolescent.

The present study showed that the perceived importance of a green environment was the strongest predictor of green space visits in adolescents, suggesting that it is the adolescents' attitude towards a green environment that impacts green space visits. The frequency of green space visits was not associated with the objectively measured quantity of residential green space. For adolescents, other environmental attributes may influence the frequency of green space visits, like the quality of green space. No information on the quality of green space was available in the present study. Other explanations for the lack of an association between green space visits and the distance to the nearest park are the relatively short distances from the homes to parks and the frequent use of bicycles in our study population. Nearly 80% of the adolescents had a park within 1000 m of their homes. In the Netherlands, teenagers bike on average 2000 km per year (Centraal Bureau voor de Statistiek 2015). In other words: parks were generally available and accessible (by bike) for our study population. It is therefore possible that the adolescents' attitudes towards green space (i.e. did the adolescents *want* to visit a green space?) influenced the frequency of green space visits more than the actual distance to residential green space.

The NDVI also includes street greenery and private green property (such as gardens), which are not included in our definition of green space visits. This may explain the absence of an association between the average NDVI in several buffers and the frequency of green space visits in our study. However, we also found no relation between the percentages of urban, agricultural and natural green spaces with the frequency of green space visits. These percentages of green space are based on Top10NL, which does not include street greenery and private green space.

In the present study, adolescents reported how often they *intentionally* visit green spaces for specific purposes. We did not find an association between the objectively measured quantity of residential green space and visiting green spaces for physical activities. However, when the quantity of residential green space is higher, adolescents may use active modes of travel instead of passive modes of travel. The quantity of residential green space could therefore influence physical activity levels in adolescents.

Our finding that the quantity of residential green space was not associated with green space visits may indicate that self-selection bias, i.e. individuals choose to reside in neighborhoods that align with their preferences for green space visits, does not play a critical role in studies examining the health effects of green space in adolescents. Our findings may also have implications for the interpretation of studies examining the health effects of green space. Those studies mostly use objective measures to assess surrounding greenness, such as the NDVI, as a proxy for greenness exposure. In those studies, there is no information on the actual green space visits by the study participants. Yet, some proposed pathways through which green space may affect health require actual green space visits (Hartig et al. 2014). Our results suggest that the quantity of residential green space as measured by the NDVI or land-use maps may not be a suitable proxy for visiting green space in adolescents because the quantity of residential green space was not associated with the frequency of green space visits. It is therefore likely that pathways that do not require actual green space visits are involved in the associations between objectively measured green space and health in adolescents that have been reported in the literature.

There is a possibility of reverse causation in our study: It is unclear whether the perceived importance of a green environment actually causes a higher frequency of green space visits, or whether a higher frequency of green space visits influences adolescents' attitudes towards a green environment. However, our finding that the perceived importance of a green environment was strongly associated with the frequency of green space visits may be relevant for public health policy. It indicates that not only the availability of residential green space, but also attitudes towards green space might be relevant targets for public health strategies. We were not able to examine the predictors of the perceived importance of a green environment, i.e. environmental attitudes. Future epidemiological studies are needed to explore the predictors of pro-environmental attitudes, so that public health strategies to promote such attitudes could be implemented.

Strengths and limitations

To our knowledge, this is the first study that has examined the perceived importance of a green environment as a predictor of green space visits in adolescents. Furthermore, we included several objective measures (the average NDVI, the percentage of urban, agricultural and natural green space and the distance to the nearest park) in several buffers to assess the quantity of residential green space in addition to perceived neighborhood greenness in the analyses.

However, this study has some limitations. The frequency of green space visits was self-reported and not objectively measured by, for example, GPS devices. We used the following question to assess the frequency of green space visits: "How often do you intentionally go to a green environment (not your own garden)?" No definition of 'a green environment' was given to the study participants. It is possible that the adolescents interpreted this term in different ways. For example, some, but not all adolescents may have considered sports fields as green spaces. Since there is no universally accepted definition of green space, it is not possible to assess whether this has resulted in an over- or underestimation of the frequency of green space visits. The lack of a definition of 'a green environment' may have resulted in differences in the reported frequencies of green space visits between adolescents that are no actual differences but caused by a different interpretation of the term 'green environment'.

Furthermore, information about the quality of green space was unavailable in the present study. Both perceived and objective quality of green space may be associated with the frequency of green space visits (Flowers et al. 2016; Lee and Maheswaran 2011; Ries et al. 2009).

Of the baseline PIAMA study population, 53% completed the questionnaire at the age of 17 years. There was selective loss to follow-up of children with lower paternal and maternal education (Wijga et al. 2014). This loss to follow-up may have influenced our observed frequencies of green space visits, since a higher level of paternal education was associated with more frequent green space visits in our study. However, we assume that the associations between potential predictors of green space visits and the frequency of green space visits would not be different in the general population of Dutch adolescents.

Our study population mainly consisted of adolescents who live in a house with a garden, which is similar to the general Dutch population (Ministerie van Binnenlandse Zaken en Koninkrijksrelaties 2013). People who live in a house without a garden may visit green spaces more often. The results of our study may therefore not be generalizable to adolescents in other countries, where the percentage of homes with a garden is lower.

The present study examined the frequency and predictors of green space visits as reported among adolescents aged 17 years. Future studies are needed to assess these associations in other age groups as well.

Conclusion

This study found that more than half of the adolescents visited a green space at least once a week in summer, mostly for physical and social activities. The strongest predictor of green space visits among adolescents was the perceived importance of a green environment. The objectively measured quantity of residential green space was not associated with green space visits. Our results suggest that subjective variables are stronger predictors of green space visits than the objectively measured quantity of residential green space.

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Supplemental material

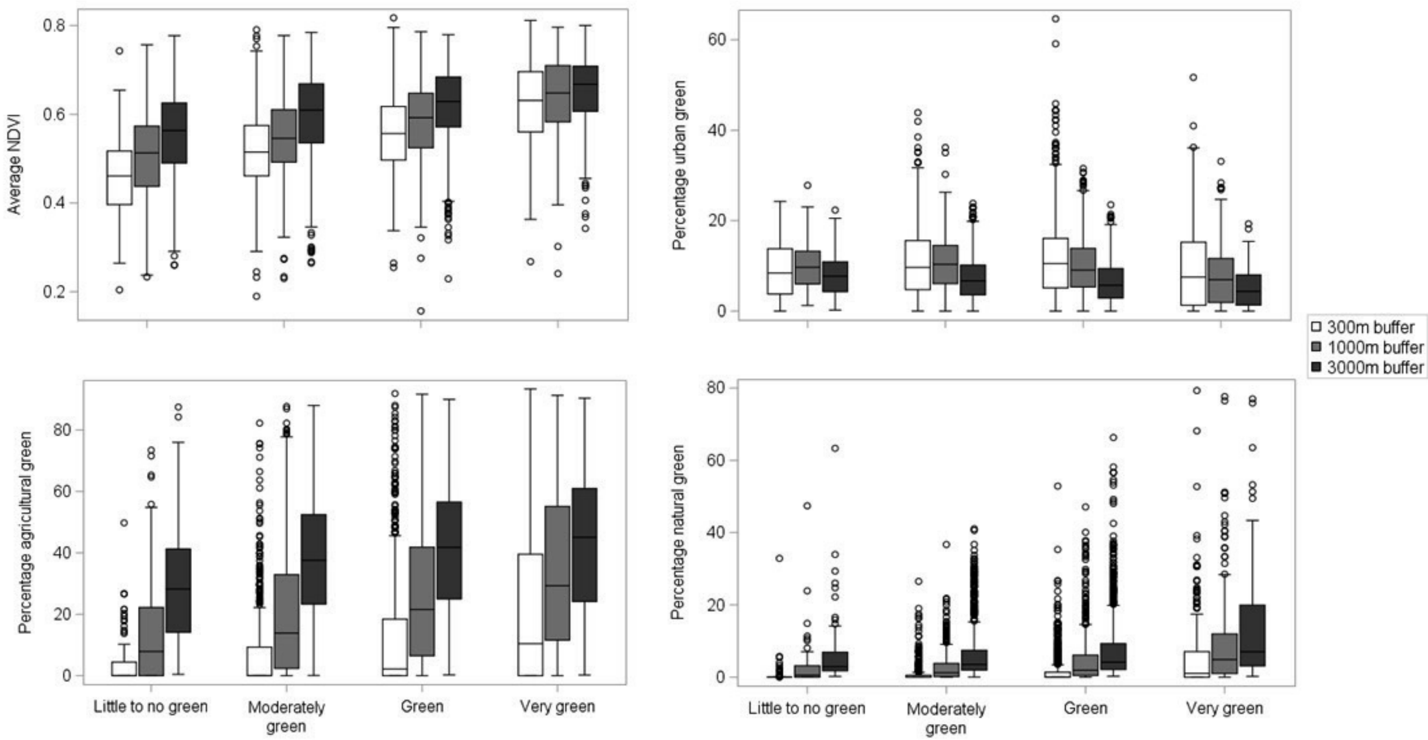

Figure S1. Boxplots of the average NDVI and percentage of urban, agricultural and natural green space stratified by 'perceived neighborhood greenness'. The length of the box represents the interquartile range and the horizontal line in the box interior represents the group median. Outliers are indicated by circles.

Table S1. Spearman correlations between the average NDVI and percentages of urban, agricultural and natural green spaces in buffers of 100m, 300m, 500m, 1000m and 3000m.

		Urban green					Agricultural green					Natural green					NDVI				
		100	**300**	**500**	**1000**	**3000**	**100**	**300**	**500**	**1000**	**3000**	**100**	**300**	**500**	**1000**	**3000**	**100**	**300**	**500**	**1000**	**3000**
Urban green	**100**	1.00	0.63	0.51	0.34	0.14	-0.27	-0.20	-0.17	-0.13	-0.02	-0.20	-0.17	-0.11	-0.07	-0.07	0.16	0.02	-0.03	-0.06	-0.03
	300		1.00	0.88	0.64	0.37	-0.46	-0.44	-0.41	-0.36	-0.20	-0.31	-0.31	-0.25	-0.17	-0.10	-0.04	-0.03	-0.11	-0.19	-0.16
	500			1.00	0.82	0.52	-0.51	-0.57	-0.56	-0.50	-0.32	-0.34	-0.39	-0.35	-0.24	-0.12	-0.11	-0.13	-0.18	-0.26	-0.23
	1000				1.00	0.75	-0.50	-0.65	-0.71	-0.71	-0.52	-0.33	-0.44	-0.45	-0.36	-0.14	-0.20	-0.26	-0.32	-0.38	-0.34
	3000					1.00	-0.40	-0.58	-0.66	-0.74	-0.76	-0.27	-0.39	-0.42	-0.37	-0.19	-0.31	-0.38	-0.43	-0.50	-0.55
Agricultural green	**100**						1.00	0.74	0.66	0.56	0.39	0.56	0.51	0.40	0.25	0.07	0.47	0.50	0.48	0.43	0.29
	300							1.00	0.93	0.80	0.56	0.45	0.65	0.60	0.40	0.07	0.40	0.55	0.59	0.56	0.36
	500								1.00	0.91	0.66	0.40	0.59	0.62	0.45	0.07	0.39	0.54	0.62	0.63	0.42
	1000									1.00	0.81	0.32	0.46	0.51	0.41	0.04	0.38	0.50	0.59	0.68	0.50
	3000										1.00	0.20	0.26	0.27	0.19	-0.07	0.33	0.40	0.46	0.54	0.61
Natural green	**100**											1.00	0.55	0.43	0.30	0.15	0.39	0.43	0.39	0.32	0.22
	300												1.00	0.82	0.61	0.30	0.40	0.54	0.56	0.49	0.31
	500													1.00	0.80	0.38	0.40	0.52	0.59	0.56	0.34
	1000														1.00	0.58	0.36	0.45	0.52	0.59	0.41
	3000															1.00	0.26	0.29	0.31	0.36	0.48
NDVI	**100**																1.00	0.83	0.73	0.62	0.49
	300																	1.00	0.93	0.77	0.57
	500																		1.00	0.89	0.63
	1000																			1.00	0.76
	3000																				1.00

Abbreviations: NDVI = normalized difference vegetation index

Table S2. Unadjusted associations between potential predictors of green space visits and visiting green space at least once a week (yes/no).

Predictor	Physical activities	Social activities	Relaxation	Experiencing nature and quietness	Any type of activity
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Sex					
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	1.17 (1.04, 1.31)	1.08 (0.96, 1.23)	0.72 (0.61, 0.85)	0.83 (0.66, 1.05)	1.06 (0.97, 1.15)
Maternal level of education					
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.01 (0.84, 1.21)	1.01 (0.84, 1.20)	0.90 (0.72, 1.11)	1.13 (0.80, 1.61)	0.96 (0.85, 1.09)
High	1.33 (1.12, 1.59)	1.09 (0.91, 1.30)	0.79 (0.64, 0.99)	1.30 (0.92, 1.83)	1.06 (0.94, 1.19)
Paternal level of education					
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.24 (1.02, 1.50)	1.15 (0.96, 1.39)	0.96 (0.77, 1.19)	1.02 (0.74, 1.41)	1.05 (0.92, 1.19)
High	1.58 (1.32, 1.89)	1.22 (1.03, 1.46)	0.88 (0.71, 1.08)	1.06 (0.78, 1.44)	1.16 (1.03, 1.30)
Educational level of adolescent					
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.20 (1.07, 1.35)	0.86 (0.76, 0.98)	0.83 (0.71, 0.98)	0.91 (0.72, 1.14)	1.01 (0.93, 1.10)
Neighborhood SES [a,b]	1.03 (0.95, 1.12)	1.05 (0.97, 1.14)	0.99 (0.89, 1.10)	0.96 (0.83, 1.11)	1.03 (0.98, 1.09)
Urbanization					
≥ 2500 addresses per km^2	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1500 - 2500 addresses per km^2	0.98 (0.78, 1.22)	1.14 (0.88, 1.46)	1.14 (0.81, 1.60)	1.27 (0.77, 2.11)	1.09 (0.92, 1.30)
1000 - 1500 addresses per km^2	0.84 (0.66, 1.08)	0.95 (0.72, 1.25)	1.10 (0.77, 1.58)	1.21 (0.71, 2.07)	0.96 (0.80, 1.16)
500 - 1000 addresses per km^2	0.96 (0.76, 1.21)	1.12 (0.86, 1.46)	1.17 (0.82, 1.65)	1.25 (0.74, 2.11)	1.12 (0.94, 1.34)
< 500 addresses per km^2	0.94 (0.73, 1.20)	1.05 (0.80, 1.40)	1.10 (0.76, 1.60)	1.44 (0.84, 2.46)	1.04 (0.86, 1.26)
Owning a dog					
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	0.92 (0.77, 1.11)	1.10 (0.92, 1.31)	1.16 (0.92, 1.47)	1.42 (1.03, 1.95)	0.98 (0.86, 1.12)
Owns a dog, and walks the dog > 1 hour per week	1.22 (1.01, 1.46)	1.06 (0.85, 1.32)	1.32 (1.02, 1.71)	1.80 (1.29, 2.52)	1.08 (0.94, 1.25)
No information available about dog ownership	0.97 (0.81, 1.16)	1.19 (1.01, 1.41)	1.23 (0.98, 1.54)	1.40 (1.01, 1.92)	1.10 (0.98, 1.24)

Importance of a green environment					
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	2.54 (1.86 - 3.47)	1.99 (1.55 - 2.56)	1.84 (1.35 - 2.51)	3.55 (1.94 - 6.51)	1.82 (1.59 - 2.07)
Important	4.64 (3.47 - 6.20)	3.74 (2.97 - 4.71)	3.54 (2.66 - 4.72)	9.66 (5.50 - 16.94)	2.17 (1.90 - 2.47)
Very important	7.35 (5.50 - 9.82)	4.93 (3.84 - 6.32)	4.96 (3.60 - 6.83)	18.01 (10.25 - 31.64)	N/A
Perceived neighborhood greenness					
Little to no green	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Moderately green	1.06 (0.76, 1.47)	0.93 (0.69, 1.26)	0.95 (0.64, 1.41)	0.96 (0.53, 1.75)	1.02 (0.82, 1.27)
Green	1.36 (0.99, 1.87)	1.08 (0.80, 1.45)	1.10 (0.74, 1.61)	1.19 (0.66, 2.13)	1.15 (0.93, 1.42)
Very green	1.45 (1.04, 2.03)	1.17 (0.86, 1.61)	1.25 (0.83, 1.90)	1.81 (0.99, 3.30)	1.21 (0.97, 1.52)
Distance from home to the nearest park					
≤ 300m	0.97 (0.82, 1.14)	1.12 (0.94, 1.34)	1.09 (0.86, 1.36)	0.80 (0.59, 1.09)	1.03 (0.91, 1.16)
300 – 1000m	1.01 (0.86, 1.17)	1.10 (0.93, 1.30)	1.10 (0.89, 1.37)	0.92 (0.69, 1.22)	1.05 (0.94, 1.18)
> 1000m	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Average NDVI in 300m buffer [b]	1.04 (0.96, 1.12)	1.00 (0.92, 1.09)	0.99 (0.89, 1.10)	1.27 (1.09, 1.49)	1.02 (0.96, 1.08)
Average NDVI in 1000m buffer [b]	1.04 (0.96, 1.13)	0.99 (0.91, 1.07)	0.95 (0.85, 1.06)	1.15 (0.98, 1.35)	1.02 (0.96, 1.08)
Average NDVI in 3000m buffer [b]	0.99 (0.91, 1.07)	0.94 (0.86, 1.02)	0.92 (0.82, 1.02)	1.11 (0.94, 1.31)	0.99 (0.93, 1.05)
Percentage urban green in 300m buffer [b]	1.03 (0.95, 1.11)	1.06 (0.98, 1.15)	1.07 (0.97, 1.19)	0.97 (0.84, 1.14)	1.02 (0.96, 1.07)
Percentage urban green in 1000m buffer [b]	1.03 (0.95, 1.12)	1.02 (0.94, 1.12)	1.05 (0.94, 1.17)	0.98 (0.84, 1.15)	1.01 (0.95, 1.07)
Percentage urban green in 3000m buffer [b]	1.05 (0.96, 1.15)	1.04 (0.95, 1.14)	0.96 (0.85, 1.09)	0.88 (0.73, 1.05)	1.02 (0.96, 1.09)
Percentage agricultural green in 300m buffer [b]	0.97 (0.92, 1.02)	0.97 (0.92, 1.03)	0.98 (0.91, 1.05)	1.06 (0.97, 1.16)	0.99 (0.95, 1.02)
Percentage agricultural green in 1000m buffer [b]	0.96 (0.88, 1.05)	0.97 (0.89, 1.07)	0.97 (0.85, 1.09)	1.07 (0.90, 1.27)	0.99 (0.93, 1.05)
Percentage agricultural green in 3000m buffer [b]	0.94 (0.86, 1.03)	0.97 (0.88, 1.07)	1.02 (0.90, 1.15)	1.05 (0.88, 1.25)	0.98 (0.92, 1.05)
Natural green in 300m buffer					
No	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	1.04 (0.92, 1.17)	1.02 (0.90, 1.16)	0.98 (0.83, 1.15)	1.29 (1.02, 1.62)	1.05 (0.97, 1.14)
Percentage natural green in 1000m buffer [b]	1.04 (1.01, 1.08)	1.01 (0.96, 1.05)	1.00 (0.94, 1.06)	1.11 (1.05, 1.17)	1.02 (1.00, 1.04)
Percentage natural green in 3000m buffer [b]	1.02 (0.98, 1.07)	0.97 (0.92, 1.02)	0.96 (0.90, 1.03)	1.10 (1.02, 1.18)	1.00 (0.96, 1.03)

Abbreviations: PR = prevalence ratio; CI = confidence interval; SES = socioeconomic status; NDVI = normalized difference vegetation index. Results are derived from log-binomial regression analysis. [a] A higher score indicates a higher SES. [b] PRs are shown for an interquartile range increase.

Table S3. Predictors associated with visiting green spaces at least once a week (yes/no) from multivariable regression analysis with the addition of the average NDVI in buffers of 300m and 3000m.

Predictor	Physical activities	Social activities	Relaxation	Experiencing nature and quietness	Any type of activity
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Sex					
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	1.12 (1.01, 1.24)	1.15 (1.03, 1.29)	0.88 (0.75, 1.04)	0.86 (0.70, 1.06)	1.07 (0.99, 1.15)
Paternal level of education					
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.09 (0.92, 1.30)	1.09 (0.92, 1.29)	1.02 (0.83, 1.24)	1.06 (0.78, 1.43)	1.03 (0.92, 1.16)
High	1.26 (1.06, 1.49)	1.22 (1.03, 1.44)	0.93 (0.76, 1.15)	0.98 (0.72, 1.32)	1.13 (1.01, 1.26)
Educational level of adolescent					
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.02 (0.92, 1.14)	0.85 (0.75, 0.96)	0.84 (0.71, 0.99)	0.83 (0.66, 1.04)	0.96 (0.88, 1.04)
Owning a dog					
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	1.02 (0.86, 1.21)	1.07 (0.91, 1.26)	1.16 (0.93, 1.45)	1.42 (1.05, 1.91)	1.01 (0.90, 1.14)
Owns a dog, and walks the dog > 1 hour per week	1.09 (0.94, 1.26)	1.04 (0.86, 1.27)	1.15 (0.90, 1.46)	1.64 (1.21, 2.22)	1.05 (0.93, 1.20)
No information available about dog ownership	0.96 (0.82, 1.12)	1.17 (1.01, 1.34)	1.16 (0.94, 1.43)	1.25 (0.93, 1.69)	1.12 (1.01, 1.24)
Importance of a green environment					
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	2.52 (1.85, 3.44)	2.04 (1.59, 2.61)	1.85 (1.35, 2.53)	3.51 (1.91, 6.44)	1.82 (1.60, 2.08)
Important	4.54 (3.40, 6.07)	3.79 (3.01, 4.78)	3.50 (2.62, 4.68)	9.41 (5.36, 16.53)	2.15 (1.89, 2.45)
Very important	6.83 (5.09, 9.15)	4.80 (3.75, 6.14)	4.84 (3.51, 6.66)	18.45 (10.50, 32.41)	N/A
Average NDVI in 300m buffer [a]	1.03 (0.95, 1.12)	1.00 (0.91, 1.09)	1.01 (0.89, 1.14)	1.13 (0.95, 1.34)	1.02 (0.96, 1.09)
Average NDVI in 3000m buffer [a]	0.94 (0.86, 1.02)	0.94 (0.85, 1.04)	0.92 (0.81, 1.04)	0.98 (0.82, 1.18)	0.97 (0.91, 1.03)

Abbreviations: PR = prevalence ratio; CI = confidence interval; NDVI = normalized difference vegetation index. Results are derived from log-binomial regression analysis. The prevalence ratios are adjusted for all variables presented in this table. Predictors that are included in at least one of the five outcome-specific models that best fit the data and the average NDVI in buffers of 300m and 3000m are presented.

[a] PRs are shown for an interquartile range increase.

Table S4. Predictors associated with visiting green spaces for physical activities in five categories from multivariable regression analysis.

Predictor	Frequency of green space visits			
	Less than once a month vs. never	1-3 times a month vs. never	Once a week vs. never	More than once a week vs. never
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex				
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	0.92 (0.68, 1.23)	0.95 (0.70, 1.29)	1.31 (0.95, 1.80)	1.50 (1.07, 2.10)
Paternal level of education				
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.25 (0.85, 1.83)	1.48 (0.99, 2.21)	1.75 (1.12, 2.74)	1.24 (0.77, 1.98)
High	1.17 (0.79, 1.72)	1.25 (0.83, 1.89)	1.87 (1.20, 2.92)	1.88 (1.19, 2.98)
Educational level of adolescent				
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.35 (0.98, 1.84)	1.54 (1.11, 2.13)	1.76 (1.25, 2.47)	1.11 (0.78, 1.59)
Owning a dog				
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	0.54 (0.36, 0.82)	0.53 (0.34, 0.82)	0.65 (0.41, 1.02)	0.64 (0.39, 1.03)
Owns a dog, and walks the dog > 1 hour per week	0.60 (0.33, 1.06)	0.96 (0.56, 1.65)	1.08 (0.62, 1.88)	1.17 (0.66, 2.07)
No information available about dog ownership	1.05 (0.69, 1.59)	0.84 (0.54, 1.32)	0.93 (0.58, 1.49)	0.94 (0.57, 1.54)
Importance of a green environment				
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	3.81 (2.70, 5.36)	6.49 (4.30, 9.78)	8.26 (5.03, 13.58)	5.97 (3.36, 10.59)
Important	4.76 (3.20, 7.07)	16.13 (10.42, 24.97)	29.21 (17.56, 48.58)	31.93 (18.26, 55.83)
Very important	2.46 (0.94, 6.41)	14.61 (6.38, 33.44)	41.35 (17.93, 95.36)	142.73 (62.16, 327.76)

Abbreviations: OR = odds ratio; CI = confidence interval.

Results are derived from polytomous logistic regression analysis. The odds ratios are adjusted for all variables presented in this table.

Table S5. Predictors associated with visiting green spaces for social activities in five categories from multivariable regression analysis.

Predictor	Frequency of green space visits			
	Less than once a month vs. never	1-3 times a month vs. never	Once a week vs. never	More than once a week vs. never
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex				
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	0.88 (0.64, 1.20)	0.68 (0.50, 0.93)	1.11 (0.79, 1.56)	1.05 (0.74, 1.49)
Paternal level of education				
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.08 (0.72, 1.60)	1.50 (1.0, 2.24)	1.82 (1.15, 2.87)	1.48 (0.93, 2.34)
High	1.65 (1.10, 2.49)	2.25 (1.48, 3.41)	2.67 (1.67, 4.26)	2.31 (1.45, 3.70)
Educational level of adolescent				
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.83 (1.31, 2.56)	2.20 (1.58, 3.07)	1.57 (1.09, 2.27)	1.21 (0.83, 1.77)
Owning a dog				
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	0.64 (0.40, 1.01)	0.88 (0.57, 1.37)	1.32 (0.83, 2.12)	0.82 (0.49, 1.36)
Owns a dog, and walks the dog > 1 hour per week	0.87 (0.51, 1.48)	0.85 (0.50, 1.45)	1.11 (0.63, 1.99)	0.79 (0.43, 1.45)
No information available about dog ownership	0.98 (0.63, 1.53)	0.74 (0.47, 1.18)	1.38 (0.85, 2.24)	1.07 (0.65, 1.77)
Importance of a green environment				
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	3.66 (2.56, 5.23)	7.70 (5.28, 11.22)	9.10 (5.74, 14.43)	6.72 (4.04, 11.20)
Important	2.86 (1.82, 4.48)	10.02 (6.44, 15.58)	21.60 (13.05, 35.74)	29.15 (17.25, 49.26)
Very important	0.81 (0.29, 2.31)	4.88 (2.19, 10.87)	14.05 (6.21, 31.77)	36.60 (16.77, 79.85)

Abbreviations: OR = odds ratio; CI = confidence interval.

Results are derived from polytomous logistic regression analysis. The odds ratios are adjusted for all variables presented in this table.

Table S6. Predictors associated with visiting green spaces for relaxation in five categories from multivariable regression analysis.

Predictor	Frequency of green space visits			
	Less than once a month vs. never	1-3 times a month vs. never	Once a week vs. never	More than once a week vs. never
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex				
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	0.90 (0.69, 1.18)	0.53 (0.40, 0.70)	0.60 (0.43, 0.82)	0.61 (0.42, 0.89)
Paternal level of education				
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.57 (1.10, 2.26)	1.81 (1.22, 2.69)	1.53 (1.0, 2.33)	1.45 (0.86, 2.43)
High	1.24 (0.87, 1.78)	1.80 (1.22, 2.64)	1.09 (0.71, 1.66)	1.40 (0.84, 2.32)
Educational level of adolescent				
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.07 (0.81, 1.41)	1.05 (0.79, 1.41)	0.77 (0.55, 1.08)	0.76 (0.51, 1.13)
Owning a dog				
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	0.69 (0.47, 1.03)	0.90 (0.60, 1.35)	1.16 (0.74, 1.81)	0.87 (0.50, 1.51)
Owns a dog, and walks the dog > 1 hour per week	0.84 (0.51, 1.38)	1.38 (0.85, 2.25)	1.45 (0.84, 2.50)	1.19 (0.63, 2.26)
No information available about dog ownership	0.75 (0.50, 1.11)	1.03 (0.69, 1.53)	1.16 (0.74, 1.82)	1.02 (0.60, 1.73)
Importance of a green environment				
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	3.81 (2.79, 5.20)	6.53 (4.52, 9.45)	6.04 (3.75, 9.71)	3.11 (1.73, 5.57)
Important	5.13 (3.57, 7.35)	11.42 (7.64, 17.09)	17.51 (10.77, 28.48)	13.77 (7.95, 23.86)
Very important	4.19 (2.01, 8.75)	12.19 (5.97, 24.87)	23.63 (11.02, 50.68)	32.55 (14.82, 71.48)

Abbreviations: OR = odds ratio; CI = confidence interval.

Results are derived from polytomous logistic regression analysis. The odds ratios are adjusted for all variables presented in this table.

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Table S7. Predictors associated with visiting green spaces for experiencing nature and quietness in five categories from multivariable regression analysis.

Predictor	Frequency of green space visits			
	Less than once a month vs. never	1-3 times a month vs. never	Once a week vs. never	More than once a week vs. never
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex				
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	1.00 (0.79, 1.27)	0.81 (0.61, 1.08)	0.80 (0.55, 1.16)	0.65 (0.40, 1.07)
Paternal level of education				
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.49 (1.08, 2.06)	1.45 (0.97, 2.17)	1.38 (0.83, 2.29)	1.42 (0.71, 2.86)
High	1.51 (1.09, 2.08)	1.59 (1.08, 2.36)	1.31 (0.79, 2.17)	1.46 (0.74, 2.89)
Educational level of adolescent				
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.16 (0.90, 1.48)	1.34 (1.0, 1.81)	0.88 (0.60, 1.31)	0.85 (0.50, 1.42)
Owning a dog				
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	0.60 (0.42, 0.86)	0.60 (0.39, 0.93)	1.25 (0.75, 2.07)	1.05 (0.51, 2.16)
Owns a dog, and walks the dog > 1 hour per week	1.08 (0.71, 1.65)	0.91 (0.54, 1.52)	1.65 (0.90, 3.03)	2.23 (1.08, 4.62)
No information available about dog ownership	1.09 (0.78, 1.54)	1.03 (0.68, 1.56)	1.43 (0.84, 2.42)	1.48 (0.74, 2.96)
Importance of a green environment				
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	3.49 (2.65, 4.60)	13.26 (8.20, 21.42)	10.32 (4.69, 22.71)	4.02 (1.32, 12.20)
Important	3.60 (2.63, 4.92)	24.79 (15.21, 40.42)	35.69 (16.69, 76.33)	24.28 (9.24, 63.78)
Very important	5.11 (2.99, 8.72)	39.70 (20.81, 75.72)	102.74 (43.28, 243.90)	127.05 (45.27, 356.52)

Abbreviations: OR = odds ratio; CI = confidence interval.

Results are derived from polytomous logistic regression analysis. The odds ratios are adjusted for all variables presented in this table.

Table S8. Predictors associated with visiting green spaces for any type of activity in five categories from multivariable regression analysis.

Predictor	Frequency of green space visits			
	Less than once a month vs. never	1-3 times a month vs. never	Once a week vs. never	More than once a week vs. never
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex				
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	0.79 (0.52, 1.19)	0.56 (0.38, 0.81)	0.81 (0.55, 1.20)	0.89 (0.60, 1.30)
Paternal level of education				
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.04 (0.63, 1.72)	1.61 (1.02, 2.56)	1.42 (0.89, 2.26)	1.41 (0.88, 2.25)
High	2.07 (1.19, 3.58)	2.69 (1.60, 4.51)	2.34 (1.39, 3.91)	3.08 (1.84, 5.18)
Educational level of adolescent				
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.91 (1.19, 3.06)	2.57 (1.66, 3.98)	2.21 (1.42, 3.44)	1.60 (1.03, 2.50)
Owning a dog				
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	0.67 (0.37, 1.19)	0.88 (0.53, 1.47)	0.91 (0.54, 1.54)	0.87 (0.52, 1.47)
Owns a dog, and walks the dog > 1 hour per week	0.81 (0.39, 1.68)	0.80 (0.41, 1.56)	1.03 (0.53, 2.0)	0.86 (0.44, 1.67)
No information available about dog ownership	1.37 (0.75, 2.51)	0.86 (0.48, 1.55)	1.47 (0.83, 2.61)	1.16 (0.65, 2.06)
Importance of a green environment				
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	1.72 (1.08, 2.75)	2.95 (1.90, 4.56)	5.07 (3.24, 7.93)	7.40 (4.68, 11.69)
Important	1.48 (0.75, 2.90)	4.64 (2.55, 8.44)	8.66 (4.74, 15.81)	19.15 (10.47, 35.03)

Abbreviations: OR = odds ratio; CI = confidence interval.

Results are derived from polytomous logistic regression analysis. The odds ratios are adjusted for all variables presented in this table.

Table S9. Unadjusted associations between potential predictors of green space visits and visiting green space at least once a week in winter (yes/no).

Predictor	Physical activities	Social activities	Any type of activity
	PR (95% CI)	PR (95% CI)	PR (95% CI)
Sex			
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	1.14 (0.92, 1.40)	1.70 (1.29, 2.24)	1.27 (1.06, 1.51)
Maternal level of education			
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.05 (0.76, 1.44)	1.03 (0.70, 1.52)	1.06 (0.81, 1.38)
High	1.38 (1.02, 1.87)	1.09 (0.74, 1.61)	1.23 (0.95, 1.59)
Paternal level of education			
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	0.89 (0.66, 1.21)	0.86 (0.59, 1.25)	0.92 (0.71, 1.19)
High	1.20 (0.91, 1.57)	1.03 (0.73, 1.46)	1.14 (0.90, 1.44)
Educational level of adolescent			
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.01 (0.82, 1.25)	0.58 (0.44, 0.77)	0.84 (0.70, 1.00)
Neighborhood SES [a,b]	1.12 (0.98, 1.29)	1.15 (0.96, 1.38)	1.09 (0.97, 1.23)
Urbanization			
≥ 2500 addresses per km^2	1.00 (reference)	1.00 (reference)	1.00 (reference)
1500 - 2500 addresses per km^2	1.15 (0.76, 1.73)	1.14 (0.66, 1.95)	1.22 (0.85, 1.74)
1000 - 1500 addresses per km^2	0.82 (0.52, 1.31)	0.89 (0.49, 1.60)	0.85 (0.57, 1.27)
500 - 1000 addresses per km^2	1.09 (0.71, 1.68)	1.17 (0.67, 2.04)	1.08 (0.75, 1.58)
< 500 addresses per km^2	1.18 (0.75, 1.85)	1.03 (0.56, 1.87)	1.20 (0.81, 1.77)
Owning a dog			
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	1.04 (0.76, 1.42)	1.13 (0.76, 1.68)	1.05 (0.81, 1.37)
Owns a dog, and walks the dog > 1 hour per week	1.40 (1.01, 1.95)	0.95 (0.57, 1.58)	1.21 (0.90, 1.63)
No information available about dog ownership	1.15 (0.86, 1.55)	1.51 (1.06, 2.14)	1.27 (0.99, 1.61)

Importance of a green environment			
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	2.64 (1.52, 4.59)	2.29 (1.30, 4.03)	2.58 (1.95, 3.41)
Important	6.74 (4.04, 11.23)	5.70 (3.38, 9.63)	3.52 (2.66, 4.65)
Very important	13.74 (8.11, 23.30)	9.71 (5.40, 17.46)	N/A
Perceived neighborhood greenness			
Little to no green	1.00 (reference)	1.00 (reference)	1.00 (reference)
Moderately green	1.24 (0.68, 2.27)	1.60 (0.64, 4.01)	1.25 (0.74, 2.10)
Green	1.70 (0.95, 3.04)	2.77 (1.13, 6.78)	1.80 (1.09, 2.99)
Very green	1.94 (1.05, 3.59)	2.27 (0.89, 5.80)	1.92 (1.13, 3.26)
Distance from home to the nearest park			
≤ 300m	0.99 (0.75, 1.32)	1.32 (0.90, 1.94)	1.07 (0.84, 1.37)
300 – 1000m	1.03 (0.78, 1.34)	1.21 (0.83, 1.76)	1.06 (0.84, 1.34)
> 1000m	1.00 (reference)	1.00 (reference)	1.00 (reference)
Average NDVI in 300m buffer [b]	1.06 (0.92, 1.22)	1.06 (0.88, 1.27)	1.10 (0.97, 1.23)
Average NDVI in 1000m buffer [b]	1.04 (0.90, 1.19)	0.99 (0.83, 1.20)	1.04 (0.92, 1.18)
Average NDVI in 3000m buffer [b]	0.97 (0.84, 1.12)	0.99 (0.82, 1.19)	0.99 (0.88, 1.12)
Percentage urban green in 300m buffer [b]	1.00 (0.87, 1.15)	1.16 (0.99, 1.37)	1.05 (0.93, 1.17)
Percentage urban green in 1000m buffer [b]	1.01 (0.88, 1.17)	1.05 (0.88, 1.26)	1.04 (0.92, 1.17)
Percentage urban green in 3000m buffer [b]	1.09 (0.94, 1.27)	1.08 (0.88, 1.31)	1.07 (0.94, 1.22)
Percentage agricultural green in 300m buffer [b]	0.98 (0.89, 1.07)	0.94 (0.83, 1.06)	0.99 (0.92, 1.07)
Percentage agricultural green in 1000m buffer [b]	0.89 (0.76, 1.05)	0.91 (0.73, 1.12)	0.93 (0.81, 1.06)
Percentage agricultural green in 3000m buffer [b]	0.83 (0.71, 0.98)	0.94 (0.76, 1.15)	0.89 (0.78, 1.02)
Natural green in 300m buffer			
No	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	1.01 (0.82, 1.25)	0.99 (0.76, 1.30)	1.05 (0.88, 1.25)
Percentage natural green in 1000m buffer [b]	1.11 (1.05, 1.17)	1.04 (0.95, 1.14)	1.08 (1.02, 1.14)
Percentage natural green in 3000m buffer [b]	1.09 (1.01, 1.17)	0.99 (0.89, 1.10)	1.06 (0.99, 1.13)

Abbreviations: PR = prevalence ratio; CI = confidence interval; SES = socioeconomic status; NDVI = normalized difference vegetation index.

Results are derived from Poisson regression analysis. [a] A higher score indicates a higher SES. [b] PRs are shown for an interquartile range increase.

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Table S10. Predictors associated with visiting green spaces at least once a week in winter (yes/no) from multivariable regression analysis.

Predictor	Physical activities	Social activities	Any type of activity
	PR (95% CI)	PR (95% CI)	PR (95% CI)
Sex			
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	1.17 (0.95, 1.44)	1.80 (1.36, 2.38)	1.32 (1.10, 1.58)
Educational level of adolescent			
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	0.90 (0.73, 1.11)	0.62 (0.46, 0.82)	0.78 (0.65, 0.93)
Importance of a green environment			
Not important	1.00 (reference)	1.00 (reference)	1.00 (reference)
Somewhat important	2.69 (1.55, 4.68)	2.48 (1.41, 4.37)	2.58 (1.95, 3.41)
Important	6.74 (4.04, 11.26)	6.00 (3.54, 10.17)	3.53 (2.66, 4.69)
Very important	13.47 (7.92, 22.92)	10.41 (5.76, 18.82)	N/A
Perceived neighborhood greenness			
Little to no green	1.00 (reference)	1.00 (reference)	1.00 (reference)
Moderately green	1.25 (0.69, 2.28)	1.56 (0.62, 3.91)	1.34 (0.79, 2.25)
Green	1.55 (0.86, 2.78)	2.57 (1.04, 6.33)	1.78 (1.07, 2.96)
Very green	1.45 (0.78, 2.70)	1.76 (0.68, 4.56)	1.71 (1.00, 2.93)
Percentage agricultural green in 3000m buffer [a]	0.85 (0.72, 1.00)	0.91 (0.74, 1.12)	0.87 (0.76, 1.00)

Abbreviations: PR = prevalence ratio; CI = confidence interval.

Results are derived from Poisson regression analysis. The prevalence ratios are adjusted for all variables presented in this table.

Predictors that are included in at least one of the three outcome-specific models that best fit the data are presented.

[a] PRs are shown for an interquartile range increase.

Table S11. Predictors associated with visiting green spaces at least once a week (yes/no) from multivariable regression analysis without the predictor 'perceived importance of a green environment'.

Predictor	Physical activities	Social activities	Relaxation	Experiencing nature and quietness	Any type of activity
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Sex					
Girl	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Boy	1.14 (1.01, 1.28)	1.06 (0.94, 1.20)	0.72 (0.61, 0.85)	0.82 (0.65, 1.03)	1.05 (0.96, 1.14)
Paternal level of education					
Low	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate	1.21 (0.99, 1.47)	1.18 (0.98, 1.42)	1.00 (0.80, 1.24)	1.07 (0.77, 1.48)	1.04 (0.92, 1.18)
High	1.48 (1.22, 1.78)	1.32 (1.10, 1.59)	0.96 (0.77, 1.20)	1.12 (0.81, 1.54)	1.15 (1.02, 1.30)
Educational level of adolescent					
Low/intermediate	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High	1.09 (0.96, 1.23)	0.82 (0.71, 0.93)	0.84 (0.71, 1.00)	0.91 (0.71, 1.16)	0.98 (0.89, 1.07)
Owning a dog					
Does not own a dog	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Owns a dog, and walks the dog ≤ 1 hour per week	0.97 (0.80, 1.16)	1.07 (0.89, 1.28)	1.08 (0.86, 1.37)	1.33 (0.96, 1.83)	0.98 (0.86, 1.11)
Owns a dog, and walks the dog > 1 hour per week	1.26 (1.06, 1.51)	1.04 (0.84, 1.30)	1.24 (0.96, 1.60)	1.76 (1.26, 2.46)	1.08 (0.94, 1.25)
No information available about dog ownership	1.01 (0.85, 1.21)	1.18 (1.00, 1.40)	1.17 (0.94, 1.47)	1.35 (0.98, 1.86)	1.11 (0.99, 1.25)
Perceived neighborhood greenness					
Little to no green	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Moderately green	1.07 (0.77, 1.48)	0.94 (0.70, 1.28)	0.91 (0.62, 1.36)	0.93 (0.51, 1.70)	1.03 (0.83, 1.29)
Green	1.33 (0.97, 1.82)	1.07 (0.80, 1.43)	1.07 (0.73, 1.57)	1.16 (0.65, 2.08)	1.15 (0.93, 1.42)
Very green	1.40 (1.00, 1.94)	1.16 (0.85, 1.58)	1.23 (0.82, 1.86)	1.75 (0.96, 3.19)	1.21 (0.96, 1.51)

Abbreviations: PR = prevalence ratio; CI = confidence interval.

Results are derived from log-binomial regression analysis. The prevalence ratios are adjusted for all variables presented in this table.

Predictors that are included in at least one of the five outcome-specific models that best fit the data are presented.

Chapter 3

The associations of air pollution, traffic noise and green space with overweight throughout childhood: the PIAMA birth cohort study

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Environ Res. 2019 Feb;169:348-356. doi: 10.1016/j.envres.2018.11.026

Abstract

Background: Air pollution, traffic noise and absence of green space may contribute to the development of overweight in children.

Objectives: To investigate the combined associations of air pollution, traffic noise and green space with overweight throughout childhood.

Methods: We used data for 3680 participants of the Dutch PIAMA birth cohort. We estimated exposure to air pollution, traffic noise and green space (i.e. the average Normalized Difference Vegetation Index (NDVI) and percentages of green space in circular buffers of 300m and 3000m) at the children's home addresses at the time of parental reported weight and height measurements. Associations of these exposures with overweight from age 3 to 17 years were analyzed by generalized linear mixed models, adjusting for potential confounders. Odds ratios (OR's) are presented for an interquartile range increase in exposure.

Results: The odds of being overweight increased with increasing exposure to NO_2 (adjusted OR 1.40 [95% confidence interval (CI) 1.12 - 1.74] per 8.90 μg/m^3) and tended to decrease with increasing exposure to green space in a 3000m buffer (adjusted OR 0.86 [95% CI 0.71 - 1.04] per 0.13 increase in the NDVI; adjusted OR 0.86 [95% CI 0.71 - 1.03] per 29.5% increase in the total percentage of green space). After adjustment for NO_2, the associations with green space in a 3000m buffer weakened. No associations of traffic noise with overweight throughout childhood were found. In children living in an urban area, living further away from a park was associated with a lower odds of being overweight (adjusted OR 0.67 [95% CI 0.52 - 0.85] per 359.6m).

Conclusions: Exposure to traffic-related air pollution, but not traffic noise or green space, may contribute to childhood overweight. Future studies examining the associations of green space with childhood overweight should account for air pollution exposure.

Introduction

Childhood overweight and obesity have emerged as major global public health problems. Air pollution, traffic noise and absence of green space may contribute to the development of overweight in children. Traffic-related air pollution may affect children's BMI through changes in basal metabolism due to effects on mitochondria and brown adipose tissue, or through pro-inflammatory central nervous system effects on appetite control (McConnell et al., 2016). Air pollution may also result in metabolic dysfunction via increased oxidative stress and adipose tissue inflammation and decreased glucose utilization in skeletal muscle (An, Ji, Yan, & Guan, 2018). Studies examining the associations of air pollution with children's weight have shown mixed results (An et al., 2018).

Traffic noise has been hypothesized to affect body composition through stress and sleep disturbances (Babisch, 2003; Pirrera, De Valck, & Cluydts, 2010). Studies in adults have found associations of exposure to road traffic and railway noise with markers of obesity (Christensen et al., 2015; Christensen, Raaschou-Nielsen, et al., 2016; Pyko et al., 2015). On the contrary, a longitudinal study in children reported that residential exposure to road and railway traffic noise during pregnancy and early childhood were not significantly associated with a higher risk of overweight at seven years of age (Christensen, Hjortebjerg, et al., 2016).

Green space has been hypothesized to have a beneficial effect on children's BMI by increasing physical activity levels or through stress reduction (Hartig, Mitchell, de Vries, & Frumkin, 2014; James, Banay, Hart, & Laden, 2015). However, there is no consistent evidence for an association between residential exposure to green space and children's weight status (James et al., 2015; Lachowycz & Jones, 2011; Sanders, Feng, Fahey, Lonsdale, & Astell-Burt, 2015).

Higher levels of green space are associated with lower concentrations of air pollution and lower levels of traffic noise (Hystad et al., 2014). Air pollution and noise share road traffic as a common source (Davies, Vlaanderen, Henderson, & Brauer, 2009; Fecht et al., 2016). Since air pollution, traffic noise and green space levels are spatially correlated, it is important to examine the combined associations of these exposures with health outcomes. However, no studies have examined the combined associations of these three environmental exposures with overweight in children. The aim of the present study is therefore to investigate the individual and combined associations of air pollution, traffic noise and green space with overweight throughout childhood.

The percentage of the global population living in urban areas is projected to increase from 54% in 2015 to 60% in 2030 (World Health Organization, 2016). Because of the high urbanization, more people live in environments that are generally more polluted and less green. Since green spaces are less available in urban areas, green spaces may play a more important role for urban residents than for those living in suburban or rural areas. For these reasons, we also assessed the associations of air pollution, traffic noise and green space with overweight in children living in an urban area.

Methods

Study design and study population

We used data from the Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. Detailed descriptions of the design of the PIAMA study have been published previously (Brunekreef et al., 2002; Wijga et al., 2014). In brief, pregnant women were recruited from the general population in three different regions of the Netherlands: north, central and west. Region north is largely rural, has a lower population density and substantially lower air pollution levels as compared to regions central and west. Region west includes the city of Rotterdam. The baseline study population consisted of 3963 children born in 1996/1997. Participating parents completed questionnaires during pregnancy, at the child's ages of three months and one year, and yearly thereafter until the child was eight. When the children were 11, 14 and 17 years old, the parents and children received separate questionnaires. The questionnaires comprised questions on growth and development, socio-demographic and lifestyle characteristics. The study protocol was approved by the medical ethical committees of the participating institutes and all parents gave written informed consent.

Assessment of overweight

Data on weight, height and the dates of the measurements were derived from the parental questionnaires. Parents were asked to report their child's weight and height measured by a medical professional, if this measurement took place within the last three months. Otherwise, parents were requested to measure their child's weight and height without shoes and heavy clothes themselves and to report it.

To facilitate longitudinal data analysis, weight and height measurements were grouped based on the exact age at the time of the weight and height measurements. This resulted in the following age categories: 0.5 - 1.5 years, 1.5 - 2.5 years, 2.5 - 3.5 years, 3.5 - 4.5 years, 4.5 - 5.5 years, 5.5 - 6.5 years, 6.5 - 7.5 years, 7.5 - 9.5 years, 10.5 - 13.5 years, 13.5 - 16.0 years, and 16.0 - 19.0 years. We restricted the dataset to one observation per child per age category. In case of multiple observations for one age category, we selected the most complete set (of weight and height) with age as close as possible to midpoint of the age category. Only data from age 2.5 - 3.5 years onwards were included in this analysis as no definition of overweight is available before the age of two years (Cole & Lobstein, 2012).

BMI (weight (kg)/height (m)^2) was calculated from the weight and height measurements and overweight (including obesity) was defined according to age and sex-specific International Obesity Task Force cut-offs (Cole & Lobstein, 2012).

In this study, we included 3680 children for whom at least one BMI measurement was available from the age of three years until the age of 17 years.

Exposure assessment

We focused on recent exposure to air pollution, traffic noise and green space in this analysis. We estimated air pollution concentrations and traffic noise levels and assessed exposure to green space at the children's current home addresses at the time of the weight and height measurements. An overview of the residential exposures included in this study is provided in Table S1.

Air pollution. We estimated annual average air pollution concentrations with land-use regression (LUR) models that were developed within the ESCAPE project. Details of the LUR model development have been described elsewhere (Beelen et al., 2013; Eeftens et al., 2012). In brief, air pollution monitoring campaigns were performed between February 2009 and February 2010 in the Netherlands/Belgium. Nitrogen dioxide (NO_2) measurements were performed in three periods of 14 days, in the cold, warm and intermediate seasons, at 80 sites. Simultaneous measurements of particulate matter with a diameter of less than 2.5µm ($PM_{2.5}$), less than 10µm (PM_{10}), 2.5-10µm (PM_{coarse}) and $PM_{2.5}$ absorbance (a marker of black carbon) were performed at half of the sites. The three measurements were averaged after temporal adjustment using data from a continuous reference site to obtain the annual average concentrations for each site (Eeftens et al., 2012). Predictor variables on population density, traffic intensity and land-use derived from Geographic Information Systems (GIS) were used to model the spatial variation of the annual average air pollution concentrations in the Netherlands/Belgium. The performance of the LUR models was evaluated using leave-one out cross validation (R^2_{LOOCV}) and ranged from 0.60 for PM_{10} to 0.89 for $PM_{2.5}$ absorbance (Table S4). We used the regression models to estimate exposure to air pollution at all ages without back-extrapolation. In the present study, we included NO_2, $PM_{2.5}$, PM_{10} and $PM_{2.5}$ absorbance.

Traffic noise. We estimated annual average traffic noise exposure by the Standard Model Instrumentation for Noise Assessments (STAMINA), which has been developed by the Dutch National Institute for Public Health and the Environment (Schreurs, Jabben, & Verheijen, 2010). The STAMINA model implements the standard Dutch Calculation method for traffic and industrial noise and uses detailed information on the types of noise source and ground data (information regarding the ground impedance (water, grass, asphalt) and the presence of buildings). The model has a resolution of 10 x 10 m around the noise sources. At increasing distances from the noise source, the resolution gradually decreases to at most 80 x 80 m (Schreurs et al., 2010).

Daily average (Lden) and nighttime average (Lnight) road traffic and railway noise exposure were estimated for 2011. Lden is the annual average A-weighted noise level weighted with 5dB(A) extra in the evening (19.00 - 23.00) and 10dB(A) extra at night (23.00 - 07.00). Because of the high correlations between Lden and Lnight (r = 0.96 for railway noise; r = 0.99 for road traffic noise), we only used Lden in the analyses.

Green space. We used the Normalized Difference Vegetation Index (NDVI) to assess greenness levels surrounding the children's homes. The NDVI was derived from Landsat 5 Thematic Mapper (TM) data at 30 m x 30 m resolution. NDVI values range from -1 to 1, with higher values indicating more greenness (Weier & Herring, 2000). Negative values correspond to water and were set to zero. We created two maps of the Netherlands by combining cloud free images of 1) the summers of 2000 and 2002 and 2) the summer of 2010. From these maps, we calculated the average NDVI in circular buffers of 300 m and 3000 m around the children's homes for each of the two years separately.

We hypothesized that different types of green space may have different effects on children's weight. To distinguish the effects of different types of green space, we defined all green spaces within a population cluster (i.e. a locality with at least 25 predominantly residential buildings (Vliegen, van Leeuwen, & Kerkvliet, 2006)) as 'urban green space'. We classified the remaining green spaces as 'agricultural green space' (fruit or tree nurseries, arable land, grassland or orchards) or 'natural green space' (heather or forests). We used two land-use maps of the Netherlands: Top10NL and Bestand Bodemgebruik. Top10NL is a detailed land-use map of the Netherlands that, in contrast to the NDVI, does not include street greenery and private green property (such as gardens) (Kadaster, 2017). Top10NL is only available from 2012 onwards. Therefore, we used Bestand Bodemgebruik to assess the percentages of green space at the time of the weight and height measurements preceding 2012. Bestand Bodemgebruik is less detailed than Top10NL (it contains fewer land-use categories), but in contrast to Top10NL, it contains a separate category for parks defined as public green spaces that can be used for relaxation (Centraal Bureau voor de Statistiek, 2008). We assessed the total percentage of green space and percentages of urban, agricultural and natural green space in buffers of 300 m and 3000 m around the children's homes for 1996, 2006 (based on Bestand Bodemgebruik) and 2016 (based on Top10NL). With Bestand Bodemgebruik and a detailed map covering all roads and paths of the Netherlands, we estimated the distance along roads (i.e. network distance) in meters from the children's homes to the nearest park entrance.

The NDVI map (2000/2002 or 2010) and land-use map (1996, 2006 or 2016) that was closest to the date of the weight and height measurement was used to assess exposure to green space at the time of the weight and height measurements. Surrounding greenness, the percentages of green space and distance to the nearest park were determined in ArcGIS 10.2.2 (Esri, Redlands, CA, USA).

Confounders

Maternal and paternal level of education (low, intermediate, high) were obtained from the 1 year questionnaire and information on maternal smoking during pregnancy (yes/no) from the pregnancy questionnaire. Parental smoking in the child's home (yes/no) was assessed through the repeated parental questionnaires from pregnancy until age 17. We used the status scores of 4-digit postal code areas from The Netherlands Institute for Social Research (SCP) of 1998 until 2014 to assess neighborhood socio-economic status (SES). Status scores include the average income, the percentage of residents with a low income, the percentage of low educated residents and the percentage unemployed subjects in a postal code area. A higher status score indicates a higher neighborhood SES (Knol, 2012).

The prevalence of overweight is different in the three regions of the Netherlands where our study participants live (north, central and west). Moreover, region north has substantially lower air pollution levels as compared to regions central and west. We have therefore adjusted our analyses for region.

Statistical analysis

First, we used natural splines to determine the linearity of the exposure-response relationships. To test whether the goodness-of-fit of the models with splines was significantly better than the goodness-of-fit of linear models (with one degree of freedom), we used the likelihood ratio test. Since there was no evidence of non-linearity, we used exposures as continuous variables in all analyses. We then analyzed the associations of air pollution, traffic noise and green space with overweight from age 3 to 17 years with generalized linear mixed models. A random subject-specific intercept was included to account for within-subject correlation across the repeated overweight measurements. We have decided not to examine the associations of the exposures with BMI growth trajectories, since we hypothesized that recent (rather than early life) exposure to green space may be associated with children's weight by increasing physical activity levels. Moreover, age-specific estimates, obtained from mixed models with exposure-age interaction terms, provide information on whether the associations of air pollution, traffic noise and green space with overweight differ across different ages.

We specified three models with increasing level of adjustment for potential confounders. Model I was adjusted for age and sex. Model II was adjusted for age, sex, maternal and paternal level of education, maternal smoking during pregnancy, parental smoking in the child's home and neighborhood SES. Model III was additionally adjusted for region (north, central or west). Associations with the percentages of urban, agricultural and natural green space were additionally adjusted for the other types of green space in the same buffer size. We considered model III as the main model and calculated age-specific estimates for model III only. Odds ratios (OR's) are presented for an interquartile range (IQR) increase in exposure. The majority of the children (between 58 to 86 percent in the different age categories) had no natural green space in a 300 m buffer around their homes. Therefore, we created a binary variable: natural green space in a buffer of 300 m yes/no.

We have additionally assessed the associations of air pollution, traffic noise and green space with overweight in children living in an urban area (≥1500 addresses/km^2). Children who have moved from an urban area to a non-urban area (or vice versa) during the study period were excluded from these analyses (n = 736). The OR's are presented for the same increase in exposure as for the main analyses to facilitate the comparison of the results. We assessed the association between the distance to the nearest park and overweight only in children who lived in an urban area.

The statistical analyses were performed with SAS version 9.4, except the spline analyses, which we performed with R version 3.4.3 (R Core Team).

3

Results

Characteristics of the study population

The number of participants decreased over the course of the follow-up period, especially from age category 10.5 - 13.5 years onwards. To show the changes in our study population throughout the study period, characteristics of the study population for the youngest and oldest age category studied are presented in Table 1. There was a selective loss to follow-up of children with lower paternal and maternal education. Moreover, 25.9% of the children with data for the youngest age category had at least one parent who smoked, whereas this percentage was 9.0 for the children with data for the oldest age category. The prevalence of overweight children ranged from 7.9% in age category 2.5-3.5 to 11.5% in age categories 6.5-7.5 and 7.5-9.5 (Figure 1).

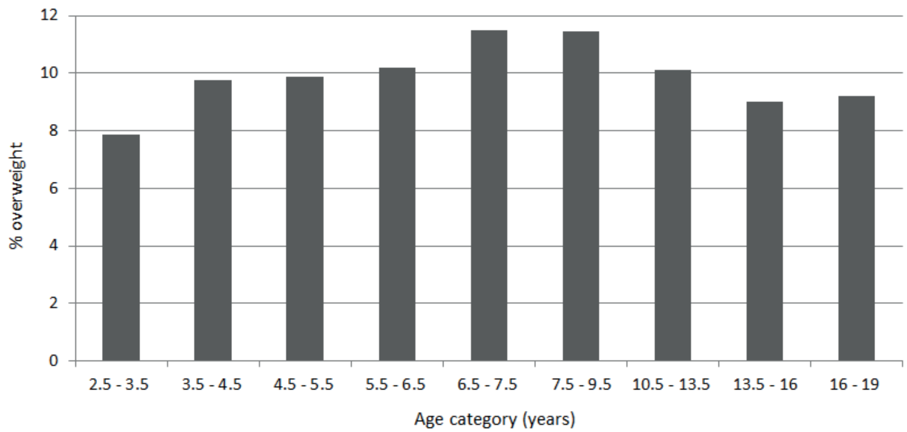

Figure 1. Percentage of overweight children per age category.

Air pollution, traffic noise and green space

The distributions of the air pollution, traffic noise and green space exposures for the youngest and oldest age categories studied are shown in Table 1. Children living in an urban area had a higher exposure to NO_2 and traffic noise and a lower exposure to green space compared to the whole study population (Table S2). Most of the children in this subgroup (96.2%) had a park within 1000 m of their homes.

Table S3 shows the Spearman correlations between the air pollutants, traffic noise and green space indicators. The correlations of the estimated concentrations of NO_2 and $PM_{2.5}$ absorbance with road traffic noise were moderate (0.41 and 0.46, respectively). Correlations between the green space indicators and traffic noise ranged from -0.35 to 0.18. The percentage of urban green space in a buffer of 3000 m was moderately positively correlated with the various air pollutants, whereas the correlations between the percentage of agricultural green space and the air pollutants were negative.

Table 1. Characteristics of the study population and the distribution of air pollution, traffic noise and green space levels for participants with data for the youngest (2.5-3.5 years) and oldest (16.0-19.0 years) age categories studied.

Characteristic	Participants with data at 2.5-3.5 years [a]	Participants with data at 16.0-19.0 years [a]
N	2735	1767
Sex (boys), n (%)	1418 (51.9)	873 (49.4)
Maternal level of education, n (%)		
Low	611 (22.6)	295 (16.8)
Intermediate	1129 (41.7)	716 (40.7)
High	967 (35.7)	750 (42.6)
Paternal level of education, n (%)		
Low	683 (25.4)	363 (20.7)
Intermediate	918 (34.2)	570 (32.5)
High	1087 (40.4)	819 (46.8)
Maternal smoking during pregnancy (yes), n (%)	446 (16.4)	231 (13.2)
Parental smoking in child's home (yes), n (%)	706 (25.9)	159 (9.0)
Neighborhood SES [b]	0.16 (-0.32 to 0.61)	0.25 (-0.50 to 0.96)
Children living in an urban area, n (%) [c]	1099 (40.2)	757 (43.1)
Region, n (%) [d]		
North	862 (31.6)	544 (31.0)
Central	1122 (41.1)	757 (43.1)
West	748 (27.4)	455 (25.9)
NO_2 (μg/m^3) [e]	23.6 (18.8 - 27.8)	22.8 (17.8 - 27.0)
$PM_{2.5}$ absorbance (10^{-5}/m) [e]	1.2 (1.1 - 1.4)	1.2 (1.0 - 1.3)
$PM_{2.5}$ (μg/m^3) [e]	16.5 (15.6 - 16.8)	16.5 (15.6 - 16.7)
PM_{10} (μg/m^3) [e]	24.6 (24.1 - 25.2)	24.5 (24.0 - 25.0)
Road traffic noise (L_{den} dB(A))	53.1 (49.9 - 56.8)	52.4 (49.3 - 56.5)
Railway noise (L_{den} dB(A))	30.6 (29.0 - 37.9)	30.7 (29.0 - 38.2)
Average NDVI in 300m buffer	0.56 (0.49 - 0.63)	0.55 (0.48 - 0.61)
Total percentage of green space in 300m buffer	12.9 (4.0 - 29.6)	19.9 (11.6 - 33.4)
Percentage urban green in 300m buffer	3.7 (0.0 - 10.5)	9.8 (4.3 - 15.6)
Percentage agricultural green in 300m buffer	0.0 (0.0 - 16.5)	1.1 (0.0 - 17.0)
Percentage natural green in 300m buffer	0.0 (0.0 - 0.0)	0.0 (0.0 - 1.3)
Average NDVI in 3000m buffer	0.64 (0.57 - 0.71)	0.62 (0.56 - 0.68)
Total percentage of green space in 3000m buffer	57.6 (42.2 - 71.2)	55.9 (42.4 - 67.0)
Percentage urban green in 3000m buffer	5.5 (1.9 - 7.9)	6.1 (2.8 - 9.7)
Percentage agricultural green in 3000m buffer	44.2 (25.0 - 62.0)	40.0 (23.3 - 55.9)
Percentage natural green in 3000m buffer	3.2 (1.1 - 9.0)	4.2 (2.1 - 10.4)

Abbreviations: SES = socioeconomic status; NDVI = Normalized Difference Vegetation Index.

[a] Values are presented as median (25th - 75th percentiles) unless otherwise indicated.

[b] A higher score indicates a higher SES.

[c] Urban area: ≥1500 addresses/km^2

[d] North: provinces Groningen, Friesland, Drenthe; Central: provinces Utrecht, Gelderland, Flevoland; West: Rotterdam and surrounding municipalities.

[e] Air pollution is modeled based upon 2009 measurements for both years.

Associations of air pollution, traffic noise and green space with overweight

The associations of air pollution, traffic noise and green space with overweight from age 3 to 17 years are shown in Table 2. The odds of being overweight increased with increasing exposure to NO_2 (adjusted OR 1.40 [95% confidence interval (CI) 1.12 - 1.74] per 8.90 µg/m^3) and $PM_{2.5}$ absorbance (adjusted OR 1.19 [95% CI 0.98 - 1.44] per 0.30 x 10^{-5}/m). The odds of being overweight decreased with increasing average NDVI and total percentage of green space in a buffer of 3000 m. These associations were not statistically significant in models II and III, though with little change in effect estimates (fully adjusted OR 0.86 [95% CI 0.71 - 1.04] per 0.13 increase in the average NDVI; fully adjusted OR 0.86 [95% CI 0.71 - 1.03] per 29.5% increase in the total percentage of green space). We found no associations of $PM_{2.5}$, PM_{10}, traffic noise and green space in a 300 m buffer with overweight from age 3 to 17 years.

Table 2. Associations of air pollution, traffic noise and green space with overweight from age 3 to 17 years.

Exposure (increment)	Model I [a]	Model II [b]	Model III [c]
	OR (95% CI)	OR (95% CI)	OR (95% CI)
NO_2 (8.90 µg/m^3)	**1.21 (1.04 - 1.40)**	**1.21 (1.04 - 1.40)**	**1.40 (1.12 - 1.74)**
$PM_{2.5}$ absorbance (0.30 x 10^{-5}/m)	1.12 (0.97 - 1.28)	1.12 (0.98 - 1.29)	1.19 (0.98 - 1.44)
PM_{10} (1.06 µg/m^3)	0.98 (0.88 - 1.09)	0.99 (0.89 - 1.11)	1.00 (0.88 - 1.12)
$PM_{2.5}$ (1.17 µg/m^3)	0.97 (0.80 - 1.18)	0.86 (0.71 - 1.05)	0.80 (0.59 - 1.09)
Road traffic noise (6.90 dB(A))	1.06 (0.93 - 1.20)	1.02 (0.90 - 1.16)	1.02 (0.90 - 1.16)
Railway noise (8.90 dB(A))	0.92 (0.80 - 1.05)	0.92 (0.80 - 1.05)	0.91 (0.79 - 1.04)
Average NDVI in 300m buffer (0.13)	0.93 (0.82 - 1.06)	0.95 (0.83 - 1.08)	0.96 (0.83 - 1.10)
Total percentage of green space in 300m buffer (25.38)	0.99 (0.89 - 1.10)	0.99 (0.88 - 1.10)	0.99 (0.88 - 1.11)
Percentage urban green in 300m buffer (10.37)	1.09 (0.99 - 1.20)	1.09 (0.98 - 1.20)	1.08 (0.98 - 1.20)
Percentage agricultural green in 300m buffer (17.55)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.05)	0.96 (0.88 - 1.05)
Natural green in 300m buffer (yes vs. no)	1.03 (0.82 - 1.29)	1.03 (0.82 - 1.29)	1.03 (0.82 - 1.30)
Average NDVI in 3000m buffer (0.13)	**0.84 (0.73 - 0.97)**	0.88 (0.76 - 1.03)	0.86 (0.71 - 1.04)
Total percentage of green space in 3000m buffer (29.47)	**0.85 (0.73 - 1.00)**	0.87 (0.74 - 1.02)	0.86 (0.71 - 1.03)
Percentage urban green in 3000m buffer (5.25)	1.04 (0.87 - 1.25)	1.06 (0.88 - 1.27)	1.05 (0.87 - 1.27)
Percentage agricultural green in 3000m buffer (35.73)	0.86 (0.68 - 1.08)	0.88 (0.69 - 1.11)	0.85 (0.66 - 1.11)
Percentage natural green in 3000m buffer (8.63)	0.99 (0.90 - 1.09)	1.01 (0.92 - 1.11)	1.01 (0.92 - 1.12)

Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index.
ORs are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnote a-c).
Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for age and sex.

[b] Adjusted for age, sex, maternal level of education, paternal level of education, maternal smoking during pregnancy, parental smoking in child's home and neighborhood socioeconomic status.

[c] Includes model II and region.

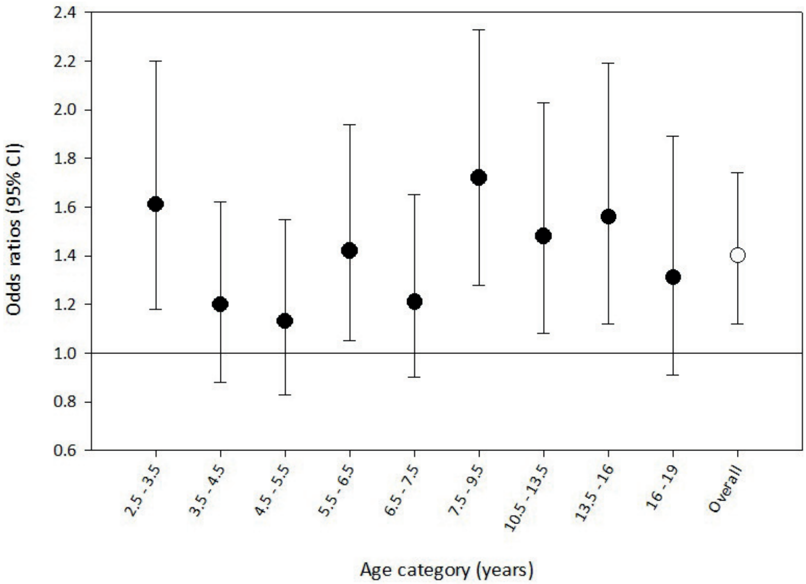

Figure 2. Age-specific associations of NO_2 with overweight from age 3 to 17 years. ORs are shown for an interquartile range increase in exposure (8.90 µg/m^3). Adjusted for age, sex, maternal level of education, paternal level of education, maternal smoking during pregnancy, parental smoking in child's home, neighborhood socioeconomic status and region.

Figures 2 and S1 show the age-specific associations of air pollution, traffic noise and green space with overweight from age 3 to 17 years. We found a positive association of NO_2 with overweight across the age categories, whereas we found no consistent pattern of associations for the other exposures with overweight across the age categories (Figure S1).

Since we observed a statistically significant association of NO_2 with overweight throughout childhood, we explored two- and three-exposure models with NO_2, road traffic noise and the average NDVI or the total percentage of green space in a 3000 m buffer (Table 3). The association of NO_2 with overweight remained after adjustment for road traffic noise (adjusted OR 1.47 [95% CI 1.16 - 1.88]) or green space in a 3000 m buffer (adjusted OR 1.36 [95% CI 1.08 - 1.72] after adjustment for the average NDVI; adjusted OR 1.44 [95% CI 1.09 - 1.90] after adjustment for the total percentage of green space). Results from three-exposure models were similar. Associations of the average NDVI and especially total percentage of green space in a 3000 m buffer with overweight weakened substantially after adjustment for NO_2.

Table 3. Associations of NO_2, road traffic noise, the average NDVI and total percentage of green space in a 3000m buffer with overweight from age 3 to 17 years from two- and three-exposure models.

Model [a]	Exposure	OR (95% CI)
NO_2 + road traffic noise	NO_2	**1.47 (1.16 - 1.88)**
	Road traffic noise	0.93 (0.80 - 1.07)
NO_2 + NDVI 3000m	NO_2	**1.36 (1.08 - 1.72)**
	Average NDVI in 3000m	0.94 (0.77 - 1.15)
NO_2 + total green 3000m	NO_2	**1.44 (1.09 - 1.90)**
	Total percentage of green space in 3000m	1.03 (0.82 - 1.29)
NO_2 + road traffic noise + NDVI 3000m	NO_2	**1.44 (1.12 - 1.86)**
	Road traffic noise	0.93 (0.80 - 1.07)
	Average NDVI in 3000m	0.94 (0.77 - 1.15)
NO_2 + road traffic noise + total green 3000m	NO_2	**1.54 (1.14 - 2.07)**
	Road traffic noise	0.92 (0.80 - 1.07)
	Total percentage of green space in 3000m	1.04 (0.82 - 1.31)

Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index.

ORs are shown for an interquartile range increase in exposure.

Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for age, sex, maternal level of education, paternal level of education, maternal smoking during pregnancy, parental smoking in child's home, neighborhood socioeconomic status and region.

In children living in an urban area, we also observed a positive association of NO_2 with overweight from age 3 to 17 years (Table 4). This association was not statistically significant in models II and III, but the effect estimates were similar to the effect estimates in the whole study population (fully adjusted OR 1.44 [95% CI 0.95 - 2.19] per 8.90 $\mu g/m^3$). A longer distance from the children's homes to the nearest park was associated with a lower odds of being overweight in this subgroup of children (adjusted OR 0.67 [95% CI 0.52 - 0.85] for an increase of 359.6 m). This was consistent across the age categories (Figure S2). Consistently, albeit non-significant, we found that an increase in the percentage of urban green space in buffers of 300 m and 3000 m was associated with a higher odds of being overweight in children living in an urban area (adjusted OR 1.15 [95% CI 0.94 - 1.40] for an increase of 10.4% in a 300 m buffer; adjusted OR 1.17 [95% CI 0.85 - 1.62] for an increase of 5.3% in a 3000 m buffer).

Table 4. Associations of air pollution, traffic noise and green space with overweight from age 3 to 17 years in children living in an urban area (≥1500 addresses/km^2).

Exposure (increment)	Model I [a]	Model II [b]	Model III [c]
	OR (95% CI)	OR (95% CI)	OR (95% CI)
NO_2 (8.90 µg/m^3)	**1.46 (1.04 - 2.03)**	1.32 (0.95 - 1.84)	1.44 (0.95 - 2.19)
$PM_{2.5}$ absorbance (0.30 x 10^{-5}/m)	1.01 (0.76 - 1.34)	1.01 (0.76 - 1.34)	0.97 (0.70 - 1.34)
PM_{10} (1.06 µg/m^3)	0.94 (0.78 - 1.12)	0.95 (0.79 - 1.14)	0.93 (0.76 - 1.12)
$PM_{2.5}$ (1.17 µg/m^3)	0.82 (0.53 - 1.27)	0.88 (0.57 - 1.35)	0.72 (0.42 - 1.23)
Road traffic noise (6.90 dB(A))	0.96 (0.74 - 1.25)	0.93 (0.72 - 1.20)	0.92 (0.71 - 1.20)
Railway noise (8.90 dB(A))	0.84 (0.65 - 1.08)	0.87 (0.67 - 1.13)	0.87 (0.68 - 1.13)
Average NDVI in 300m buffer (0.13)	0.86 (0.65 - 1.14)	0.94 (0.71 - 1.26)	0.96 (0.71 - 1.29)
Total percentage of green space in 300m buffer (25.38)	1.11 (0.78 - 1.59)	1.10 (0.77 - 1.56)	1.09 (0.76 - 1.56)
Percentage urban green in 300m buffer (10.37)	1.16 (0.95 - 1.40)	1.15 (0.95 - 1.40)	1.15 (0.94 - 1.40)
Average NDVI in 3000m buffer (0.13)	**0.73 (0.56 - 0.97)**	0.82 (0.61 - 1.10)	0.76 (0.52 - 1.13)
Total percentage of green space in 3000m buffer (29.47)	0.80 (0.53 - 1.21)	0.79 (0.51 - 1.21)	0.79 (0.50 - 1.25)
Percentage urban green in 3000m buffer (5.25)	1.17 (0.86 - 1.61)	1.15 (0.84 - 1.58)	1.17 (0.85 - 1.62)
Distance from home to the nearest park (359.57m)	**0.64 (0.50 - 0.81)**	**0.67 (0.53 - 0.85)**	**0.67 (0.52 - 0.85)**

Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index.

Associations with the percentage of urban green space are adjusted for the percentage of agricultural and natural green space in the same buffer size (plus additional confounders as detailed in footnote a-c).

Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for age and sex.

[b] Adjusted for age, sex, maternal level of education, paternal level of education, maternal smoking during pregnancy, parental smoking in child's home and neighborhood socioeconomic status.

[c] Includes model II and region.

3

Discussion

Main findings

We found that the odds of being overweight from age 3 to 17 years increased with increasing exposure to NO_2 and decreased with an increasing average NDVI and total percentage of green space in a buffer of 3000 m. The association of NO_2 with overweight remained after adjustment for road traffic noise, the average NDVI or total percentage of green space in a buffer of 3000 m. After adjustment for NO_2, the associations of green space in a buffer of 3000 m with overweight weakened substantially. We found no significant associations of particulate matter air pollution, traffic noise and green space in a buffer of 300 m with overweight. In children living in an urban area, living further away from a park was associated with a lower odds of being overweight.

Comparison with other studies and interpretation of the findings

We found a positive association of NO_2 with overweight across the age categories. The 95% confidence intervals of the age-specific estimates overlapped, however, and there were no indications for a consistent trend in associations across the age categories.

Our finding of an increased odds of being overweight with increasing exposure to NO_2 is in line with the findings from the Southern California Children's Health Study (CHS). McConnell et al. showed in 2944 participants of the 1993/1996 cohort that a higher exposure to NO_x at the homes was associated with a larger increase in BMI from age 10 to 18 and a higher attained BMI at age 18 (McConnell et al., 2015). Jerrett et al. found in 4550 participants of the 2002/2003 cohort a 13.6% increase in annual BMI growth from age 5 to 11 when comparing the lowest to the highest tenth percentile of exposure to NO_x, which resulted in an increase of nearly 0.4 BMI units on attained BMI at age 10 (Jerrett et al., 2014).

We found an increased odds of being overweight with increasing exposure to NO_2 and $PM_{2.5}$ absorbance, but not with exposure to $PM_{2.5}$ and PM_{10}, which are less determined by traffic than NO_2 and $PM_{2.5}$ absorbance (European Environment Agency, 2017). Model performance was higher for NO_2 and $PM_{2.5}$ absorbance than for $PM_{2.5}$ and PM_{10} (Table S4), which may at least partly explain why we did not find associations with particulate matter air pollution. Our findings may also indicate that specifically traffic-related air pollution is associated with children's weight. Traffic-related air pollution may affect children's weight through pro-inflammatory central nervous system effects on appetite control (McConnell et al., 2016). Air pollution may also result in metabolic dysfunction via increased oxidative stress and adipose tissue inflammation and decreased glucose utilization in skeletal muscle (An et al., 2018).

Alternatively, NO_2 concentrations may not be causally related to childhood overweight, but may represent traffic intensity near the children's homes. Traffic around the home may be associated with perceived lack of safety among children and parents, which may inhibit children's outdoor play or mobility on bicycle or foot. A previous analysis within the PIAMA study, however, has shown that the correlation between NO_2 and traffic intensity on the nearest street is low (0.2 for the birth and 8-year addresses) (Gehring et al., 2013). The low correlation between NO_2 and traffic intensity on the nearest street can be explained by the fact that traffic intensity on the nearest street is a determinant of NO_2 concentrations, but by far not the only one. The LUR model, used to estimate NO_2 concentrations, also includes regional NO_2 levels, the number of inhabitants in a 5000 m buffer and several traffic variables, such as the length of major roads in a 1000 m buffer. Moreover, no associations of overweight with road traffic noise, which is also determined by traffic density, were found in the present study. We therefore consider it unlikely that the association of NO_2 with childhood overweight in our study is explained by decreased physical activity levels associated with increased traffic density near the children's homes.

Future studies are needed to replicate our findings and to explore the pathways through which air pollution concentrations may be associated with children's weight.

Only two previous studies have assessed associations of traffic noise with children's weight (Christensen, Hjortebjerg, et al., 2016; Weyde et al., 2018). Weyde et al. found that exposure to road traffic noise during early childhood was not associated with BMI trajectories from age 18 months to 8 years in 6403 children in Norway (Weyde et al., 2018). A study from Denmark did not find associations of road traffic and railway noise with the risk for overweight at seven years of age in 40,974 children (OR 1.06 [95% CI 0.99 - 1.12] per 10 dB increase in road traffic noise) (Christensen, Hjortebjerg, et al., 2016). In the present study, we also observed a non-significant positive association of road traffic noise with overweight in single-exposure models (OR 1.02 [95% CI 0.90 - 1.16] per 6.90 dB(A)). Since the association of traffic noise with childhood overweight has been sparsely investigated, more epidemiological studies are needed to explore this association.

In single-exposure models, we found that the odds of being overweight decreased with increasing average NDVI and total percentage of green space in a buffer of 3000 m. These associations were not robust against adjustment of multiple potential confounders. Findings from previous studies examining the associations of residential exposure to green space with children's weight have been inconsistent (James et al., 2015; Lachowycz & Jones, 2011; Sanders et al., 2015). Those studies differed in the assessment of exposure to green space (i.e. different buffer sizes or green space metrics were used), which may have contributed to the mixed findings. Our results are in line with a study by Dadvand et al. that has shown that a higher average NDVI in several buffers around the children's homes was associated with a lower prevalence of overweight/obesity in children aged 9 - 12 years in Spain (Dadvand et al., 2014). Our findings are also consistent with a study from the United States that found that a higher average NDVI in a buffer of 1000 m around the children's homes was associated with lower BMI z-scores and a lower odds of increasing BMI z-scores over two years in children aged 3 - 16 years (Bell, Wilson, & Liu, 2008).

Results from two-exposure models indicate that the associations of green space in a buffer of 3000 m with overweight were confounded by NO_2 levels. The associations of green space in a buffer of 3000 m with overweight weakened after adjustment for NO_2. Higher levels of green space in a buffer of 3000 m are associated with lower concentrations of NO_2 (Table S3). This means that the associations of green space in a buffer of 3000 m with overweight can be partly explained by lower NO_2 concentrations (as a result of less traffic in places with more green space). This indicates that not green space itself (by increasing physical activity levels or through stress reduction), but lower levels of traffic-related air pollution may decrease the odds of being overweight throughout childhood. To our knowledge, this is the first study that has examined the associations of both air pollution and green space on childhood overweight.

We observed that a longer distance from the children's homes to the nearest park was associated with a significantly lower odds of being overweight in children who live in an urban area. This is an unexpected finding, since it is hypothesized that green space has a beneficial effect on children's weight by providing opportunities for physical activity. The evidence for a beneficial effect of the availability of parks on children's weight is limited. The CHS found that more park acres within a 500 m distance from children's homes was associated with a lower BMI at age 18 (Wolch et al., 2011). The study by Dadvand et al. has shown that living within 300 m of a park was not associated with overweight/obesity in children aged 9 - 12 years in Spain (Dadvand et al., 2014). Likewise, two studies from Canada found no associations of distance to the nearest park with overweight in children (Potestio et al., 2009; Potwarka, Kaczynski, & Flack, 2008).

We do not have an explanation for our finding that living further away from a park was associated with a lower odds of being overweight throughout childhood. In an earlier analysis within the PIAMA study, we found no association between distance to parks and the frequency of green space visits in adolescents aged 17 years (Bloemsma et al., 2018). This may indicate that children who live closest to a park do not necessarily visit parks more often than children who live further away from a park. In Dutch cities, parks tend to be located at some distance from the city centers. We may be dealing with some aspects of deprivation, associated with increasing distance from city centers, which is not adequately captured by including parental level of education and neighborhood SES in our analyses.

Strengths and limitations

Strengths of this study include the repeated measurements of children's weight and height from age 3 to 17 years and data on multiple environmental exposures that may be associated with childhood overweight. This enabled us to study the combined associations of air pollution, traffic noise and green space with overweight throughout childhood. We had detailed address histories for all children, which allowed the collection of virtually complete residential exposure data. Furthermore, we used several indicators to assess exposure to green space. Most previous studies only used the average NDVI or percentage of green space in several buffers around participant's homes to assess exposure to green space (James et al., 2015). We additionally examined the associations of different types of green space (urban, agricultural and natural) and distance to the nearest park with overweight in children.

Some potential limitations need to be addressed. Parents measured their child's weight and height themselves if the child's weight and height had not been measured by a medical professional within the last three months before completion of the questionnaire. The agreement between parental reported and measured weight and height has been investigated at ages four and eight within the PIAMA study and the mean difference between measured and parental reported BMI was small. Parents of children with a high

BMI tended to underreport their child's weight (Bekkers et al., 2011; Scholtens et al., 2007). This indicates that some overweight children may have been misclassified as non-overweight in the present study, resulting in an underestimation of overweight prevalence. However, we consider it unlikely that this underestimation is associated with modeled levels of air pollution and traffic noise or objectively measured green space. Thus, misclassification of the outcome is most likely unrelated to the environmental determinants, indicating that spurious associations are unlikely.

We have adjusted our analyses for several important lifestyle indicators: maternal smoking during pregnancy, parental smoking in the child's home, parental level of education and neighborhood SES. The adjustment for these potential confounders has hardly changed the associations of the exposures with childhood overweight. We nevertheless have considered including indicators of physical activity and nutrition in our study, but we have decided not to adjust our analyses for physical activity or nutrition for several reasons. Firstly, physical activity is a potential mediator, rather than a confounder, of the association between green space and overweight. We did not perform a formal mediation analysis, because in two- and three-exposure models no associations of green space with childhood overweight were found. Secondly, there is no hypothesis on how physical activity or diet could be related to air pollution, traffic noise and green space levels. SES may be an underlying variable that is related to both health behavior (including physical activity and diet) and residential exposure to air pollution, traffic noise and green space (persons with a higher SES may live in neighborhoods with higher levels of green space and lower air pollution and noise levels). We have adjusted our analyses for both maternal and paternal level of education and neighborhood SES. Finally, previous analyses within the PIAMA study have shown that questionnaire reported snacking and fast food intake were not associated with childhood overweight, which was another reason not to consider these indicators as potential confounders in the current study (Berentzen et al., 2014; Wijga et al., 2010).

Given the number of associations that we have examined in this study, we cannot rule out the fact that our finding of an association between NO_2 and childhood overweight could have occurred by chance alone. However, the association of NO_2 with overweight was consistent across different models (models I, II and III and multi-exposure models) and across the age categories. We therefore consider it unlikely that this association is a chance finding.

A limitation of the current study is that we used purely spatial air pollution models that were based on measurement campaigns performed in 2009 and that we only had estimates for traffic noise for the year 2011. However, we have good reasons to assume stable spatial contrasts in levels of air pollution and traffic noise since the start of the follow-up in our study (1999/2000). Several studies from Europe have shown that the spatial variation in air pollution and noise levels remained stable over periods of seven years and more (Cesaroni et al., 2012; Eeftens et al., 2011; Fecht et al., 2016). Moreover, a study by Gulliver et al. showed that spatial patterns of air pollution concentrations in Great Britain, estimated by LUR models, were broadly similar over a period of nearly 30 years (1962-1991) (Gulliver et al., 2011). In addition, measurement data from the Dutch National Air Quality Monitoring Network demonstrated that the annual average concentrations of PM_{10} and NO_2 have not substantially changed between 2000 and 2007 (Beijk, Mooibroek, & Hoogerbrugge, 2008).

We examined associations of residential exposure to air pollution, traffic noise and green space with childhood overweight and disregarded exposures at the school addresses, where children also spend a substantial amount of time. However, a previous analysis within the PIAMA study has shown that the correlations between air pollution concentrations at home and school addresses were moderate to high (Milanzi et al., 2018). This indicates that measurement error, resulting from including residential exposure to air pollution only, is likely small. Another limitation is that we only had information on traffic noise levels outside the home and lacked information on potential individual level noise modifiers such as data on window type, indoor insulation and orientation of the bedroom. This may have led to misclassification of individual exposure to traffic noise.

We only had information on the quantity of green space and did not know if and how often our study population used the green areas located within the specified buffers around the homes. Information on green space visits was available when the children were 17 years old, but we did not know the frequency of green space visits throughout the study period (Bloemsma et al., 2018). Finally, information on the quality of green spaces was unavailable in the present study. Quality characteristics of green spaces such as aesthetics, safety and sport/play facilities may affect the use of green spaces for physical activity (McCormack, Rock, Toohey, & Hignell, 2010).

Conclusion

Exposure to traffic-related air pollution, but not traffic noise or green space, may contribute to childhood overweight. Our results indicate that future studies examining the associations of green space with childhood overweight should account for air pollution concentrations.

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Supplemental Material

Table S1. Overview of the residential exposures included in this study, with the corresponding sources and years of data availability.

Exposure	**Source**	**Years of data availability**
NO_2, $PM_{2.5}$ absorbance, $PM_{2.5}$ and PM_{10} concentrations	LUR models developed within the ESCAPE project	2009
Road traffic and railway noise (L_{den} dB(A))	STAMINA model	2011
Average NDVI in buffers of 300m and 3000m	Landsat 5 Thematic Mapper data	2000/2002, 2010
Percentages of green space in buffers of 300m and 3000m	Bestand Bodemgebruik Top10NL	1996, 2006 2016
Distance to the nearest park	Bestand Bodemgebruik	1996, 2006, 2010

Abbreviations: NDVI = Normalized Difference Vegetation Index; LUR = land-use regression; STAMINA = Standard Model Instrumentation for Noise Assessments.

Table S2. The distribution of air pollution, traffic noise and green space levels for children who have lived in an urban area (≥1500 addresses/km^2) throughout the study period (n = 1147).

Exposure	**Median (25th - 75th percentiles) or n (%)**
NO_2 (μg/m^3)	27.72 (24.43 - 31.91)
$PM_{2.5}$ absorbance (10^{-5}/m)	1.34 (1.27 - 1.50)
$PM_{2.5}$ (μg/m^3)	16.65 (16.49 - 16.93)
PM_{10} (μg/m^3)	25.08 (24.68 - 25.96)
Road traffic noise (L_{den} dB(A))	54.40 (51.50 - 57.70)
Railway noise (L_{den} dB(A))	33.60 (29.00 - 39.80)
Average NDVI in 300m buffer	0.51 (0.45 - 0.57)
Total percentage of green space in 300m buffer	7.43 (0.44 - 16.22)
Percentage urban green in 300m buffer	4.59 (0.00 - 11.47)
Percentage agricultural green in 300m buffer	0.0 (0.0 - 0.0)
Percentage natural green in 300m buffer	0.0 (0.0 - 0.0)
Average NDVI in 3000m buffer	0.58 (0.52 - 0.65)
Total percentage of green space in 3000m buffer	37.39 (25.58 - 49.92)
Percentage urban green in 3000m buffer	6.88 (4.25 - 10.15)
Percentage agricultural green in 3000m buffer	22.20 (11.33 - 32.95)
Percentage natural green in 3000m buffer	2.47 (0.89 - 7.19)
Distance from home to the nearest park in meters	360.91 (213.20 - 572.78)
Distance from home to the nearest park	
≤ 300m	2779 (39.94)
300 – 1000m	3913 (56.24)
> 1000m	266 (3.82)

Abbreviations: NDVI = Normalized Difference Vegetation Index.

Table S3. Spearman correlations between the air pollutants, traffic noise and green space indicators.

		Air pollutants				Noise		NDVI		Urban green		Agricultural green		Natural green	
		NO_2	$PM_{2.5}$ abs	PM_{10}	$PM_{2.5}$	Road traffic	Railway	300m	3000m	300m	3000m	300m	3000m	300m	3000m
Air pollutants	NO_2	1.00	0.91	0.80	0.70	0.41	0.31	-0.53	-0.49	0.16	0.58	-0.53	-0.67	-0.25	-0.29
	$PM_{2.5}$ abs		1.00	0.88	0.83	0.46	0.32	-0.42	-0.37	0.09	0.52	-0.43	-0.67	-0.16	-0.16
	PM_{10}			1.00	0.67	0.48	0.28	-0.40	-0.41	0.15	0.64	-0.48	-0.70	-0.16	-0.22
	$PM_{2.5}$				1.00	0.40	0.25	-0.28	-0.12	0.02	0.30	-0.31	-0.46	-0.11	-0.02
Noise	Road traffic					1.00	0.15	-0.21	-0.16	0.00	0.22	-0.19	-0.26	-0.11	-0.12
	Railway						1.00	-0.15	-0.22	0.04	0.18	-0.20	-0.35	-0.08	-0.05
NDVI	300m							1.00	0.50	-0.01	-0.37	0.48	0.37	0.36	0.33
	3000m								1.00	-0.18	-0.50	0.27	0.49	0.18	0.51
Urban green	300m									1.00	0.40	-0.26	-0.20	-0.08	-0.07
	3000m										1.00	-0.50	-0.70	-0.17	-0.23
Agricultural green	300m											1.00	0.57	0.32	0.11
	3000m												1.00	0.09	-0.02
Natural green	300m													1.00	0.30
	3000m														1.00

Abbreviations: NDVI = Normalized Difference Vegetation Index.

Table S4. Land-use regression models with model performance (leave-one-out cross-validation R^2, R^2_{LOOCV}).

Exposure	Land-use regression model	R^2_{LOOCV}
NO_2	-7.80 + 1.18 × REGIONALESTIMATE + 2.30 × 10^{-5} × POP_5000 + 2.46 × 10^{-6} × TRAFLOAD_50 + 1.06 × 10^{-4} × ROADLENGTH_1000 + 9.84 × 10^{-5} × HEAVYTRAFLOAD_25 +12.19 × DISTINVNEARC1 + 4.47 × 10^{-7} × HEAVYTRAFLOAD_25_500	0.81
$PM_{2.5}$ abs	0.07 + 2.95 × 10^{-9} × TRAFLOAD_500 + 2.93 × 10^{-3} × MAJORROADLENGTH_50 + 0.85 × REGIONALESTIMATE + 7.90 × 10^{-9} × HLDRES_5000 + 1.72 × 10^{-6} × HEAVYTRAFLOAD_50	0.89
PM_{10}	23.71 + 2.16 × 10^{-8} × TRAFMAJORLOAD_500 + 6.68 × 10^{-6} × POP_5000 + 0.02 × MAJORROADLENGTH_50	0.60
$PM_{2.5}$	9.46 + 0.42 × REGIONALESTIMATE + 0.01 × MAJORROADLENGTH_50 + 2.28 × 10^{-9} × TRAFMAJORLOAD_1000	0.61

DISTINVMAJOR1: inverse distance (m^{-1}) to the nearest road of the local road network; DISTINVNEARC1: Inverse distance to the nearest road; HEAVYTRAFLOAD_X: Total heavy-duty traffic load of all roads in X m buffer (sum of (heavy-duty traffic intensity *length of all segments)); HLDRES_X: Sum of high density and low density residential land in X m buffer; MAJORROADLENGTH_X: Road length of major roads in X m buffer; POP_X: Number of inhabitants in X m buffer; PORT: port in X m buffer; REGIONALESTIMATE: Regional estimate; ROADLENGTH_X: Road length of major roads in X m buffer; TRAFLOAD_X: Total traffic load of all roads in X m buffer (sum of (traffic intensity * length of all segments)); TRAFMAJORLOAD_X: Total traffic load of major roads in X m buffer (sum of (traffic intensity * length of all segments)); TRAFNEAR: Traffic intensity on nearest road.

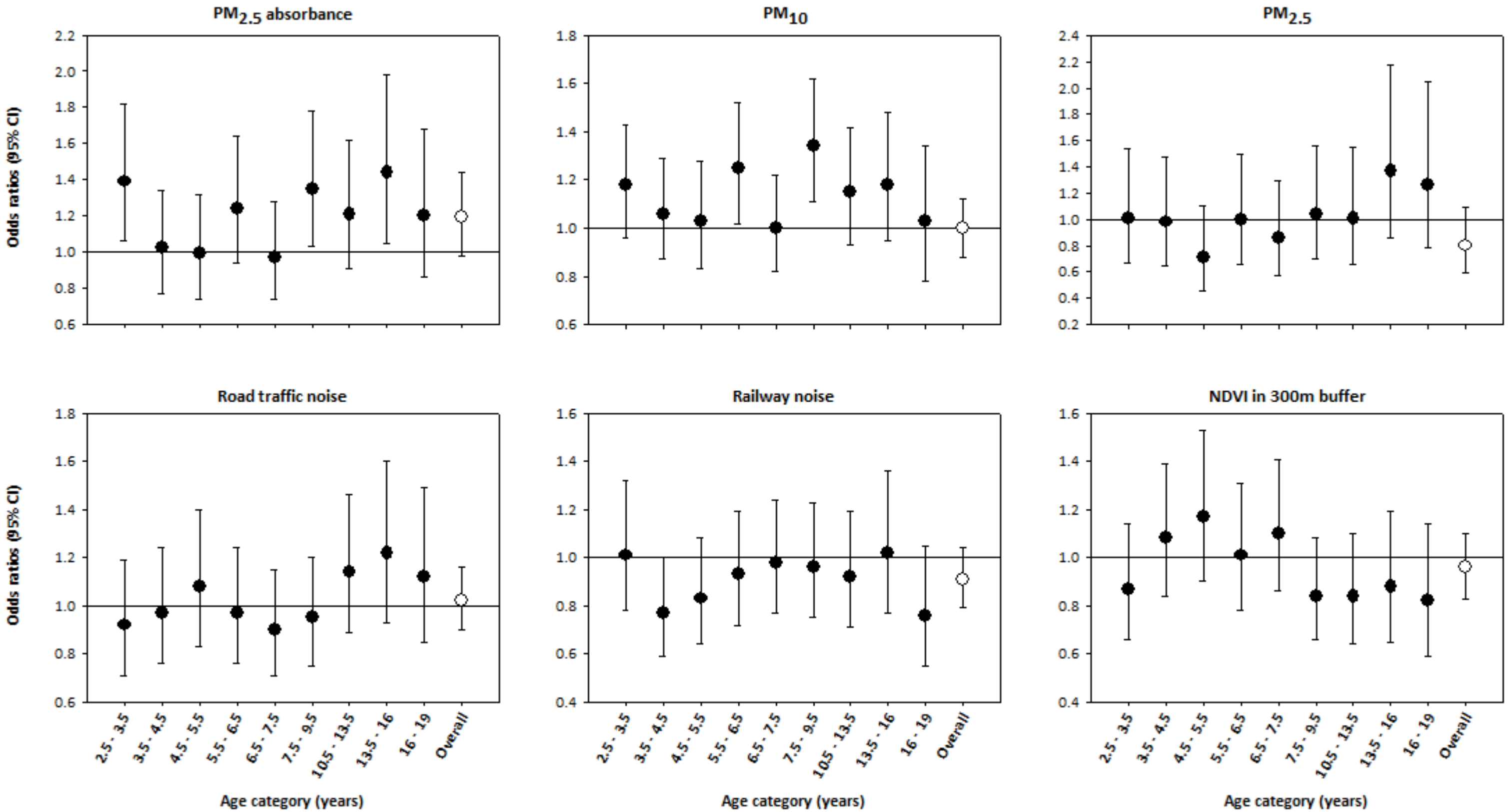
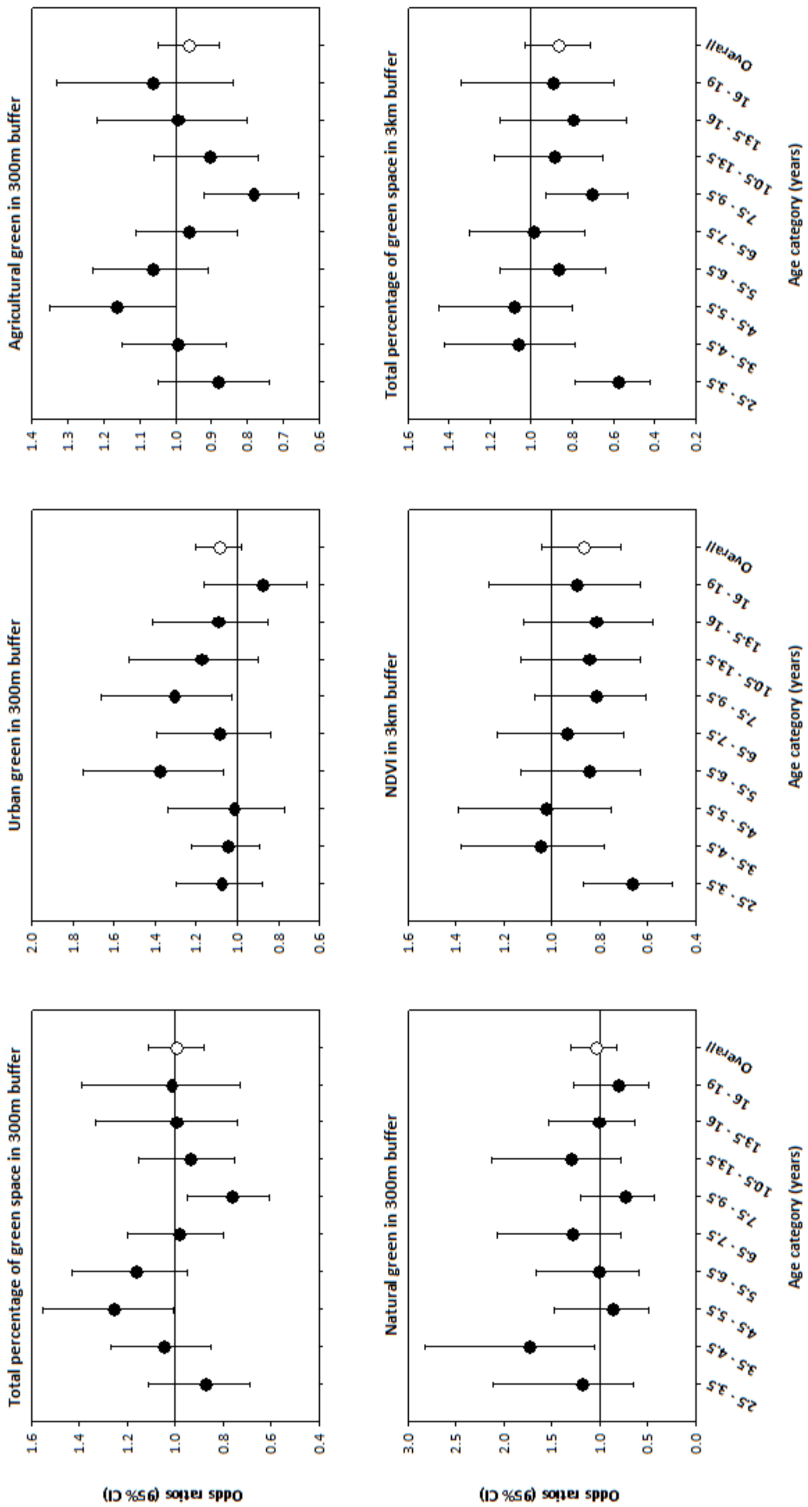


Figure S1. Age-specific associations of air pollution, traffic noise and green space with overweight from age 3 to 17 years. ORs are shown for an interquartile range increase in exposure, except for natural green in a 300m buffer. Adjusted for age, sex, maternal level of education, paternal level of education, maternal smoking during pregnancy, parental smoking in child's home, neighborhood socioeconomic status and region. Associations with the percentages of urban, agricultural and natural green space are also adjusted for the other types of green space in the same buffer size.



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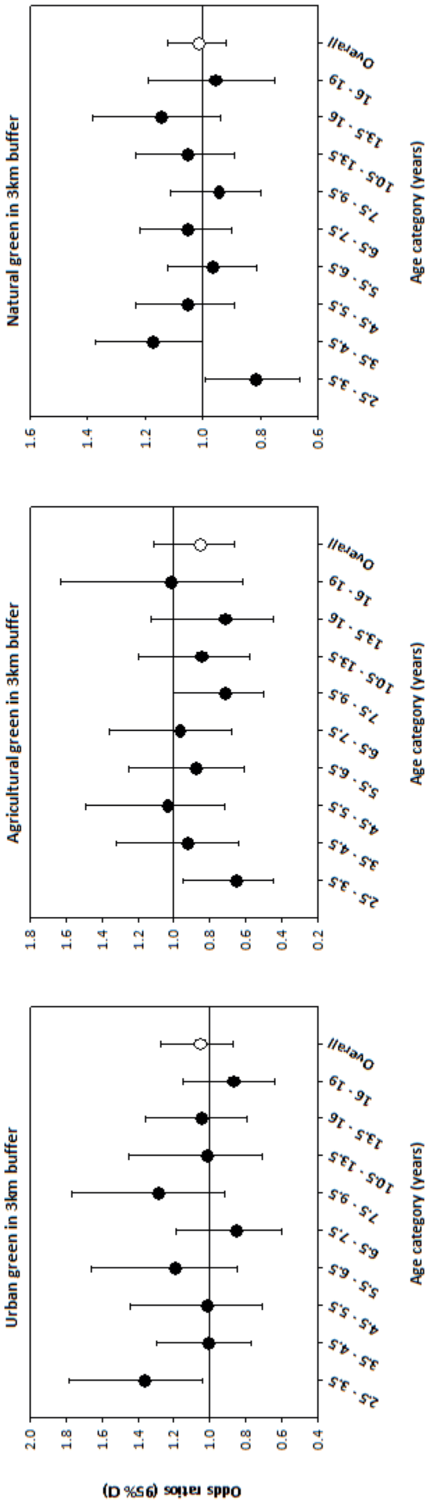

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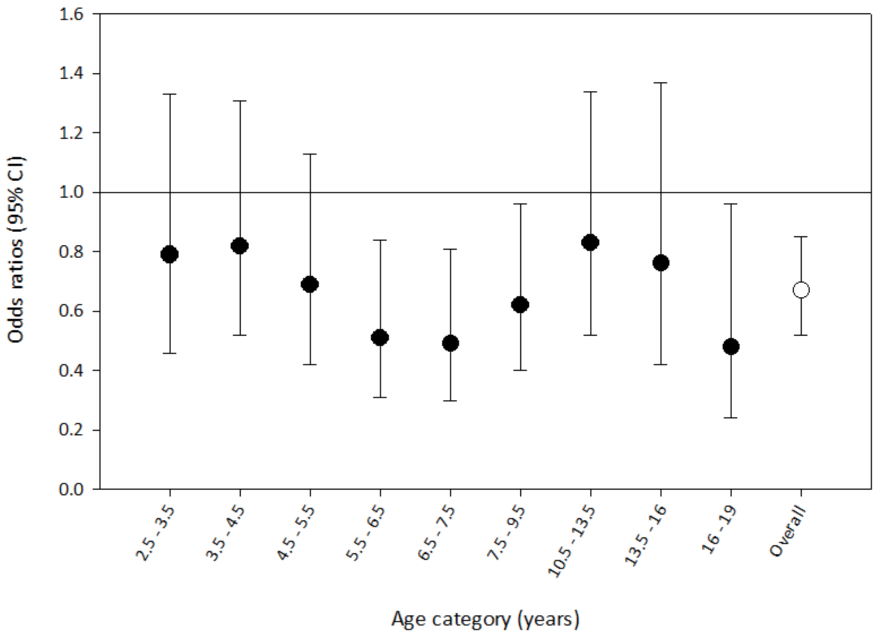

Figure S2. Age-specific associations of the distance to the nearest park with overweight from age 3 to 17 years in children living in an urban area. ORs are shown for an interquartile range increase in exposure (359.57m). Adjusted for age, sex, maternal level of education, paternal level of education, maternal smoking during pregnancy, parental smoking in child's home, neighborhood socioeconomic status and region.

Chapter 4

Green space, air pollution, traffic noise and cardiometabolic health in adolescents: the PIAMA birth cohort

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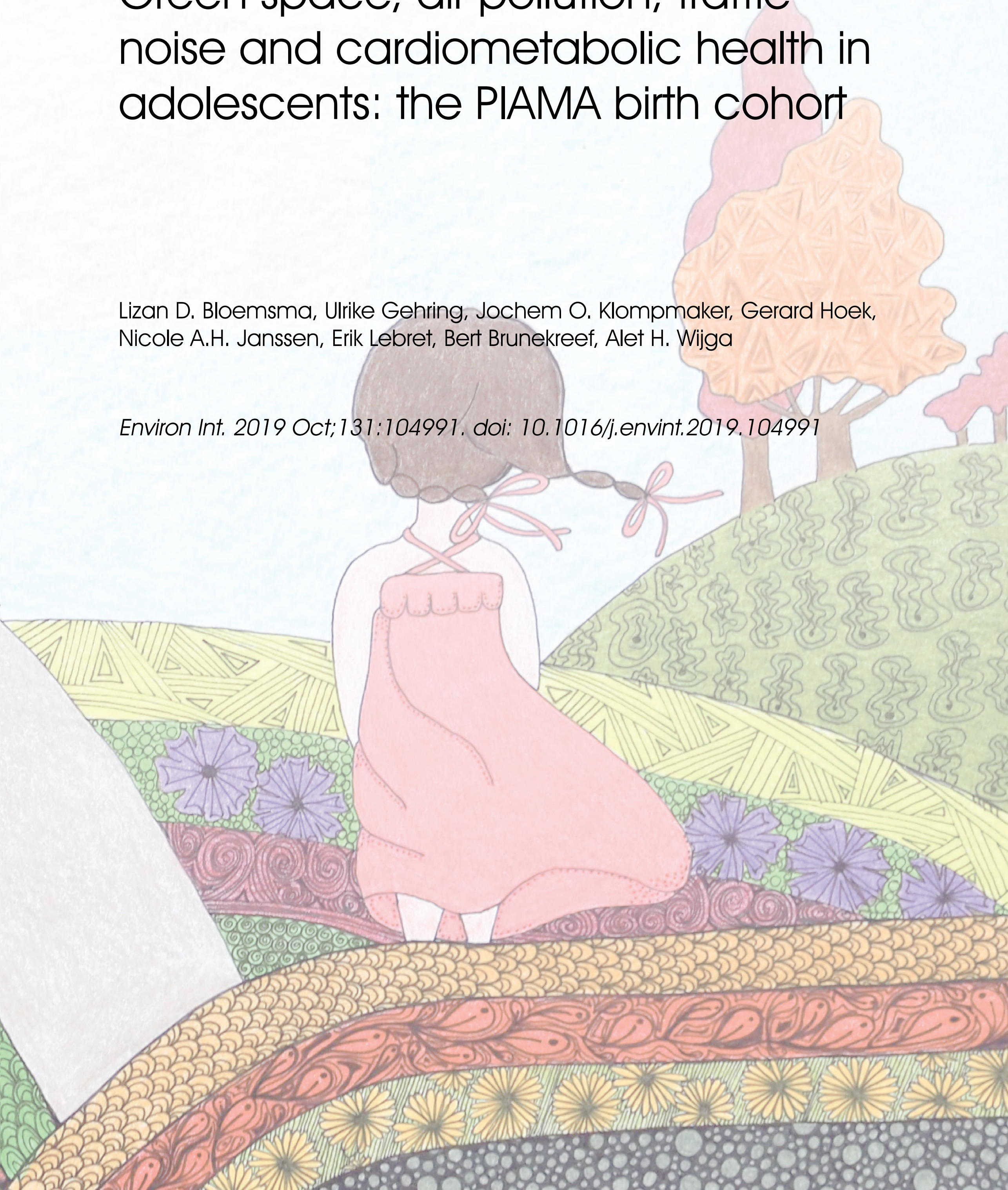
Environ Int. 2019 Oct;131:104991. doi: 10.1016/j.envint.2019.104991



Abstract

Background: Green space has been hypothesized to improve cardiometabolic health of adolescents, whereas air pollution and traffic noise may negatively impact cardiometabolic health.

Objectives: To examine the associations of green space, air pollution and traffic noise with cardiometabolic health in adolescents aged 12 and 16 years.

Methods: Waist circumference, blood pressure, cholesterol and glycated hemoglobin (HbA1c) were measured in subsets of participants of the Dutch PIAMA birth cohort, who participated in medical examinations at ages 12 (n=1505) and/or 16 years (n=797). We calculated a combined cardiometabolic risk score for each participant, with a higher score indicating a higher cardiometabolic risk. We estimated exposure to green space (i.e. the average Normalized Difference Vegetation Index (NDVI) and percentages of green space in circular buffers of 300m and 3000m), air pollution (by land-use regression models) and traffic noise (using the Standard Model Instrumentation for Noise Assessments (STAMINA) model) at the adolescents' home addresses at the time of the medical examinations. We assessed associations of these exposures with cardiometabolic health outcomes at ages 12 and 16 by multiple linear regression, adjusting for potential confounders.

Results: We did not observe consistent patterns of associations of green space, air pollution and traffic noise with the cardiometabolic risk score, blood pressure, total cholesterol levels, the total/HDL cholesterol ratio and HbA1c. We found inverse associations of air pollution with waist circumference at both age 12 and 16. These associations weakened after adjustment for region, except for particulate matter with a diameter of less than 2.5µm ($PM_{2.5}$) at age 12. The association of $PM_{2.5}$ with waist circumference at age 12 remained after adjustment for green space and road traffic noise (adjusted difference -1.42 cm [95% CI -2.50, -0.35 cm] per 1.16 $\mu g/m^3$ increase in $PM_{2.5}$).

Conclusion: This study does not provide evidence for beneficial effects of green space or adverse effects of air pollution and traffic noise on cardiometabolic health in adolescents.

Introduction

Cardiovascular diseases (CVDs) are the leading cause of death globally (World Health Organization, 2017). Atherosclerosis progresses from childhood and adolescence to adulthood. This process is related to the presence of cardiometabolic markers such as obesity, high blood pressure, glucose intolerance, high levels of total cholesterol, and low levels of high-density lipoprotein (HDL) cholesterol (Berenson et al., 1998). Furthermore, studies have suggested that cardiometabolic markers, such as blood pressure and body mass index (BMI), track from childhood and adolescence into adulthood (Juhola et al., 2011; Katzmarzyk et al., 2001; Morrison, Glueck, Woo, & Wang, 2012). Therefore, it is important to assess the impact of modifiable determinants on cardiometabolic health in children and adolescents.

Green space, air pollution and traffic noise are among the modifiable risk factors that may influence cardiometabolic health of children and adolescents. Green space has been hypothesized to improve cardiometabolic health outcomes by increasing physical activity levels, through stress reduction or reduced exposure to air pollution and noise (Hartig, Mitchell, de Vries, & Frumkin, 2014; James, Banay, Hart, & Laden, 2015). Air pollution may negatively impact cardiometabolic health through autonomic nervous system imbalance, pulmonary and systemic inflammation and oxidative stress (Araujo, 2010; Giorgini et al., 2016). Noise may affect cardiometabolic health through a stress response or sleep disturbances (Babisch, 2011; Munzel, Gori, Babisch, & Basner, 2014).

A meta-analysis has shown that increased exposure to green space was associated with decreased diastolic blood pressure and high-density lipoprotein (HDL) cholesterol and a decreased risk of type II diabetes (Twohig-Bennett & Jones, 2018). However, studies examining the associations of green space with cardiometabolic health in children or adolescents are scarce. A study by Gutiérrez-Zornoza et al. found no associations between the distance from children's homes to green spaces and cardiometabolic risk in children aged 10 to 12 years in Spain (Gutierrez-Zornoza et al., 2015). A study conducted within the German GINIplus and LISAplus birth cohorts has shown that 10-year-old children with a lower exposure to residential greenness had a higher systolic (SBP) and diastolic blood pressure (DBP) (Markevych et al., 2014). In the same German birth cohorts, no associations of residential greenness with blood lipids were found at ages 10 and 15 years (Markevych et al., 2016). A study in Iranian children aged 7-18 years showed that children who spent more time in green spaces had lower fasting blood glucose levels and a reduced risk of impaired fasting glucose (Dadvand et al., 2018).

Several epidemiological studies assessed the associations of air pollution or traffic noise with blood pressure in children. A study from Pakistan found that 8-12 year old children attending a school located in an area with high levels of air pollution had a higher blood pressure than children attending a school located in an area with lower levels of air pollution (Sughis, Nawrot, Ihsan-ul-Haque, Amjad, & Nemery, 2012). A previous analysis within the PIAMA study has shown that long-term exposure to nitrogen dioxide (NO_2) and $PM_{2.5}$ absorbance were associated with increased DBP in children aged 12 years who have lived at the same address since birth (Bilenko et al., 2015). No associations of road traffic noise with blood pressure were observed in that study (Bilenko et al., 2015). In contrast, a study by Liu et al. found positive associations of traffic noise with blood pressure, but no associations of air pollution with blood pressure in children aged 10 years from the GINIplus and LISAplus birth cohorts (Liu et al., 2014). A recent meta-analysis reported a non-significant increase of 0.20 mmHg in SBP and 0.03 mmHg in DBP per 5 dB increase in road traffic noise levels at home in children (Dzhambov & Dimitrova, 2017). No studies have examined the associations of air pollution or traffic noise with other cardiometabolic health outcomes in children or adolescents, such as blood glucose or cholesterol levels.

Road traffic is a source of both air pollution and noise (Davies, Vlaanderen, Henderson, & Brauer, 2009; Fecht et al., 2016). Higher levels of green space are associated with lower levels of air pollution and traffic noise (Hystad et al., 2014). Since green space, air pollution and traffic noise levels are spatially correlated, it is important to examine the combined associations of these exposures with health outcomes. Few studies have assessed the relationships of both air pollution and traffic noise with blood pressure in children (Bilenko et al., 2015; Liu et al., 2014). However, no previous epidemiological studies have examined the associations of green space, air pollution and traffic noise with different markers of cardiometabolic health in children or adolescents. The aim of the present study is therefore to evaluate the associations of green space, air pollution and traffic noise with cardiometabolic health outcomes (waist circumference, SBP, DBP, glycated hemoglobin, total cholesterol levels and the total/HDL cholesterol ratio) in adolescents aged 12 and 16 years.

Methods

Study design and population

We used data from the Dutch population-based Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. The design of the PIAMA study has been described elsewhere (Brunekreef et al., 2002; Wijga et al., 2014). Briefly, pregnant women were recruited in 1996/1997 in three different regions of the Netherlands: north, central and west. Region west includes the city of Rotterdam and surrounding municipalities and region central includes the provinces of Utrecht, Gelderland and Flevoland. Region north is largely rural, has a lower population density and substantially lower air pollution and traffic noise levels than regions central and west. Green space levels are highest in region north and lowest in region west. The baseline study population consisted of 3963 children. Data on growth and development, socio-demographic and lifestyle characteristics were collected through parental questionnaires at the child's age of three months, yearly until age eight years, and when the children were 11, 14 and 17 years old. Additionally, cardiometabolic health outcomes were measured during medical examinations at ages 12 and 16 years. Due to funding restrictions, only adolescents from regions north and central (n=2159) were invited for the medical examination at age 16. The study protocol has been approved by the medical ethics committees of the participating institutes and all parents and children gave written informed consent.

In this study, we included adolescents who participated in the medical examination at ages 12 (n=1505) and/or 16 (n=797), and had data on at least one cardiometabolic health outcome.

Assessment of cardiometabolic health

Medical examinations were performed by trained staff during home visits at age 12 and at the University Medical Centers of Utrecht and Groningen at age 16. Height, weight and waist circumference were measured while the adolescents were only wearing underwear. Waist circumference is a measure of central obesity. The distribution of body fat has been found to be more important than total fat mass in predicting obesity-related health risks. Excess fat located in the upper abdominal region is associated with a greater risk than fat located in other areas. Accumulation of fat mass in the abdominal area increases the risk of metabolic complications such as diabetes, hypertension and dyslipidemia (Coulston, Rock, & Monsen, 2001). Therefore, we have included waist circumference in the present study. Waist circumference was measured twice at both ages. If the two measurements differed by >2 cm, two new measurements were taken. We used the mean of the two measurements in our analyses.

SBP and DBP were measured using an Omron M6 monitor (Omron M6, Omron Healthcare Europe BV, Hoofddorp, the Netherlands) according to the recommendations of the American Heart Association Council on High Blood Pressure Research (Pickering et al., 2005). The cuff (15-22cm or >22cm, depending on the mid-upper arm circumference) was placed at the non-dominant upper arm. At both ages 12 and 16 years, BP was measured at least twice with intervals of five minutes according to a standardized protocol while the adolescent was seated. If two consecutive measures differed by >5 mmHg, another measurement was taken. We used the mean of the BP measurements in the present study.

Blood was drawn for the measurement of cholesterol and glycated hemoglobin (HbA1c). Serum levels of total and HDL cholesterol were determined enzymatically using Roche automated clinical chemistry analyzers (Roche Diagnostics, Indianapolis, IN, USA). We included total cholesterol levels and the total/HDL cholesterol ratio in our analyses. HbA1c was determined by ion-exchange chromatography using the Adams A1c HA-8160 HPLC Auto analyzer (Menarini Diagnostics Benelux, Valkenswaard, the Netherlands).

We also calculated a continuous cardiometabolic risk score for each participant, based on well-known CVD risk factors. This risk score combines the components used to define the metabolic syndrome in adults: excess adiposity, blood pressure, blood lipids and blood glucose (Ahrens et al., 2014). Previous studies in children and adolescents have used similar cardiometabolic risk scores (Rioux et al., 2017; Stratakis et al., 2018). We constructed the risk score without including triglyceride levels, since triglyceride levels have not been measured during the medical examination at age 12 years. We first calculated sex- and age-specific z-scores of waist circumference using the reference data of the Dutch Fourth Nation-wide Growth Study carried out in 1997 (Fredriks et al., 2000). We also computed sex- and age-specific z-scores of total cholesterol, non-HDL cholesterol and HbA1c as standardized regression residuals of linear regression models with cholesterol or HbA1c as outcomes and age and sex as independent variables. Sex-, age- and height- specific z-scores of SBP and DBP were calculated using reference data provided by the American Academy of Pediatrics (Flynn et al., 2017). The z-scores of SBP and DBP and the z-scores of total cholesterol and non-HDL cholesterol were averaged. In this way, blood pressure and cholesterol received the same weight as the other two components of the score (i.e. waist circumference and HbA1c). Finally, the z-scores described above were summed to create a single cardiometabolic risk score. A higher score reflects a higher cardiometabolic risk.

Exposure assessment

We estimated exposure to green space, air pollution and traffic noise at the adolescents' current home addresses at the time of the medical examinations at age 12 and 16 years. A detailed description of the exposure assessment has been published previously (Bloemsma, Wijga, et al., 2018).

Green space. We used multiple indicators to estimate residential exposure to green space. We used the Normalized Difference Vegetation Index (NDVI) to assess greenness levels around the adolescents' home addresses (Weier & Herring, 2000). The NDVI was derived from Landsat 5 Thematic Mapper data at a spatial resolution of 30 m x 30 m. NDVI values range from -1 to 1, with higher values indicating a higher density of green vegetation. Negative values correspond to water and were set to zero. We combined cloud free images of the summer of 2010 to create a map of the Netherlands. From this map, we calculated the average NDVI in circular buffers of 300 m and 3000 m around the adolescents' home addresses at the time of the medical examinations at ages 12 and 16.

We hypothesized that different types of green space may have different effects on cardiometabolic health in adolescents. We assessed the total percentage of green space and percentages of urban, agricultural and natural green space in circular buffers of 300 m and 3000 m around the adolescents' homes. We used TOP10NL of 2016, a highly detailed land-use map of the Netherlands, to assess the percentages of green space at the time of the medical examinations at age 16 (Kadaster, 2017). Since TOP10NL was not available before 2016, Bestand Bodemgebruik was used to assess the percentages of green space at the time of the medical examinations at age 12. Bestand Bodemgebruik is another land-use map of the Netherlands, which contains fewer land-use categories than TOP10NL (Centraal Bureau voor de Statistiek, 2008). Both TOP10NL and Bestand Bodemgebruik do not include private green property (such as gardens) and street greenery, in contrast to the NDVI. We assessed surrounding greenness and the percentages of green space in ArcGIS 10.2.2 (Esri, Redlands, CA, USA).

Air pollution. We used land-use regression (LUR) models to estimate annual average concentrations of NO_2, particulate matter with diameters of less than 2.5μm ($PM_{2.5}$) and less than 10μm (PM_{10}), $PM_{2.5}$ absorbance (a marker of black carbon) and the oxidative potential of $PM_{2.5}$ (electron spin resonance (OP^{ESR}) and dithiothreitol (OP^{DTT})) at the adolescents' home addresses. Details of the LUR model development have been described elsewhere (Beelen et al., 2013; Eeftens et al., 2012; Yang et al., 2015). Substantial variability in annual average air pollution concentrations was explained for NO_2, $PM_{2.5}$ absorbance, PM_{10}, $PM_{2.5}$ and OP^{ESR} (leave-one-out cross validation (R^2_{LOOCV}) = 0.60 - 0.89) but not for OP^{DTT} (R^2_{LOOCV} = 0.47) (Table S1).

Traffic noise. We estimated annual average road traffic and railway noise exposure using the STAMINA model (Standard Model Instrumentation for Noise Assessments), which has been developed at the Dutch National Institute for Public Health and the Environment (Schreurs, Jabben, & Verheijen, 2010). Daily average (Lden) and nighttime average (Lnight) road traffic and railway noise exposure at the adolescents' home addresses were estimated for 2011. Lden is the A-weighted noise level over a whole day with a penalty of 5dB(A) for evening noise (19.00 - 23.00) and a penalty of 10dB(A) for nighttime noise (23.00 - 07.00). It does not capture occasional very high noise levels (noise peaks). For the road and rail traffic noise in this study, the noise level patterns are relatively stable over the year. Because Lden and Lnight were highly correlated (r = 0.99 for road traffic noise; r = 0.95 for railway noise), we only included Lden in our analyses.

Potential confounders

We obtained the following information from parental questionnaires: Parental level of education as an indicator of family socioeconomic status (SES) (defined as the maximum of the mother's and father's educational level and categorized as low/intermediate and high), maternal smoking during pregnancy (yes/no) and any smoking in the adolescent's home at ages 11 and 16 (yes/no).Pubertal development (puberty development scale: 1 = not yet started; 2 = barely started; 3 = definitely started; and 4 = seems complete) was reported by the adolescents at ages 11 and 16 (Carskadon & Acebo, 1993). We assessed neighborhood SES with the status scores of 4-digit postal code areas from The Netherlands Institute for Social Research (SCP) of 2010 and 2014. Status scores include the average income, the percentage of low educated residents, the percentage of residents with a low income and the percentage unemployed persons in a postal code area. A higher status score indicates a higher neighborhood SES (Knol, 2012).

Epidemiological studies have suggested that ambient temperature and short-term air pollution concentrations are associated with blood pressure (Giorgini et al., 2016; Hu et al., 2019; Modesti, 2013; Zeng et al., 2017). Therefore, when we examined the associations of long-term exposure to air pollution with blood pressure, we adjusted these for short-term ambient air pollution concentrations and ambient temperature observed just before the medical examinations took place. We obtained daily data on ambient temperature from automatic weather stations of the Royal Netherlands Meteorological Institute and data on short-term air pollution concentrations, defined as the average of the air pollution concentrations on the seven days preceding the medical examinations, from routine background monitoring sites of the Dutch National Air Quality Monitoring Network.

We observed substantial differences in waist circumference between adolescents living in different regions of the Netherlands (north, central and west). The average waist circumference was highest in adolescents living in region north. We have fitted models with a random intercept for region to examine the clustering of participants within regions. The model fit of the models with a random intercept for region did not improve compared to models without a random intercept (data not shown). We have therefore decided not to include a random intercept for region in our analyses, but we have included region as a potential confounder in a separate model.

Statistical analyses
We examined the shapes of the unadjusted relationships between the continuous exposures and cardiometabolic health outcomes by generalized additive models with integrated smoothness estimation and an identity link (GAM function; The R Project for Statistical Computing 2.8.0, www.r-project.org) (Figures S1 and S2). Since the majority of the adolescents (82.6% at age 12 and 55.8% at age 16) had no natural green space in a buffer of 300 m around their homes, we created a binary variable: natural green space in a buffer of 300 m yes/no.

The Longitudinal Study of Australian Children has found that associations of green space with BMI and waist circumference are stronger in older children (Sanders, Feng, Fahey, Lonsdale, & Astell-Burt, 2015a, 2015b). It is possible that the benefits of green space exposure accumulate across childhood. Additionally, as children grow older, they will initiate or withdraw from activities that involve contact with nature while also developing different levels of independence from their parents (Sanders et al., 2015b). Associations between residential exposure to green space and children's cardiometabolic health may therefore not be consistent across childhood. Children have a larger lung surface area per unit of body weight and breathe considerably more air per unit of body weight than adults. The highest breathing rates are found in the youngest children (Bateson & Schwartz, 2008). Due to higher breathing rates and longer periods spent outdoors, younger children may be more exposed to ambient air pollution than older children. Since the associations of environmental exposures with adolescent's health may differ between ages 12 and 16 years, we decided to perform separate cross-sectional analyses and show the associations for both age groups separately. We assessed associations of green space, air pollution and traffic noise with cardiometabolic health outcomes (waist circumference, SBP, DBP, HbA1c, total cholesterol levels, the total/HDL cholesterol ratio and the cardiometabolic risk score) at ages 12 and 16 years in single-exposure models by multiple linear regression analyses.

We specified three models with increasing level of adjustment for potential confounders. Model I was the unadjusted model. Model II was adjusted for sex, exact age at the time of the medical examination, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development and neighborhood SES. Model III was additionally adjusted for region (north, central or west). Associations with the percentages of urban, agricultural and natural green space were adjusted for the other types of green space in the same buffer. In models II and III, analyses of HbA1c were additionally adjusted for the storage time of the blood samples and analyses of blood pressure were additionally adjusted for cuff size (15-22cm or >22cm), the room temperature during the medical examination and the average ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure were also adjusted for short-term air pollution levels.

To investigate the relevance of long-term (non-movers) versus more recent exposures, we excluded adolescents who had moved in the two years preceding the medical examinations (n=138 at age 12; n=41 at age 16) and repeated the analyses in the subgroup of non-movers. The statistical analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), except the analyses of the linearity of the associations, which we performed with R version 3.4.3 (R Core Team).

Results

Population characteristics

Characteristics of the study population and the distributions of the green space, air pollution and traffic noise levels at ages 12 and 16 are presented in Table 1. The cardiometabolic risk score ranged from -4.9 to 9.6 at age 12 and from -6.1 to 7.5 at age 16. The majority of the adolescents had at least one highly educated parent (57.8% at age 12; 62.8% at age 16). Eleven percent of the participants at age 12 had at least one parent who smoked, whereas this percentage was 6.6 at age 16. At both ages 12 and 16, most adolescents lived in region central (45.4% and 58.6%, respectively).

Table 1. Characteristics of the study population and the distribution of green space, air pollution and traffic noise levels.

	n (%), mean ± SD or median (25th - 75th percentiles)	
Characteristic	**Age 12**	**Age 16**
N	1505	797
Waist circumference (cm)	66.5 ± 6.7	72.3 ± 6.7
HbA1c (mmol/mol)	32.3 ± 2.5	33.1 ± 2.2
Systolic blood pressure (mmHg)	115.0 ± 9.6	116.3 ± 9.9
Diastolic blood pressure (mmHg)	66.7 ± 6.5	66.3 ± 6.8
Total cholesterol levels (mmol/L)	4.1 ± 0.6	3.9 ± 0.7
Total/HDL cholesterol ratio	3.1 ± 0.8	3.0 ± 0.8
Cardiometabolic risk score [a]	0.7 ± 1.9	0.2 ± 2.0
Boys	735 (48.8)	385 (48.3)
Parental level of education		
Low/intermediate	632 (42.2)	294 (37.2)
High	866 (57.8)	496 (62.8)
Maternal smoking during pregnancy (yes)	212 (14.2)	103 (13.0)
Smoking in adolescent's home (yes)	162 (11.0)	50 (6.6)
Puberty development scale	1.5 ± 0.5	3.4 ± 0.4
Neighborhood SES [b]	0.25 (-0.43 - 1.09)	0.47 (-0.30 - 1.06)
Region [c]		
North	474 (31.5)	330 (41.4)
Central	683 (45.4)	467 (58.6)
West	347 (23.1)	0 (0.0)
Average NDVI in 300m	0.55 (0.49 - 0.62)	0.57 (0.51 - 0.63)
Total percentage of green space in 300m	11.46 (2.44 - 28.83)	19.80 (11.74 - 35.14)
Percentage urban green in 300m	0.79 (0.00 - 7.65)	10.23 (4.41 - 15.63)
Percentage agricultural green in 300m	0.00 (0.00 - 19.13)	0.81 (0.00 - 17.67)
Percentage natural green in 300m	0.00 (0.00 - 0.00)	0.00 (0.00 - 1.68)
Buffers that have no natural green	1240 (82.6)	444 (55.8)
Average NDVI in 3000m	0.63 (0.56 - 0.69)	0.66 (0.61 - 0.70)
Total percentage of green space in 3000m	55.91 (39.94 - 70.33)	58.79 (48.83 - 68.58)
Percentage urban green in 3000m	2.76 (0.90 - 4.79)	5.71 (2.53 - 9.67)
Percentage agricultural green in 3000m	43.43 (24.56 - 61.56)	42.69 (25.27 - 56.89)
Percentage natural green in 3000m	3.81 (1.46 - 10.79)	5.61 (2.45 - 15.07)
NO_2 ($\mu g/m^3$)	22.7 (18.0 - 26.6)	21.2 (16.7 - 24.6)

Table 1. Continued

	n (%), mean ± SD or median (25th - 75th percentiles)	
Characteristic	**Age 12**	**Age 16**
$PM_{2.5}$ absorbance (10^{-5}/m)	1.2 (1.0 - 1.3)	1.2 (1.0 - 1.3)
PM_{10} (μg/m^3)	24.5 (24.0 - 25.0)	24.4 (24.0 - 24.8)
$PM_{2.5}$ (μg/m^3)	16.5 (15.6 - 16.7)	16.5 (15.5 - 16.7)
OP^{ESR} (A.U./m^3)	934.9 (777.7 - 1027.3)	933.1 (765.6 - 1035.8)
OP^{DTT} (nmol DTT/min/m^3)	1.1 (1.0 - 1.2)	1.1 (0.9 - 1.2)
Road traffic noise (L_{den} dB(A))	52.4 (49.4 - 56.3)	52.1 (49.0 - 55.7)
Railway noise (L_{den} dB(A))	30.1 (29.0 - 37.5)	29.0 (29.0 - 36.6)

Abbreviations: SES = socioeconomic status; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol; NDVI = Normalized Difference Vegetation Index.

[a] A higher cardiometabolic risk score reflects a higher cardiometabolic risk.
[b] A higher score indicates a higher SES.
[c] North: provinces Friesland, Groningen, Drenthe; Central: provinces Utrecht, Gelderland, Flevoland; West: Rotterdam and surrounding municipalities.

Green space, air pollution and traffic noise

The percentage of urban green space and total percentage of green space in a buffer of 300 m were higher at age 16 than at age 12 (Table 1). Table S2 shows the Spearman correlations between the air pollutants, traffic noise and green space indicators at ages 12 and 16. The estimated concentrations of NO_2 and $PM_{2.5}$ absorbance were moderately, positively correlated with road traffic noise levels (r=0.40 to 0.47). Correlations of the green space indicators with the various air pollutants ranged from -0.14 to -0.71 and the correlations of the green space indicators with traffic noise ranged from -0.17 to -0.46 (Table S2).

Associations of green space, air pollution and traffic noise with cardiometabolic health

Most of the associations of green space, air pollution and traffic noise with cardiometabolic health were linear or almost linear (Figures S1 and S2). We have therefore decided to use all exposures as continuous variables in our analyses. We have expressed the associations as the change in cardiometabolic health outcome per interquartile range increase (IQR) in exposure. For model III, we have additionally categorized exposures into quartiles when exposures were not linearly associated with at least one cardiometabolic health outcome. The results of the analyses with quartiles of exposure are displayed in Table S8 and Figure S3. Figure 1 and Table S3 show the associations of green space, air pollution and traffic noise with the cardiometabolic risk score at ages 12 and 16. We found no associations of the exposures with the cardiometabolic risk score at age 12. At age 16, we observed negative relationships between the air pollutants (except OP^{DTT}) and the cardiometabolic risk score in models I and II (Table S3). These relationships weakened and were no longer statistically significant after adjustment for region (Figure 1).

The associations of green space, air pollution and traffic noise with the individual cardiometabolic health outcomes are presented in Tables 2 and 3 and Tables S4-S7. We found no consistent pattern of associations between the exposures and blood pressure, total cholesterol levels, the total/HDL cholesterol ratio and HbA1c at either age 12 or 16.

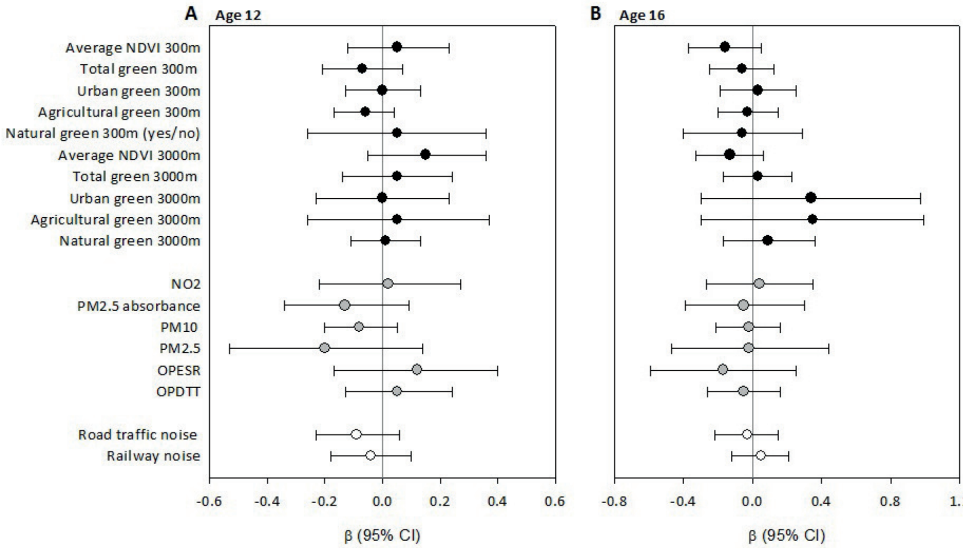


Figure 1. Associations of green space, air pollution and traffic noise with the cardiometabolic risk score at age 12 and 16 years. Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m. Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.

At both ages 12 and 16, we observed inverse associations of the air pollutants with waist circumference. After adjustment for region, these associations attenuated and were no longer statistically significant, except for $PM_{2.5}$ at age 12 (adjusted difference -1.11 cm [95% confidence interval (CI) -2.08, -0.13 cm] per 1.16 μg/m^3 increase in $PM_{2.5}$) (Tables 2 and 3). We also found associations of the total percentage of green space in buffers of 300 m and 3000 m with waist circumference at age 12 (Table S8). However, these associations were not consistent across quartiles of exposure. We found no associations between traffic noise and waist circumference.

In multi-exposure models with adjustment for green space in a buffer of 300 m and traffic noise, we still observed inverse associations of the air pollutants with waist circumference at both age 12 and 16 (except for OP^{DTT} at age 12) (Table 4). These associations weakened after adjustment for region, except for $PM_{2.5}$ absorbance (adjusted difference -0.89 cm [95% CI -1.62, -0.17 cm] per 0.29 x 10^{-5}/m increase) and $PM_{2.5}$ at age 12 (adjusted difference -1.42 cm [95% CI -2.50, -0.35 cm] per 1.16 μg/m^3 increase).

Excluding adolescents who had moved in the two years preceding the medical examinations did not influence the results (Tables S9-S11).

Table 2. Associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c at age 12 – model III.[a]

Exposure (increment)	WC (cm)	SBP (mmHg) [b]	DBP (mmHg) [b]	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol) [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.13)	-0.02 (-0.54, 0.50)	0.39 (-0.36, 1.14)	0.17 (-0.35, 0.70)	0.03 (-0.03, 0.08)	-0.04 (-0.11, 0.03)	-0.10 (-0.32, 0.11)
Total green space in 300m (26.38)	-0.08 (-0.48, 0.33)	0.24 (-0.34, 0.82)	-0.05 (-0.46, 0.36)	0.00 (-0.04, 0.05)	-0.01 (-0.06, 0.04)	**-0.17 (-0.33, 0.00)**
Urban green in 300m (7.65)	0.19 (-0.19, 0.58)	0.32 (-0.23, 0.88)	0.21 (-0.17, 0.60)	-0.03 (-0.08, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.20, 0.12)
Agricultural green in 300m (19.17)	-0.05 (-0.36, 0.26)	0.22 (-0.23, 0.66)	0.05 (-0.26, 0.36)	-0.01 (-0.04, 0.03)	0.00 (-0.04, 0.04)	**-0.15 (-0.27, -0.02)**
Natural green in 300m (yes vs. no)	0.01 (-0.91, 0.94)	-0.37 (-1.70, 0.97)	**-1.15 (-2.08, -0.22)**	0.07 (-0.03, 0.17)	-0.05 (-0.18, 0.07)	0.10 (-0.29, 0.48)
Average NDVI in 3000m (0.12)	0.29 (-0.31, 0.89)	0.57 (-0.31, 1.45)	0.45 (-0.16, 1.06)	-0.01 (-0.08, 0.05)	-0.02 (-0.10, 0.06)	0.10 (-0.15, 0.35)
Total green space in 3000m (30.39)	0.37 (-0.19, 0.94)	0.13 (-0.69, 0.95)	0.13 (-0.44, 0.70)	-0.01 (-0.07, 0.05)	0.01 (-0.07, 0.08)	-0.02 (-0.25, 0.22)
Urban green in 3000m (3.86)	-0.15 (-0.82, 0.53)	0.46 (-0.51, 1.44)	0.32 (-0.36, 1.00)	0.01 (-0.06, 0.08)	-0.04 (-0.13, 0.05)	-0.04 (-0.32, 0.24)
Agricultural green in 3000m (37.01)	0.27 (-0.65, 1.19)	0.49 (-0.85, 1.82)	0.46 (-0.47, 1.40)	0.00 (-0.10, 0.10)	-0.02 (-0.14, 0.11)	-0.02 (-0.41, 0.37)
Natural green in 3000m (9.33)	0.09 (-0.25, 0.44)	0.27 (-0.23, 0.77)	0.02 (-0.33, 0.37)	-0.01 (-0.04, 0.03)	-0.02 (-0.07, 0.02)	-0.08 (-0.22, 0.07)
NO_2 (8.58 μg/m^3)	-0.13 (-0.85, 0.59)	0.06 (-1.00, 1.13)	0.12 (-0.63, 0.86)	0.00 (-0.08, 0.08)	0.02 (-0.07, 0.12)	0.16 (-0.14, 0.46)
$PM_{2.5}$ absorbance (0.29 x 10^{-5}/m)	-0.60 (-1.22, 0.03)	0.02 (-0.92, 0.96)	0.32 (-0.33, 0.97)	0.01 (-0.06, 0.08)	-0.07 (-0.15, 0.01)	-0.12 (-0.38, 0.15)
PM_{10} (0.97 μg/m^3)	-0.30 (-0.68, 0.09)	0.03 (-0.54, 0.60)	0.13 (-0.26, 0.53)	0.01 (-0.04, 0.05)	-0.04 (-0.09, 0.01)	-0.05 (-0.21, 0.11)
$PM_{2.5}$ (1.16 μg/m^3)	**-1.11 (-2.08, -0.13)**	0.07 (-1.41, 1.55)	0.83 (-0.19, 1.86)	0.00 (-0.11, 0.11)	-0.11 (-0.24, 0.02)	-0.26 (-0.66, 0.15)
OP^{ESR} (249.57 A.U./m^3)	-0.42 (-1.26, 0.42)	0.41 (-0.82, 1.63)	0.37 (-0.48, 1.22)	0.03 (-0.06, 0.12)	0.01 (-0.10, 0.13)	0.24 (-0.10, 0.59)
OP^{DTT} (0.26 nmol DTT/min/m^3)	0.29 (-0.26, 0.84)	-0.24 (-1.04, 0.56)	0.18 (-0.37, 0.74)	-0.02 (-0.08, 0.04)	0.06 (-0.02, 0.13)	0.13 (-0.10, 0.35)
Road traffic noise (6.90 dB(A))	0.06 (-0.38, 0.50)	0.18 (-0.45, 0.81)	-0.07 (-0.50, 0.37)	-0.01 (-0.06, 0.04)	0.00 (-0.06, 0.06)	**-0.22 (-0.40, -0.05)**
Railway noise (8.45 dB(A))	-0.27 (-0.70, 0.16)	-0.15 (-0.77, 0.46)	0.01 (-0.42, 0.44)	0.02 (-0.02, 0.07)	-0.01 (-0.07, 0.04)	-0.07 (-0.24, 0.10)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-c).
Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.
[b] Additionally adjusted for cuff size, the room temperature during the medical examination and the average of the ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure are also adjusted for short-term air pollution levels.
[c] Additionally adjusted for the storage time of the blood samples.

Table 3. Associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c at age 16 – model III.[a]

Exposure (increment)	WC (cm)	SBP (mmHg) [b]	DBP (mmHg) [b]	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol) [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.12)	-0.28 (-0.92, 0.36)	0.13 (-0.86, 1.12)	0.20 (-0.50, 0.90)	-0.01 (-0.08, 0.06)	-0.06 (-0.14, 0.03)	-0.23 (-0.46, 0.01)
Total green space in 300m (23.40)	-0.30 (-0.85, 0.25)	0.35 (-0.50, 1.20)	0.33 (-0.27, 0.93)	0.00 (-0.06, 0.07)	-0.06 (-0.14, 0.01)	-0.16 (-0.36, 0.05)
Urban green in 300m (11.24)	-0.17 (-0.84, 0.50)	-0.57 (-1.60, 0.45)	0.49 (-0.24, 1.21)	-0.03 (-0.11, 0.04)	-0.01 (-0.10, 0.08)	0.07 (-0.18, 0.33)
Agricultural green in 300m (17.69)	-0.23 (-0.76, 0.29)	0.38 (-0.43, 1.19)	0.42 (-0.15, 1.00)	0.01 (-0.05, 0.07)	-0.03 (-0.10, 0.05)	-0.17 (-0.37, 0.03)
Natural green in 300m (yes vs. no)	0.04 (-1.01, 1.10)	-0.40 (-2.02, 1.22)	-0.47 (-1.61, 0.68)	-0.02 (-0.14, 0.10)	-0.09 (-0.23, 0.05)	0.15 (-0.24, 0.55)
Average NDVI in 3000m (0.09)	0.06 (-0.54, 0.67)	-0.02 (-0.97, 0.93)	-0.38 (-1.05, 0.29)	-0.04 (-0.11, 0.03)	0.00 (-0.08, 0.08)	-0.16 (-0.38, 0.07)
Total green space in 3000m (19.76)	0.26 (-0.35, 0.88)	0.33 (-0.62, 1.28)	-0.22 (-0.89, 0.45)	0.02 (-0.05, 0.09)	0.04 (-0.04, 0.12)	-0.14 (-0.37, 0.09)
Urban green in 3000m (7.10)	0.61 (-1.36, 2.57)	0.01 (-2.98, 3.01)	-0.07 (-2.18, 2.03)	0.12 (-0.09, 0.34)	0.19 (-0.06, 0.45)	0.16 (-0.57, 0.88)
Agricultural green in 3000m (31.62)	0.81 (-1.17, 2.78)	0.63 (-2.39, 3.65)	0.07 (-2.06, 2.19)	0.15 (-0.07, 0.37)	0.22 (-0.04, 0.48)	-0.10 (-0.84, 0.63)
Natural green in 3000m (12.53)	0.41 (-0.42, 1.23)	-0.14 (-1.40, 1.13)	-0.82 (-1.71, 0.08)	0.03 (-0.06, 0.13)	0.08 (-0.03, 0.19)	0.06 (-0.25, 0.37)
NO_2 (7.92 μg/m^3)	-0.23 (-1.19, 0.73)	-0.25 (-1.72, 1.23)	0.23 (-0.81, 1.28)	-0.05 (-0.16, 0.05)	-0.06 (-0.19, 0.07)	0.33 (-0.03, 0.68)
$PM_{2.5}$ absorbance (0.31 x 10^{-5}/m)	-0.18 (-1.24, 0.88)	0.16 (-1.47, 1.80)	0.13 (-1.03, 1.28)	-0.03 (-0.15, 0.09)	**-0.18 (-0.32, -0.04)**	0.13 (-0.26, 0.53)
PM_{10} (0.84 μg/m^3)	0.12 (-0.45, 0.70)	0.19 (-0.69, 1.07)	0.28 (-0.34, 0.90)	-0.03 (-0.09, 0.03)	**-0.11 (-0.18, -0.03)**	0.04 (-0.17, 0.25)
$PM_{2.5}$ (1.22 μg/m^3)	-0.68 (-2.06, 0.70)	0.48 (-1.64, 2.59)	0.62 (-0.87, 2.12)	-0.02 (-0.18, 0.13)	**-0.20 (-0.39, -0.02)**	0.20 (-0.32, 0.72)
OP^{ESR} (269.95 A.U./m^3)	-1.16 (-2.45, 0.13)	-0.56 (-2.55, 1.43)	-0.31 (-1.71, 1.10)	-0.02 (-0.16, 0.13)	-0.06 (-0.23, 0.11)	0.19 (-0.29, 0.67)
OP^{DTT} (0.25 nmol DTT/min/m^3)	-0.16 (-0.81, 0.48)	-0.58 (-1.56, 0.41)	0.34 (-0.36, 1.03)	-0.03 (-0.10, 0.04)	0.02 (-0.06, 0.10)	0.11 (-0.13, 0.35)
Road traffic noise (6.70 dB(A))	-0.06 (-0.62, 0.51)	0.29 (-0.58, 1.15)	-0.10 (-0.71, 0.51)	-0.01 (-0.08, 0.05)	0.00 (-0.08, 0.07)	-0.04 (-0.25, 0.17)
Railway noise (7.60 dB(A))	-0.28 (-0.78, 0.22)	-0.09 (-0.85, 0.67)	0.08 (-0.46, 0.62)	0.03 (-0.03, 0.08)	-0.02 (-0.08, 0.05)	0.07 (-0.12, 0.25)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-c).
Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.
[b] Additionally adjusted for cuff size, the room temperature during the medical examination and the average of the ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure are also adjusted for short-term air pollution levels.
[c] Additionally adjusted for the storage time of the blood samples.

Table 4. Associations of air pollution with waist circumference at age 12 and 16, adjusted for the total percentage of green space in a 300m buffer and road traffic noise.

Exposure	Age 12			Age 16		
	Model I [a]	Model II [b]	Model III [c]	Model I [a]	Model II [b]	Model III [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
NO_2	**-0.82 (-1.41, -0.24)**	**-0.61 (-1.20, -0.03)**	-0.36 (-1.25, 0.53)	**-1.46 (-2.31, -0.61)**	**-1.06 (-1.95, -0.18)**	-0.61 (-1.80, 0.57)
$PM_{2.5}$ absorbance	**-1.13 (-1.64, -0.61)**	**-0.87 (-1.40, -0.35)**	**-0.89 (-1.62, -0.17)**	**-1.43 (-2.30, -0.56)**	**-0.95 (-1.85, -0.05)**	-0.34 (-1.61, 0.92)
PM_{10}	**-0.57 (-0.97, -0.17)**	**-0.47 (-0.87, -0.07)**	-0.41 (-0.83, 0.02)	-0.39 (-1.02, 0.24)	-0.07 (-0.71, 0.57)	0.14 (-0.52, 0.80)
$PM_{2.5}$	**-1.61 (-2.27, -0.95)**	**-1.24 (-1.93, -0.55)**	**-1.42 (-2.50, -0.35)**	**-1.55 (-2.46, -0.65)**	**-1.23 (-2.17, -0.28)**	-0.83 (-2.34, 0.68)
OP^{ESR}	**-1.02 (-1.64, -0.39)**	**-0.80 (-1.44, -0.17)**	-0.56 (-1.46, 0.34)	**-1.70 (-2.58, -0.81)**	**-1.46 (-2.39, -0.53)**	-1.34 (-2.71, 0.04)
OP^{DTT}	0.06 (-0.53, 0.64)	0.06 (-0.51, 0.64)	0.33 (-0.34, 1.01)	**-1.01 (-1.81, -0.21)**	-0.66 (-1.44, 0.12)	-0.53 (-1.32, 0.26)

Abbreviations: CI = confidence interval; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure.
Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for the total percentage of green space in a 300m buffer and road traffic noise.
[b] Adjusted for the total percentage of green space in a 300m buffer, road traffic noise, sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development and neighborhood socioeconomic status.
[c] Includes model II and region.

Discussion

Main findings

We found no consistent pattern of associations of green space, air pollution and traffic noise with the cardiometabolic risk score, blood pressure, total cholesterol levels, the total/HDL cholesterol ratio and HbA1c in adolescents aged 12 and 16 years. We observed inverse associations of air pollution with waist circumference at both ages 12 and 16, which attenuated after adjustment for region.

Comparison with other studies in children or adolescents and possible explanations for our findings

Green space

We did not find associations of green space with cardiometabolic health in adolescents aged 12 and 16 years. This is in line with a study by Gutiérrez-Zornoza et al. that found no associations between the distance from children's homes to green spaces and cardiometabolic risk in 956 schoolchildren aged 10 to 12 years in rural areas in Spain (Gutierrez-Zornoza et al., 2015). Our results are also in line with a study by Markevych et al. that found no associations of residential greenness with blood lipids at ages 10 and 15 years in 1552 children participating in two German birth cohorts (Markevych et al., 2016). Our findings are, however, inconsistent with a study in the same German birth cohorts (GINIplus and LISAplus) that has shown that 10-year-old children with a lower average NDVI in buffers of 500 m around their homes had a higher SBP and DBP (Markevych et al., 2014). We did not include the average NDVI in buffers of 500 m around the adolescents' homes in our study, since the green space indicators in the 300 m and 500 m buffers were highly correlated. Because of the high correlations, we expect that we would also observe no associations between blood pressure and the green space indicators in a 500 m buffer. No previous studies have examined the associations of green space with HbA1c in children or adolescents. However, a study by Dadvand et al. showed that Iranian schoolchildren who spent more time in green spaces had lower fasting blood glucose levels and a reduced risk of impaired fasting glucose (Dadvand et al., 2018).

Findings from previous studies examining associations of residential exposure to green space with children's adiposity have been inconsistent (James et al., 2015; Lachowycz & Jones, 2011). Most of these studies used BMI as a measure of adiposity and did not include waist circumference. We have previously shown that green space was not associated with overweight from age 3 to 17 years in the PIAMA study (Bloemsma, Wijga, et al., 2018), consistent with the results from the present study. Only one previous study has assessed the relationship between green space and waist circumference in children or adolescents. That study has shown that a higher proportion of neighborhood green space was associated with a lower waist circumference in 4423 Australian children aged 6-13 years (Sanders et al., 2015a).

Air pollution

In this study, no associations of air pollution with the cardiometabolic risk score, blood pressure, cholesterol and HbA1c in adolescents were found. This is in line with a study by Liu et al. that found that air pollution was not consistently associated with SBP and DBP in 2368 children aged 10 years from the GINIplus and LISAplus birth cohorts (Liu et al., 2014). In contrast, a study from Pakistan found that 8-12 year old children attending a school situated in an area with high levels of air pollution had higher SBP and DBP than children attending a school located in an area with lower levels of air pollution (Sughis et al., 2012). The mean daily concentration of $PM_{2.5}$ was 28.5 µg/m^3 in the low pollution area and 183 µg/m^3 in the high pollution area (Sughis et al., 2012), which is considerably higher than the $PM_{2.5}$ concentrations in our study (median $PM_{2.5}$ concentration of 16.5 µg/m^3 at both ages 12 and 16). No previous epidemiological studies have assessed the associations of air pollution with cholesterol or HbA1c in adolescents.

We found inverse associations of the air pollutants with waist circumference at both ages 12 and 16. After adjustment for region, these associations attenuated and were no longer statistically significant, except for $PM_{2.5}$ at age 12. The inclusion of region in our analyses may, however, have resulted in over-adjustment, because the estimated residential exposures differ between regions. Air pollution concentrations are lowest in region north, where the average waist circumference of our study participants was highest. On the other hand, there is a possibility of residual confounding if we would not adjust for region (e.g. due to differences in lifestyle). We have therefore decided to include region as a potential confounder in a separate model and show the results of the analyses with and without adjustment for region.

To our knowledge, no previous studies have examined associations of air pollution with waist circumference in children. Our previous analysis within the PIAMA study, however, has shown that the odds of being overweight from age 3 to 17 years increased with increasing exposure to NO_2 (Bloemsma, Wijga, et al., 2018).

Traffic noise
We found no relationships between road traffic or railway noise and cardiometabolic health at ages 12 and 16. Findings from previous studies that assessed associations of traffic noise with children's blood pressure are inconsistent (Paunovic, Stansfeld, Clark, & Belojevic, 2011). A meta-analysis showed a non-significant increase of 0.20 mmHg in SBP and 0.03 mmHg in DBP per 5 dB increase in road traffic noise levels at children's homes (Dzhambov & Dimitrova, 2017). In line with the findings from this meta-analysis, we did not observe statistically significant associations between residential exposure to road traffic noise and blood pressure in adolescents. No previous studies have assessed the relationships of traffic noise with waist circumference, cholesterol or HbA1c in children or adolescents.

Strengths and limitations
Strengths of our study include the availability of multiple objectively measured cardiometabolic health outcomes, which allowed us to calculate a combined risk score to estimate an adolescent's individual cardiometabolic risk. Moreover, we had data on multiple spatially correlated environmental exposures that may be associated with cardiometabolic health in adolescents. The inclusion of detailed and specific indicators of exposure to green space is another strength of this study. We used several indicators to assess residential exposure to green space. Most previous studies only used the total percentage of green space or average NDVI in several buffers around participants' homes to assess exposure to

green space (James et al., 2015). We additionally had information on specific types of green spaces (urban, agricultural and natural), potentially giving an indication of the usability of these green spaces for our study participants.

This study has also some potential limitations. Because of the cross-sectional design of our study, it is not possible to distinguish causes from effects. Moreover, while we have a more detailed set of green space indicators compared to other studies, we did not know if and how often our study population used the green spaces located within the specified buffers. In the PIAMA study, information on green space visits was available when the children were 17 years old. We have previously shown that these 17-year-olds did make use of green spaces, but that the frequency of green space visits was not associated with the amount of green space in buffers around their homes (Bloemsma, Gehring, et al., 2018). Another limitation is that we used purely spatial air pollution models that were based on measurement campaigns performed in 2009 to estimate air pollution exposure during the medical examinations at age 12 (in 2008-2010) and 16 (in 2012-2014). However, our assumption of constant spatial contrasts in air pollution levels is supported by several studies from Europe that have shown that the spatial variation in air pollution concentrations remain stable over periods of seven years and more (Cesaroni et al., 2012; Eeftens et al., 2011; Fecht et al., 2016). Like most previous epidemiological studies, we only had information on traffic noise levels outside the adolescents' home addresses and no information on orientation of the bedroom, window type and indoor insulation, which may affect an adolescent's actual exposure to noise. We therefore cannot rule out the possibility of misclassification of individual exposure to traffic noise.

Children in the PIAMA cohort were recruited from the general population, but children of lower educated parents were underrepresented. There was selective loss to follow-up of children with lower paternal and maternal education, i.e. parents of children in the current study population were higher educated than parents of the baseline PIAMA study population. Exposure to secondhand smoke also decreased between the medical examinations at ages 12 and 16 years, which partly reflects the general trend of a decreasing percentage of smokers in the Dutch population (Volksgezondheidenzorg.info, 2019). The associations of air pollution and traffic noise with cardiometabolic health may be assumed to be in the same direction for children of parents with low or high education, implying that generalizability of these findings is not limited to highly educated populations. It has been suggested that persons with lower levels of education have a greater health benefit from green space exposure compared to those with higher levels of education (James et al., 2015). If this also applies to children of lower educated parents in the Netherlands, it would imply that we may have missed beneficial effects of green space in our study population that has a relatively low proportion of children of lower educated parents.

Conclusion

This study does not provide evidence for beneficial effects of green space or adverse effects of air pollution and traffic noise on cardiometabolic health in adolescents aged 12 and 16 years.

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Supplemental Material

Table S1. Land-use regression models with model performance (leave-one-out cross-validation R^2, R^2_{LOOCV}).

Exposure	Land-use regression model	R^2_{LOOCV}
NO_2	-7.80 + 1.18 × REGIONALESTIMATE + 2.30 × 10^{-5} × POP_5000 + 2.46 × 10^{-6} × TRAFLOAD_50 + 1.06 × 10^{-4} × ROADLENGTH_1000 + 9.84 × 10^{-5} × HEAVYTRAFLOAD_25 +12.19 × DISTINVNEARC1 + 4.47 × 10^{-7} × HEAVYTRAFLOAD_25_500	0.81
$PM_{2.5}$ abs	0.07 + 2.95 × 10^{-9} × TRAFLOAD_500 + 2.93 × 10^{-3} × MAJORROADLENGTH_50 + 0.85 × REGIONALESTIMATE + 7.90 × 10^{-9} × HLDRES_5000 + 1.72 × 10^{-6} × HEAVYTRAFLOAD_50	0.89
PM_{10}	23.71 + 2.16 × 10^{-8} × TRAFMAJORLOAD_500 + 6.68 × 10^{-6} × POP_5000 + 0.02 × MAJORROADLENGTH_50	0.60
$PM_{2.5}$	9.46 + 0.42 × REGIONALESTIMATE + 0.01 × MAJORROADLENGTH_50 + 2.28 × 10^{-9} × TRAFMAJORLOAD_1000	0.61
OP^{ESR}	327 + 434 x REGIONALESTIMATE + 587 x TRAFLOAD_50 + 305 x POP_5000	0.60
OP^{DTT}	0.08 + 0.33 x REGIONALESTIMATE + 0.31 x ROADLENGTH_500 + 0.15 x INTMAJORINVDIST - 0.11 x NATURAL_1000	0.47

DISTINVMAJOR1: inverse distance (m^{-1}) to the nearest road of the local road network; DISTINVNEARC1: Inverse distance to the nearest road; HEAVYTRAFLOAD_X: Total heavy-duty traffic load of all roads in X m buffer (sum of (heavy-duty traffic intensity *length of all segments)); HLDRES_X: Sum of high density and low density residential land in X m buffer; INTMAJORINVDIST: Product of traffic intensity on nearest major road and inverse of distance to the nearest major road; MAJORROADLENGTH_X: Road length of major roads in X m buffer; NATURAL_X: Surface area of semi-natural and forested areas in X m buffer; POP_X: Number of inhabitants in X m buffer; PORT: port in X m buffer; REGIONALESTIMATE: Regional estimate; ROADLENGTH_X: Road length of major roads in X m buffer; TRAFLOAD_X: Total traffic load of all roads in X m buffer (sum of (traffic intensity * length of all segments)); TRAFMAJORLOAD_X: Total traffic load of major roads in X m buffer (sum of (traffic intensity * length of all segments)); TRAFNEAR: Traffic intensity on nearest road.

Table S2. Spearman correlations between the air pollutants, traffic noise and green space at age 12 (top right) and age 16 (bottom left, *in italics*).

		Air pollutants						Noise		NDVI		Total percentage green space	
		NO_2	$PM_{2.5}$ abs	PM_{10}	$PM_{2.5}$	OP^{ESR}	OP^{DTT}	Road traffic	Railway	300m	3000m	300m	3000m
Air pollutants	**NO_2**		0.89	0.76	0.66	0.65	0.71	0.40	0.31	-0.60	-0.64	-0.46	-0.71
	$PM_{2.5}$ abs	*0.88*		0.87	0.82	0.73	0.53	0.46	0.32	-0.46	-0.50	-0.38	-0.64
	PM_{10}	*0.75*	*0.85*		0.64	0.56	0.47	0.46	0.29	-0.40	-0.52	-0.37	-0.70
	$PM_{2.5}$	*0.72*	*0.88*	*0.66*		0.81	0.38	0.41	0.26	-0.33	-0.23	-0.29	-0.36
	OP^{ESR}	*0.76*	*0.82*	*0.58*	*0.82*		0.31	0.36	0.28	-0.28	-0.19	-0.34	-0.40
	OP^{DTT}	*0.62*	*0.40*	*0.39*	*0.31*	*0.30*		0.26	0.19	-0.68	-0.56	-0.53	-0.55
Noise	**Road traffic**	*0.40*	*0.47*	*0.50*	*0.39*	*0.35*	*0.21*		0.14	-0.26	-0.21	-0.20	-0.26
	Railway	*0.36*	*0.36*	*0.34*	*0.28*	*0.34*	*0.20*	*0.13*		-0.18	-0.28	-0.17	-0.37
NDVI	**300m**	*-0.56*	*-0.42*	*-0.39*	*-0.31*	*-0.29*	*-0.65*	*-0.25*	*-0.21*		0.58	0.64	0.51
	3000m	*-0.48*	*-0.35*	*-0.50*	*-0.14*	*-0.19*	*-0.43*	*-0.20*	*-0.40*	*0.50*		0.30	0.84
Total percentage green space	**300m**	*-0.50*	*-0.40*	*-0.37*	*-0.31*	*-0.35*	*-0.56*	*-0.18*	*-0.22*	*0.77*	*0.36*		0.45
	3000m	*-0.66*	*-0.58*	*-0.66*	*-0.37*	*-0.45*	*-0.48*	*-0.25*	*-0.46*	*0.51*	*0.84*	*0.49*	

Abbreviations: OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol; NDVI = Normalized Difference Vegetation Index.

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Table S3. Associations of green space, air pollution and traffic noise with the cardiometabolic risk score at age 12 and 16 – models I and II. Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.

	Age 12		Age 16	
	Model I [a]	Model II [b]	Model I [a]	Model II [b]
Exposure	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**
Average NDVI in 300m	0.00 (-0.15, 0.15)	0.04 (-0.12, 0.20)	-0.10 (-0.29, 0.10)	-0.07 (-0.28, 0.13)
Total percentage of green space in 300m	-0.08 (-0.20, 0.04)	-0.06 (-0.19, 0.07)	0.00 (-0.17, 0.17)	0.01 (-0.17, 0.19)
Urban green in 300m	0.02 (-0.10, 0.14)	0.01 (-0.12, 0.13)	0.03 (-0.18, 0.24)	0.07 (-0.14, 0.29)
Agricultural green in 300m	-0.07 (-0.16, 0.03)	-0.06 (-0.16, 0.05)	0.04 (-0.12, 0.20)	0.04 (-0.13, 0.21)
Natural green in 300m (yes vs. no)	0.02 (-0.28, 0.32)	0.05 (-0.26, 0.37)	-0.07 (-0.40, 0.27)	-0.05 (-0.40, 0.30)
Average NDVI in 3000m	0.02 (-0.13, 0.16)	0.06 (-0.09, 0.21)	-0.11 (-0.30, 0.08)	-0.12 (-0.31, 0.08)
Total percentage of green space in 3000m	0.01 (-0.15, 0.17)	0.04 (-0.13, 0.21)	0.16 (-0.02, 0.34)	0.12 (-0.08, 0.31)
Urban green in 3000m	-0.02 (-0.23, 0.19)	0.01 (-0.21, 0.24)	0.41 (-0.17, 1.00)	0.54 (-0.07, 1.15)
Agricultural green in 3000m	0.00 (-0.28, 0.29)	0.06 (-0.23, 0.36)	**0.57 (0.01, 1.14)**	**0.63 (0.04, 1.23)**
Natural green in 3000m	-0.03 (-0.13, 0.08)	0.00 (-0.12, 0.11)	0.15 (-0.11, 0.40)	0.13 (-0.13, 0.40)
NO_2	0.03 (-0.12, 0.19)	0.00 (-0.16, 0.16)	**-0.26 (-0.47, -0.05)**	-0.22 (-0.44, 0.01)
$PM_{2.5}$ absorbance	-0.06 (-0.20, 0.08)	-0.08 (-0.23, 0.07)	**-0.32 (-0.54, -0.10)**	**-0.28 (-0.52, -0.05)**
PM_{10}	-0.06 (-0.18, 0.05)	-0.06 (-0.18, 0.05)	-0.15 (-0.31, 0.01)	-0.12 (-0.29, 0.06)
$PM_{2.5}$	-0.09 (-0.28, 0.10)	-0.11 (-0.32, 0.09)	**-0.36 (-0.61, -0.11)**	**-0.34 (-0.61, -0.07)**
OP^{ESR}	0.02 (-0.16, 0.20)	0.01 (-0.19, 0.20)	**-0.42 (-0.66, -0.17)**	**-0.39 (-0.66, -0.11)**
OP^{DTT}	0.09 (-0.06, 0.24)	0.04 (-0.12, 0.20)	-0.14 (-0.33, 0.05)	-0.13 (-0.33, 0.07)
Road traffic noise	-0.10 (-0.24, 0.03)	-0.09 (-0.23, 0.050	-0.12 (-0.29, 0.06)	-0.11 (-0.29, 0.07)
Railway noise	-0.03 (-0.16, 0.10)	-0.04 (-0.18, 0.09)	-0.05 (-0.20, 0.10)	-0.01 (-0.17, 0.15)

Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-b).

Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Unadjusted model.

[b] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development and neighborhood socioeconomic status.

Table S4. Unadjusted associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c at age 12.

Exposure (increment)	WC (cm)	SBP (mmHg)	DBP (mmHg)	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol)
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.13)	0.10 (-0.36, 0.56)	0.46 (-0.21, 1.13)	-0.03 (-0.49, 0.43)	0.03 (-0.02, 0.08)	-0.05 (-0.11, 0.01)	-0.13 (-0.31, 0.06)
Total green space in 300m (26.38)	0.02 (-0.35, 0.40)	0.30 (-0.25, 0.85)	-0.16 (-0.53, 0.21)	0.01 (-0.03, 0.05)	-0.01 (-0.06, 0.04)	**-0.17 (-0.32, -0.02)**
Urban green in 300m (7.65)	0.29 (-0.09, 0.67)	0.31 (-0.23, 0.86)	0.21 (-0.17, 0.58)	-0.03 (-0.07, 0.01)	-0.03 (-0.08, 0.02)	-0.01 (-0.17, 0.14)
Agricultural green in 300m (19.17)	0.02 (-0.27, 0.31)	0.27 (-0.15, 0.68)	-0.02 (-0.31, 0.26)	0.00 (-0.03, 0.03)	0.00 (-0.03, 0.04)	**-0.16 (-0.27, -0.04)**
Natural green in 300m (yes vs. no)	0.13 (-0.77, 1.04)	-0.37 (-1.68, 0.95)	**-1.16 (-2.05, -0.26)**	0.06 (-0.04, 0.15)	-0.07 (-0.19, 0.05)	0.16 (-0.21, 0.53)
Average NDVI in 3000m (0.12)	0.17 (-0.28, 0.61)	0.40 (-0.26, 1.05)	0.04 (-0.40, 0.49)	0.00 (-0.05, 0.05)	-0.04 (-0.10, 0.01)	0.01 (-0.17, 0.19)
Total green space in 3000m (30.39)	0.44 (-0.05, 0.93)	0.22 (-0.50, 0.93)	-0.07 (-0.57, 0.42)	0.00 (-0.06, 0.05)	-0.01 (-0.07, 0.06)	-0.06 (-0.26, 0.14)
Urban green in 3000m (3.86)	0.11 (-0.54, 0.76)	0.47 (-0.48, 1.41)	0.17 (-0.47, 0.82)	0.00 (-0.07, 0.06)	-0.05 (-0.13, 0.04)	-0.09 (-0.35, 0.18)
Agricultural green in 3000m (37.01)	0.66 (-0.21, 1.52)	0.59 (-0.66, 1.84)	0.11 (-0.75, 0.96)	-0.01 (-0.10, 0.09)	-0.04 (-0.15, 0.07)	-0.13 (-0.49, 0.22)
Natural green in 3000m (9.33)	0.01 (-0.32, 0.34)	0.32 (-0.16, 0.80)	-0.04 (-0.37, 0.29)	-0.01 (-0.05, 0.02)	-0.03 (-0.07, 0.01)	-0.07 (-0.20, 0.07)
NO_2 (8.58 μg/m^3)	**-0.55 (-1.02, -0.09)**	-0.32 (-1.00, 0.36)	0.21 (-0.25, 0.68)	0.00 (-0.05, 0.05)	0.03 (-0.03, 0.09)	0.19 (0.00, 0.38)
$PM_{2.5}$ absorbance (0.29 x 10^{-5}/m)	**-0.80 (-1.24, -0.37)**	-0.23 (-0.86, 0.40)	0.24 (-0.19, 0.67)	0.01 (-0.04, 0.05)	-0.02 (-0.08, 0.03)	0.06 (-0.12, 0.23)
PM_{10} (0.97 μg/m^3)	**-0.44 (-0.79, -0.10)**	-0.09 (-0.59, 0.42)	0.09 (-0.26, 0.44)	0.01 (-0.03, 0.04)	-0.02 (-0.07, 0.02)	-0.02 (-0.16, 0.12)
$PM_{2.5}$ (1.16 μg/m^3)	**-1.28 (-1.86, -0.70)**	-0.39 (-1.24, 0.47)	0.47 (-0.11, 1.05)	0.01 (-0.05, 0.07)	-0.04 (-0.12, 0.03)	0.11 (-0.13, 0.35)
OP^{ESR} (249.57 A.U./m^3)	**-0.84 (-1.39, -0.28)**	-0.25 (-1.06, 0.56)	0.29 (-0.26, 0.84)	0.01 (-0.05, 0.07)	-0.02 (-0.09, 0.06)	**0.25 (0.02, 0.47)**
OP^{DTT} (0.26 nmol DTT/min/m^3)	0.01 (-0.45, 0.47)	-0.36 (-1.03, 0.31)	0.29 (-0.17, 0.74)	-0.02 (-0.06, 0.03)	0.06 (0.00, 0.12)	0.17 (-0.02, 0.35)
Road traffic noise (6.90 dB(A))	-0.03 (-0.46, 0.39)	-0.02 (-0.64, 0.59)	-0.08 (-0.50, 0.34)	-0.02 (-0.06, 0.03)	-0.01 (-0.06, 0.05)	**-0.17 (-0.34, 0.00)**
Railway noise (8.45 dB(A))	-0.35 (-0.77, 0.07)	-0.18 (-0.78, 0.43)	0.08 (-0.33, 0.50)	0.02 (-0.02, 0.06)	-0.01 (-0.06, 0.05)	-0.02 (-0.18, 0.15)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer.
Statistically significant results are highlighted in bold (p <0.05).

Table S5. Associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c at age 12 – model II.[a]

Exposure (increment)	WC (cm)	SBP (mmHg) [b]	DBP (mmHg) [b]	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol) [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.13)	0.17 (-0.30, 0.64)	0.47 (-0.22, 1.15)	0.02 (-0.46, 0.50)	0.02 (-0.03, 0.07)	-0.05 (-0.11, 0.01)	-0.10 (-0.30, 0.09)
Total green space in 300m (26.38)	0.05 (-0.34, 0.45)	0.36 (-0.21, 0.93)	-0.09 (-0.48, 0.31)	0.00 (-0.04, 0.05)	-0.01 (-0.07, 0.04)	**-0.17 (-0.33, -0.01)**
Urban green in 300m (7.65)	0.24 (-0.14, 0.62)	0.37 (-0.18, 0.92)	0.21 (-0.17, 0.60)	-0.03 (-0.07, 0.01)	-0.03 (-0.08, 0.02)	-0.04 (-0.20, 0.12)
Agricultural green in 300m (19.17)	0.05 (-0.25, 0.34)	0.31 (-0.13, 0.74)	0.02 (-0.28, 0.32)	-0.01 (-0.04, 0.03)	0.00 (-0.04, 0.04)	**-0.15 (-0.27, -0.03)**
Natural green in 300m (yes vs. no)	0.06 (-0.86, 0.98)	-0.34 (-1.67, 1.00)	**-1.17 (-2.10, -0.24)**	0.07 (-0.03, 0.17)	-0.06 (-0.18, 0.07)	0.10 (-0.29, 0.48)
Average NDVI in 3000m (0.12)	0.30 (-0.14, 0.75)	0.38 (-0.28, 1.04)	0.09 (-0.38, 0.55)	-0.01 (-0.06, 0.04)	-0.04 (-0.10, 0.02)	0.04 (-0.15, 0.23)
Total green space in 3000m (30.39)	0.49 (-0.01, 0.99)	0.29 (-0.45, 1.02)	-0.03 (-0.54, 0.49)	-0.01 (-0.06, 0.05)	-0.01 (-0.08, 0.05)	-0.03 (-0.24, 0.18)
Urban green in 3000m (3.86)	-0.05 (-0.71, 0.61)	0.58 (-0.38, 1.54)	0.32 (-0.35, 0.99)	0.01 (-0.06, 0.08)	-0.03 (-0.12, 0.06)	-0.06 (-0.33, 0.22)
Agricultural green in 3000m (37.01)	0.53 (-0.34, 1.40)	0.84 (-0.44, 2.11)	0.30 (-0.59, 1.19)	0.00 (-0.09, 0.10)	-0.04 (-0.15, 0.08)	-0.07 (-0.43, 0.30)
Natural green in 3000m (9.33)	0.06 (-0.27, 0.39)	0.24 (-0.24, 0.71)	-0.01 (-0.34, 0.32)	0.00 (-0.04, 0.03)	-0.03 (-0.08, 0.01)	-0.07 (-0.20, 0.07)
NO_2 (8.58 μg/m^3)	-0.45 (-0.93, 0.02)	-0.12 (-0.97, 0.74)	0.29 (-0.31, 0.89)	0.00 (-0.05, 0.05)	0.03 (-0.03, 0.10)	0.12 (-0.08, 0.31)
$PM_{2.5}$ absorbance (0.29 x 10^{-5}/m)	**-0.66 (-1.09, -0.22)**	-0.41 (-1.08, 0.27)	0.30 (-0.16, 0.77)	0.00 (-0.05, 0.05)	-0.02 (-0.07, 0.04)	-0.01 (-0.19, 0.17)
PM_{10} (0.97 μg/m^3)	**-0.39 (-0.74, -0.04)**	-0.13 (-0.65, 0.39)	0.17 (-0.19, 0.53)	0.00 (-0.03, 0.04)	-0.02 (-0.07, 0.02)	-0.03 (-0.17, 0.12)
$PM_{2.5}$ (1.16 μg/m^3)	**-1.01 (-1.62, -0.41)**	-0.69 (-1.64, 0.25)	0.54 (-0.11, 1.19)	-0.01 (-0.07, 0.06)	-0.03 (-0.11, 0.05)	-0.02 (-0.27, 0.23)
OP^{ESR} (249.57 A.U./m^3)	**-0.69 (-1.25, -0.12)**	-0.40 (-1.25, 0.45)	0.28 (-0.31, 0.88)	0.01 (-0.05, 0.07)	0.00 (-0.07, 0.08)	0.18 (-0.06, 0.41)
OP^{DTT} (0.26 nmol DTT/min/m^3)	-0.01 (-0.48, 0.46)	-0.35 (-1.03, 0.33)	0.28 (-0.19, 0.75)	-0.01 (-0.06, 0.04)	0.06 (0.00, 0.12)	0.11 (-0.08, 0.31)
Road traffic noise (6.90 dB(A))	-0.07 (-0.50, 0.35)	0.04 (-0.57, 0.65)	-0.02 (-0.44, 0.41)	-0.01 (-0.06, 0.03)	0.00 (-0.05, 0.06)	**-0.20 (-0.37, -0.02)**
Railway noise (8.45 dB(A))	-0.36 (-0.78, 0.05)	-0.26 (-0.87, 0.34)	0.04 (-0.38, 0.46)	0.02 (-0.02, 0.07)	-0.01 (-0.06, 0.05)	-0.06 (-0.23, 0.11)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-c).
Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development and neighborhood socioeconomic status.
[b] Additionally adjusted for cuff size, the room temperature during the medical examination and the average of the ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure are also adjusted for short-term air pollution levels.
[c] Additionally adjusted for the storage time of the blood samples.

Table S6. Unadjusted associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c at age 16.

Exposure (increment)	WC (cm)	SBP (mmHg)	DBP (mmHg)	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol)
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.12)	-0.05 (-0.68, 0.59)	0.24 (-0.71, 1.20)	-0.13 (-0.78, 0.52)	-0.02 (-0.09, 0.05)	-0.06 (-0.14, 0.02)	-0.08 (-0.31, 0.14)
Total green space in 300m (23.40)	-0.11 (-0.65, 0.44)	0.63 (-0.18, 1.45)	0.09 (-0.47, 0.64)	0.00 (-0.06, 0.06)	-0.05 (-0.12, 0.02)	-0.05 (-0.24, 0.14)
Urban green in 300m (11.24)	-0.07 (-0.76, 0.61)	-0.52 (-1.54, 0.50)	0.27 (-0.43, 0.97)	-0.03 (-0.11, 0.05)	-0.02 (-0.10, 0.06)	0.10 (-0.14, 0.34)
Agricultural green in 300m (17.69)	-0.24 (-0.75, 0.28)	0.35 (-0.42, 1.12)	0.19 (-0.33, 0.72)	0.02 (-0.04, 0.08)	-0.02 (-0.08, 0.05)	-0.04 (-0.22, 0.14)
Natural green in 300m (yes vs. no)	0.71 (-0.37, 1.79)	0.48 (-1.14, 2.09)	-0.60 (-1.70, 0.51)	-0.08 (-0.21, 0.04)	-0.09 (-0.22, 0.05)	0.12 (-0.26, 0.49)
Average NDVI in 3000m (0.09)	0.20 (-0.41, 0.81)	0.12 (-0.81, 1.05)	-0.45 (-1.09, 0.18)	-0.05 (-0.12, 0.01)	0.00 (-0.08, 0.07)	-0.09 (-0.30, 0.12)
Total green space in 3000m (19.76)	**0.65 (0.06, 1.25)**	0.65 (-0.24, 1.53)	-0.44 (-1.04, 0.17)	0.03 (-0.03, 0.10)	0.04 (-0.03, 0.11)	0.03 (-0.18, 0.24)
Urban green in 3000m (7.10)	1.41 (-0.51, 3.34)	-0.07 (-2.95, 2.81)	-1.66 (-3.62, 0.30)	0.10 (-0.12, 0.31)	0.10 (-0.14, 0.33)	0.52 (-0.15, 1.18)
Agricultural green in 3000m (31.62)	**2.00 (0.16, 3.85)**	0.89 (-1.88, 3.65)	-1.78 (-3.66, 0.09)	0.13 (-0.07, 0.34)	0.12 (-0.10, 0.35)	0.47 (-0.17, 1.12)
Natural green in 3000m (12.53)	0.83 (0.00, 1.66)	0.03 (-1.23, 1.28)	**-1.19 (-2.04, -0.34)**	0.02 (-0.07, 0.11)	0.07 (-0.03, 0.17)	0.16 (-0.12, 0.45)
NO_2 (7.92 μg/m^3)	**-0.92 (-1.60, -0.23)**	-0.76 (-1.78, 0.27)	**0.80 (0.10, 1.49)**	-0.06 (-0.13, 0.02)	-0.02 (-0.10, 0.06)	**-0.24 (-0.47, 0.00)**
$PM_{2.5}$ absorbance (0.31 x 10^{-5}/m)	**-1.00 (-1.72, -0.27)**	-0.64 (-1.72, 0.44)	**0.81 (0.08, 1.54)**	-0.06 (-0.14, 0.02)	-0.07 (-0.15, 0.02)	**-0.33 (-0.58, -0.08)**
PM_{10} (0.84 μg/m^3)	-0.30 (-0.84, 0.23)	-0.29 (-1.10, 0.51)	0.35 (-0.20, 0.89)	-0.05 (-0.10, 0.01)	**-0.09 (-0.15, -0.03)**	-0.10 (-0.28, 0.09)
$PM_{2.5}$ (1.22 μg/m^3)	**-1.25 (-2.06, -0.44)**	-0.49 (-1.70, 0.72)	**1.25 (0.43, 2.08)**	-0.06 (-0.15, 0.03)	-0.05 (-0.15, 0.05)	**-0.41 (-0.69, -0.13)**
OP^{ESR} (269.95 A.U./m^3)	**-1.40 (-2.21, -0.60)**	-0.82 (-2.03, 0.39)	**0.88 (0.06, 1.70)**	-0.06 (-0.15, 0.03)	-0.01 (-0.11, 0.09)	**-0.43 (-0.71, -0.16)**
OP^{DTT} (0.25 nmol DTT/min/m^3)	-0.56 (-1.19, 0.07)	**-0.95 (-1.89, -0.01)**	0.59 (-0.05, 1.23)	-0.02 (-0.09, 0.05)	0.01 (-0.07, 0.09)	-0.05 (-0.27, 0.16)
Road traffic noise (6.70 dB(A))	-0.09 (-0.66, 0.48)	0.11 (-0.74, 0.96)	0.08 (-0.50, 0.65)	-0.04 (-0.10, 0.02)	-0.01 (-0.08, 0.06)	-0.09 (-0.29, 0.11)
Railway noise (7.60 dB(A))	**-0.53 (-1.04, -0.03)**	-0.29 (-1.04, 0.46)	0.13 (-0.38, 0.64)	0.01 (-0.05, 0.06)	-0.02 (-0.08, 0.04)	-0.01 (-0.18, 0.16)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size.
Statistically significant results are highlighted in bold ($p < 0.05$).

Table S7. Associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c at age 16 – model II.[a]

Exposure (increment)	WC (cm)	SBP (mmHg) [b]	DBP (mmHg) [b]	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol) [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.12)	-0.08 (-0.69, 0.54)	0.28 (-0.69, 1.25)	0.02 (-0.66, 0.71)	0.00 (-0.07, 0.07)	-0.06 (-0.15, 0.02)	-0.11 (-0.34, 0.12)
Total green space in 300m (23.40)	-0.12 (-0.66, 0.41)	0.48 (-0.35, 1.31)	0.16 (-0.43, 0.75)	0.01 (-0.05, 0.07)	-0.07 (-0.14, 0.01)	-0.06 (-0.26, 0.14)
Urban green in 300m (11.24)	-0.05 (-0.72, 0.62)	-0.49 (-1.51, 0.53)	0.37 (-0.35, 1.10)	-0.03 (-0.10, 0.05)	-0.01 (-0.10, 0.08)	0.14 (-0.11, 0.39)
Agricultural green in 300m (17.69)	-0.07 (-0.59, 0.44)	0.51 (-0.28, 1.30)	0.25 (-0.31, 0.81)	0.02 (-0.04, 0.07)	-0.03 (-0.10, 0.04)	-0.07 (-0.27, 0.12)
Natural green in 300m (yes vs. no)	0.08 (-0.97, 1.14)	-0.41 (-2.03, 1.21)	-0.45 (-1.60, 0.70)	-0.02 (-0.14, 0.10)	-0.09 (-0.23, 0.05)	0.16 (-0.24, 0.56)
Average NDVI in 3000m (0.09)	0.10 (-0.50, 0.71)	0.03 (-0.92, 0.98)	-0.43 (-1.10, 0.24)	-0.04 (-0.11, 0.03)	0.00 (-0.08, 0.08)	-0.14 (-0.36, 0.09)
Total green space in 3000m (19.76)	0.46 (-0.13, 1.04)	0.51 (-0.40, 1.43)	-0.42 (-1.07, 0.22)	0.03 (-0.03, 0.10)	0.03 (-0.05, 0.11)	-0.02 (-0.24, 0.21)
Urban green in 3000m (7.10)	1.09 (-0.81, 2.99)	0.37 (-2.53, 3.27)	-0.78 (-2.83, 1.27)	0.13 (-0.08, 0.34)	0.15 (-0.10, 0.40)	0.51 (-0.20, 1.22)
Agricultural green in 3000m (31.62)	1.52 (-0.31, 3.34)	1.15 (-1.66, 3.97)	-0.98 (-2.97, 1.01)	0.16 (-0.04, 0.36)	0.16 (-0.08, 0.40)	0.41 (-0.28, 1.10)
Natural green in 3000m (12.53)	0.51 (-0.31, 1.33)	-0.05 (-1.31, 1.21)	**-0.99 (-1.88, -0.10)**	0.04 (-0.05, 0.13)	0.07 (-0.04, 0.18)	0.13 (-0.18, 0.43)
NO_2 (7.92 μg/m^3)	-0.69 (-1.39, 0.01)	-0.90 (-2.11, 0.32)	0.54 (-0.32, 1.40)	-0.06 (-0.13, 0.02)	-0.01 (-0.10, 0.08)	-0.14 (-0.40, 0.12)
$PM_{2.5}$ absorbance (0.31 x 10^{-5}/m)	-0.72 (-1.45, 0.02)	-0.52 (-1.71, 0.67)	0.73 (-0.11, 1.58)	-0.05 (-0.13, 0.04)	-0.06 (-0.15, 0.04)	**-0.29 (-0.57, -0.01)**
PM_{10} (0.84 μg/m^3)	-0.13 (-0.67, 0.41)	-0.04 (-0.87, 0.78)	0.48 (-0.11, 1.07)	-0.04 (-0.10, 0.02)	**-0.08 (-0.15, -0.01)**	-0.09 (-0.29, 0.11)
$PM_{2.5}$ (1.22 μg/m^3)	**-1.03 (-1.86, -0.21)**	-0.58 (-1.94, 0.79)	**1.11 (0.15, 2.08)**	-0.05 (-0.14, 0.05)	-0.04 (-0.15, 0.07)	**-0.38 (-0.69, -0.06)**
OP^{ESR} (269.95 A.U./m^3)	**-1.25 (-2.09, -0.41)**	-1.02 (-2.40, 0.35)	0.68 (-0.30, 1.65)	-0.04 (-0.14, 0.05)	0.01 (-0.10, 0.12)	**-0.35 (-0.66, -0.03)**
OP^{DTT} (0.25 nmol DTT/min/m^3)	-0.35 (-0.97, 0.27)	-0.72 (-1.67, 0.23)	0.52 (-0.16, 1.19)	-0.04 (-0.11, 0.03)	0.03 (-0.05, 0.11)	-0.01 (-0.24, 0.22)
Road traffic noise (6.70 dB(A))	-0.22 (-0.77, 0.33)	0.13 (-0.72, 0.97)	0.07 (-0.53, 0.66)	-0.02 (-0.08, 0.04)	0.01 (-0.07, 0.08)	-0.13 (-0.34, 0.08)
Railway noise (7.60 dB(A))	-0.40 (-0.88, 0.09)	-0.21 (-0.95, 0.54)	0.21 (-0.32, 0.74)	0.02 (-0.03, 0.08)	-0.01 (-0.07, 0.06)	-0.01 (-0.19, 0.17)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-c).
Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development and neighborhood socioeconomic status.
[b] Additionally adjusted for cuff size, the room temperature during the medical examination and the average of the ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure are also adjusted for short-term air pollution levels.
[c] Additionally adjusted for the storage time of the blood samples.

Table S8. Associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c for quartiles of exposure at age 12 and 16.[a]

Exposure (increment)	WC (cm)	SBP (mmHg) [b]	DBP (mmHg) [b]	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol) [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Age 12						
Total percentage of green space in 300m						
Quartile 1 (< 2.44)	ref	ref	ref	ref	ref	ref
Quartile 2 (2.44 - 11.46)	**1.21 (0.26, 2.17)**	0.96 (-0.42, 2.34)	0.18 (-0.79, 1.15)	0.00 (-0.11, 0.10)	0.05 (-0.08, 0.17)	-0.07 (-0.47, 0.33)
Quartile 3 (11.46 - 28.83)	**1.06 (0.10, 2.02)**	0.79 (-0.59, 2.17)	0.12 (-0.85, 1.09)	-0.06 (-0.17, 0.04)	-0.07 (-0.20, 0.05)	-0.19 (-0.59, 0.21)
Quartile 4 (≥ 28.83)	0.48 (-0.52, 1.47)	0.85 (-0.58, 2.28)	0.10 (-0.90, 1.10)	0.02 (-0.09, 0.13)	0.00 (-0.13, 0.13)	-0.29 (-0.70, 0.12)
Total percentage of green space in 3000m						
Quartile 1 (<39.98)	ref	ref	ref	ref	ref	ref
Quartile 2 (39.98 - 55.93)	**1.07 (0.10, 2.05)**	**1.54 (0.13, 2.95)**	0.51 (-0.47, 1.50)	-0.01 (-0.11, 0.10)	0.08 (-0.05, 0.22)	0.23 (-0.18, 0.64)
Quartile 3 (55.93 - 70.29)	0.94 (-0.08, 1.95)	0.81 (-0.65, 2.27)	0.56 (-0.46, 1.58)	-0.02 (-0.13, 0.09)	-0.01 (-0.14, 0.12)	0.26 (-0.16, 0.68)
Quartile 4 (≥70.29)	0.36 (-0.69, 1.42)	0.06 (-1.46, 1.58)	0.10 (-0.97, 1.16)	-0.01 (-0.12, 0.11)	-0.01 (-0.15, 0.13)	0.10 (-0.34, 0.54)
Agricultural green in 3000m						
Quartile 1 (< 24.64)	ref	ref	ref	ref	ref	ref
Quartile 2 (24.64 - 43.46)	0.10 (-0.99, 1.19)	1.56 (-0.01, 3.12)	1.00 (-0.09, 2.09)	0.00 (-0.12, 0.13)	0.10 (-0.05, 0.24)	-0.04 (-0.50, 0.42)
Quartile 3 (43.46 - 61.55)	0.63 (-0.61, 1.88)	1.18 (-0.61, 2.96)	0.94 (-0.31, 2.19)	-0.04 (-0.17, 0.10)	0.00 (-0.17, 0.16)	0.23 (-0.30, 0.75)
Quartile 4 (≥61.55)	-0.40 (-1.89, 1.08)	0.08 (-2.05, 2.22)	0.57 (-0.93, 2.06)	0.02 (-0.14, 0.18)	-0.03 (-0.22, 0.17)	-0.03 (-0.65, 0.59)
PM_{10} (µg/m^3)						
Quartile 1 (< 24.02)	ref	ref	ref	ref	ref	ref
Quartile 2 (24.02 - 24.47)	0.13 (-0.87, 1.12)	0.18 (-1.30, 1.65)	0.42 (-0.60, 1.44)	0.02 (-0.08, 0.13)	0.02 (-0.11, 0.15)	0.02 (-0.39, 0.43)
Quartile 3 (24.47 - 24.99)	0.57 (-0.47, 1.61)	0.51 (-1.03, 2.05)	0.28 (-0.79, 1.34)	0.09 (-0.03, 0.20)	0.07 (-0.07, 0.20)	0.35 (-0.08, 0.78)
Quartile 4 (≥ 24.99)	-0.71 (-1.76, 0.35)	-0.32 (-1.89, 1.25)	0.32 (-0.76, 1.41)	-0.03 (-0.14, 0.09)	-0.08 (-0.22, 0.06)	0.01 (-0.42, 0.45)
Road traffic noise (dB(A))						
Quartile 1 (< 49.40)	ref	ref	ref	ref	ref	ref
Quartile 2 (49.40 - 52.40)	0.37 (-0.61, 1.34)	-0.07 (-1.48, 1.34)	0.54 (-0.44, 1.52)	-0.04 (-0.14, 0.06)	0.03 (-0.10, 0.16)	-0.24 (-0.63, 0.16)
Quartile 3 (52.40 - 56.30)	-0.03 (-1.01, 0.94)	-0.09 (-1.50, 1.32)	-0.05 (-1.04, 0.94)	-0.07 (-0.18, 0.03)	0.01 (-0.12, 0.14)	-0.33 (-0.73, 0.07)
Quartile 4 (≥ 56.30)	0.14 (-0.85, 1.13)	0.10 (-1.32, 1.53)	-0.14 (-1.14, 0.85)	-0.04 (-0.14, 0.07)	-0.03 (-0.16, 0.10)	**-0.47 (-0.87, -0.07)**
Age 16						
Total percentage of green space in 300m						
Quartile 1 (< 11.82)	ref	ref	ref	ref	ref	ref
Quartile 2 (11.82 - 19.88)	0.65 (-0.62, 1.92)	0.10 (-1.84, 2.04)	0.99 (-0.38, 2.37)	-0.09 (-0.23, 0.05)	-0.06 (-0.22, 0.11)	0.15 (-0.32, 0.63)
Quartile 3 (19.88 - 35.13)	0.71 (-0.57, 1.99)	-0.63 (-2.61, 1.35)	1.03 (-0.37, 2.42)	**-0.15 (-0.29, -0.01)**	-0.01 (-0.18, 0.16)	0.20 (-0.27, 0.68)
Quartile 4 (≥ 35.13)	-0.24 (-1.55, 1.07)	0.89 (-1.12, 2.90)	0.87 (-0.55, 2.29)	-0.04 (-0.19, 0.10)	-0.11 (-0.29, 0.06)	-0.25 (-0.74, 0.24)

Total percentage of green space in 3000m						
Quartile 1 (< 48.88)	ref	ref	ref	ref	ref	ref
Quartile 2 (48.88 - 58.78)	0.01 (-1.29, 1.30)	0.08 (-1.91, 2.07)	0.34 (-1.06, 1.75)	0.01 (-0.14, 0.15)	0.12 (-0.05, 0.30)	-0.15 (-0.63, 0.34)
Quartile 3 (58.78 - 68.32)	0.61 (-0.69, 1.92)	-0.24 (-2.25, 1.77)	0.82 (-0.60, 2.24)	-0.03 (-0.18, 0.11)	0.15 (-0.03, 0.32)	-0.03 (-0.52, 0.45)
Quartile 4 (≥ 68.32)	0.19 (-1.18, 1.57)	0.63 (-1.49, 2.75)	-0.27 (-1.77, 1.23)	0.09 (-0.06, 0.25)	0.08 (-0.10, 0.26)	-0.48 (-0.99, 0.04)
Agricultural green in 3000m						
Quartile 1 (< 25.37)	ref	ref	ref	ref	ref	ref
Quartile 2 (25.37 - 42.68)	-0.59 (-2.23, 1.05)	0.18 (-2.33, 2.69)	1.35 (-0.42, 3.11)	0.12 (-0.06, 0.30)	0.20 (-0.01, 0.42)	-0.01 (-0.62, 0.59)
Quartile 3 (42.68 - 56.85)	-0.17 (-2.41, 2.06)	-0.94 (-4.34, 2.47)	1.51 (-0.88, 3.91)	0.02 (-0.22, 0.27)	0.24 (-0.05, 0.54)	-0.31 (-1.13, 0.52)
Quartile 4 (≥ 56.85)	-0.65 (-3.57, 2.26)	-1.01 (-5.44, 3.43)	1.66 (-1.46, 4.78)	0.14 (-0.18, 0.46)	0.29 (-0.10, 0.67)	-0.35 (-1.43, 0.73)
PM_{10} (μg/m^3)						
Quartile 1 (<23.99)	ref	ref	ref	ref	ref	ref
Quartile 2 (23.99 - 24.37)	**-1.34 (-2.66, -0.02)**	-1.78 (-3.82, 0.26)	0.38 (-1.06, 1.82)	-0.13 (-0.28, 0.01)	0.03 (-0.15, 0.20)	0.14 (-0.36, 0.63)
Quartile 3 (24.37 - 24.83)	-0.57 (-1.94, 0.79)	-0.74 (-2.83, 1.36)	0.31 (-1.18, 1.79)	0.06 (-0.09, 0.21)	0.06 (-0.12, 0.24)	0.19 (-0.32, 0.71)
Quartile 4 (≥ 24.83)	-0.40 (-1.83, 1.02)	-1.24 (-3.42, 0.95)	-0.28 (-1.83, 1.26)	-0.12 (-0.28, 0.03)	**-0.19 (-0.38, 0.00)**	0.21 (-0.32, 0.74)
Road traffic noise (dB(A))						
Quartile 1 (<49.00)	ref	ref	ref	ref	ref	ref
Quartile 2 (49.00 - 52.10)	0.16 (-1.13, 1.45)	-0.96 (-2.95, 1.03)	-1.24 (-2.64, 0.16)	-0.03 (-0.18, 0.12)	0.15 (-0.03, 0.32)	0.28 (-0.20, 0.77)
Quartile 3 (52.10 - 55.70)	-0.05 (-1.34, 1.25)	-0.74 (-2.72, 1.24)	-1.23 (-2.63, 0.17)	-0.03 (-0.17, 0.12)	0.14 (-0.03, 0.31)	0.29 (-0.20, 0.77)
Quartile 4 (≥ 55.70)	-0.50 (-1.80, 0.81)	0.25 (-1.76, 2.27)	-0.40 (-1.82, 1.02)	-0.03 (-0.17, 0.12)	0.00 (-0.18, 0.17)	-0.13 (-0.63, 0.36)

Associations with the percentage of agricultural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-c). Statistically significant results are highlighted in bold (p <0.05).

[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.

[b] Additionally adjusted for cuff size, the room temperature during the medical examination and the average of the ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure are also adjusted for short-term air pollution levels.

[c] Additionally adjusted for the storage time of the blood samples.

Table S9. Associations of green space, air pollution and traffic noise with the cardiometabolic risk score at age 12 and 16 in adolescents who have lived ≥ two years at their current home address.[a]

Exposure	Age 12 (n=1367)	Age 16 (n=756)
	β (95% CI)	**β (95% CI)**
Average NDVI in 300m	0.03 (-0.15, 0.22)	-0.18 (-0.40, 0.04)
Total percentage of green space in 300m		
Quartile 1	ref	ref
Quartile 2	0.19 (-0.15, 0.53)	0.07 (-0.36, 0.50)
Quartile 3	0.05 (-0.29, 0.40)	0.14 (-0.29, 0.57)
Quartile 4	0.00 (-0.36, 0.35)	-0.05 (-0.50, 0.40)
Urban green in 300m	0.02 (-0.11, 0.16)	-0.02 (-0.25, 0.22)
Agricultural green in 300m	-0.08 (-0.19, 0.03)	-0.03 (-0.21, 0.15)
Natural green in 300m (yes vs. no)	0.07 (-0.26, 0.40)	-0.07 (-0.43, 0.29)
Average NDVI in 3000m	0.12 (-0.10, 0.33)	-0.14 (-0.35, 0.06)
Total percentage of green space in 3000m		
Quartile 1	ref	ref
Quartile 2	0.31 (-0.04, 0.66)	-0.14 (-0.58, 0.30)
Quartile 3	0.34 (-0.03, 0.70)	0.06 (-0.38, 0.50)
Quartile 4	0.05 (-0.33, 0.44)	-0.02 (-0.49, 0.45)
Urban green in 3000m	-0.01 (-0.23, 0.22)	-0.13 (-0.71, 0.44)
Agricultural green in 3000m		
Quartile 1	ref	ref
Quartile 2	0.26 (-0.14, 0.66)	0.08 (-0.48, 0.63)
Quartile 3	0.28 (-0.17, 0.73)	-0.28 (-1.03, 0.47)
Quartile 4	-0.04 (-0.58, 0.50)	-0.23 (-1.21, 0.76)
Natural green in 3000m	0.01 (-0.11, 0.14)	-0.07 (-0.32, 0.18)
NO_2	0.09 (-0.17, 0.35)	0.06 (-0.27, 0.39)
$PM_{2.5}$ absorbance	-0.09 (-0.31, 0.14)	-0.06 (-0.41, 0.30)
PM_{10}		
Quartile 1	ref	ref
Quartile 2	0.16 (-0.19, 0.51)	**-0.45 (-0.90, -0.01)**
Quartile 3	**0.48 (0.11, 0.85)**	-0.06 (-0.52, 0.40)
Quartile 4	-0.05 (-0.43, 0.33)	-0.27 (-0.75, 0.20)
$PM_{2.5}$	-0.14 (-0.50, 0.22)	-0.03 (-0.49, 0.44)
OP^{ESR}	0.14 (-0.18, 0.45)	-0.15 (-0.59, 0.29)
OP^{DTT}	0.08 (-0.12, 0.28)	-0.05 (-0.27, 0.17)
Road traffic noise		
Quartile 1	ref	ref
Quartile 2	-0.09 (-0.43, 0.26)	0.13 (-0.31, 0.56)
Quartile 3	-0.27 (-0.62, 0.08)	0.04 (-0.40, 0.47)
Quartile 4	-0.16 (-0.51, 0.19)	-0.15 (-0.60, 0.30)
Railway noise	0.00 (-0.15, 0.14)	0.03 (-0.14, 0.20)

Abbreviations: CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure or quartiles of exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnote a).
Statistically significant results are highlighted in bold ($p < 0.05$).
[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.

Table S10. Associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c in adolescents aged 12 years who have lived at their current home address ≥ two years (n=1367).[a]

Exposure (increment)	WC (cm)	SBP (mmHg) [b]	DBP (mmHg) [b]	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol) [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.13)	-0.16 (-0.71, 0.39)	0.39 (-0.41, 1.19)	0.21 (-0.34, 0.77)	0.03 (-0.03, 0.09)	-0.05 (-0.13, 0.02)	-0.09 (-0.32, 0.13)
Total percentage of green space in 300m						
Quartile 1 (< 2.44)	ref	ref	ref	ref	ref	ref
Quartile 2 (2.44 - 11.46)	**1.34 (0.34, 2.34)**	0.87 (-0.58, 2.31)	0.28 (-0.73, 1.28)	0.01 (-0.10, 0.12)	0.04 (-0.09, 0.18)	-0.13 (-0.55, 0.29)
Quartile 3 (11.46 - 28.83)	**1.09 (0.10, 2.09)**	0.90 (-0.54, 2.34)	0.31 (-0.69, 1.31)	-0.04 (-0.15, 0.07)	-0.07 (-0.20, 0.07)	-0.18 (-0.60, 0.23)
Quartile 4 (≥ 28.83)	0.27 (-0.77, 1.31)	0.93 (-0.57, 2.44)	0.19 (-0.85, 1.24)	0.01 (-0.10, 0.13)	0.00 (-0.14, 0.14)	-0.32 (-0.76, 0.12)
Urban green in 300m (7.65)	0.24 (-0.16, 0.64)	0.35 (-0.24, 0.94)	0.26 (-0.14, 0.67)	-0.03 (-0.07, 0.02)	-0.03 (-0.09, 0.02)	-0.03 (-0.20, 0.14)
Agricultural green in 300m (19.17)	-0.12 (-0.45, 0.20)	0.25 (-0.23, 0.72)	0.04 (-0.29, 0.37)	-0.01 (-0.05, 0.02)	0.01 (-0.04, 0.05)	**-0.17 (-0.30, -0.03)**
Natural green in 300m (yes vs. no)	0.23 (-0.73, 1.18)	-0.38 (-1.77, 1.00)	**-1.00 (-1.96, -0.04)**	0.08 (-0.02, 0.19)	-0.07 (-0.20, 0.06)	0.07 (-0.33, 0.47)
Average NDVI in 3000m (0.12)	0.08 (-0.57, 0.73)	0.34 (-0.61, 1.29)	0.48 (-0.18, 1.14)	-0.01 (-0.08, 0.07)	-0.03 (-0.11, 0.06)	0.11 (-0.16, 0.38)
Total percentage of green space in 3000m						
Quartile 1 (<39.98)	ref	ref	ref	ref	ref	ref
Quartile 2 (39.98 - 55.93)	1.01 (-0.02, 2.03)	1.35 (-0.13, 2.83)	0.55 (-0.48, 1.57)	-0.01 (-0.13, 0.10)	0.09 (-0.05, 0.22)	0.24 (-0.19, 0.67)
Quartile 3 (55.93 - 70.29)	0.86 (-0.21, 1.93)	1.08 (-0.47, 2.63)	0.87 (-0.20, 1.95)	-0.02 (-0.14, 0.10)	0.01 (-0.13, 0.16)	**0.47 (0.02, 0.92)**
Quartile 4 (≥70.29)	0.18 (-0.93, 1.30)	-0.02 (-1.63, 1.60)	0.22 (-0.91, 1.34)	0.00 (-0.12, 0.12)	-0.01 (-0.16, 0.14)	0.07 (-0.40, 0.54)
Urban green in 3000m (3.86)	-0.52 (-1.18, 0.15)	0.14 (-0.83, 1.11)	0.32 (-0.36, 0.99)	0.03 (-0.05, 0.10)	-0.05 (-0.14, 0.04)	-0.01 (-0.28, 0.27)
Agricultural green in 3000m						
Quartile 1 (< 24.64)	ref	ref	ref	ref	ref	ref
Quartile 2 (24.64 - 43.46)	-0.20 (-1.35, 0.94)	1.47 (-0.19, 3.12)	1.12 (-0.04, 2.27)	0.02 (-0.11, 0.15)	0.10 (-0.06, 0.26)	-0.03 (-0.52, 0.46)
Quartile 3 (43.46 - 61.55)	0.44 (-0.88, 1.76)	1.18 (-0.73, 3.08)	1.06 (-0.26, 2.38)	-0.04 (-0.18, 0.11)	0.01 (-0.18, 0.17)	0.32 (-0.24, 0.88)
Quartile 4 (≥61.55)	-0.94 (-2.52, 0.63)	-0.02 (-2.30, 2.25)	0.85 (-0.73, 2.44)	0.04 (-0.14, 0.21)	-0.05 (-0.26, 0.17)	-0.10 (-0.77, 0.56)
Natural green in 3000m (9.33)	-0.02 (-0.38, 0.34)	0.20 (-0.31, 0.71)	0.08 (-0.28, 0.44)	0.00 (-0.04, 0.04)	-0.02 (-0.07, 0.02)	-0.05 (-0.20, 0.10)
NO_2 (8.58 μg/m^3)	0.00 (-0.76, 0.76)	-0.07 (-1.19, 1.05)	0.11 (-0.67, 0.88)	0.01 (-0.07, 0.09)	0.03 (-0.07, 0.13)	0.21 (-0.11, 0.53)
$PM_{2.5}$ absorbance (0.29 x 10^{-5}/m)	-0.51 (-1.17, 0.15)	-0.08 (-1.08, 0.91)	0.29 (-0.40, 0.97)	0.02 (-0.06, 0.09)	-0.06 (-0.15, 0.02)	-0.09 (-0.37, 0.19)

PM_{10} (µg/m³)						
Quartile 1 (< 24.02)	ref	ref	ref	ref	ref	ref
Quartile 2 (24.02 - 24.47)	0.37 (-0.67, 1.42)	0.45 (-1.10, 2.01)	0.61 (-0.46, 1.68)	0.04 (-0.08, 0.15)	0.03 (-0.11, 0.16)	0.14 (-0.30, 0.57)
Quartile 3 (24.47 - 24.99)	0.84 (-0.25, 1.93)	0.87 (-0.75, 2.49)	0.46 (-0.66, 1.58)	0.10 (-0.02, 0.23)	0.05 (-0.09, 0.20)	**0.48 (0.02, 0.93)**
Quartile 4 (≥ 24.99)	-0.45 (-1.56, 0.66)	-0.15 (-1.81, 1.50)	0.49 (-0.66, 1.63)	-0.02 (-0.14, 0.11)	-0.08 (-0.23, 0.07)	0.08 (-0.38, 0.54)
$PM_{2.5}$ (1.16 µg/m³)	-1.02 (-2.04, 0.01)	0.14 (-1.42, 1.70)	0.77 (-0.31, 1.84)	0.00 (-0.12, 0.12)	-0.10 (-0.24, 0.05)	-0.18 (-0.62, 0.25)
OP^{ESR} (249.57 A.U./m³)	-0.45 (-1.35, 0.44)	0.09 (-1.22, 1.40)	0.39 (-0.52, 1.30)	0.02 (-0.08, 0.12)	0.03 (-0.09, 0.15)	0.31 (-0.07, 0.69)
OP^{DTT} (0.26 nmol DTT/min/m³)	0.33 (-0.25, 0.91)	-0.25 (-1.09, 0.59)	0.16 (-0.42, 0.74)	-0.01 (-0.08, 0.05)	0.05 (-0.02, 0.13)	0.17 (-0.07, 0.41)
Road traffic noise (dB(A))						
Quartile 1 (< 49.40)	ref	ref	ref	ref	ref	ref
Quartile 2 (49.40 - 52.40)	0.10 (-0.92, 1.12)	0.21 (-1.27, 1.69)	0.80 (-0.22, 1.83)	-0.06 (-0.17, 0.06)	0.01 (-0.12, 0.14)	-0.19 (-0.61, 0.23)
Quartile 3 (52.40 - 56.30)	0.04 (-0.99, 1.07)	0.28 (-1.21, 1.78)	0.07 (-0.96, 1.11)	-0.08 (-0.20, 0.03)	0.00 (-0.14, 0.13)	-0.32 (-0.74, 0.11)
Quartile 4 (≥ 56.30)	0.19 (-0.84, 1.23)	0.35 (-1.15, 1.85)	0.12 (-0.92, 1.15)	-0.04 (-0.15, 0.08)	-0.02 (-0.16, 0.11)	-0.42 (-0.85, 0.01)
Railway noise (8.45 dB(A))	-0.13 (-0.58, 0.31)	-0.11 (-0.75, 0.54)	-0.03 (-0.48, 0.42)	0.02 (-0.03, 0.07)	0.00 (-0.06, 0.06)	-0.04 (-0.22, 0.14)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure or quartiles of exposure, except for natural green in a buffer of 300m.

Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-c).

Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.

[b] Additionally adjusted for cuff size, the room temperature during the medical examination and the average of the ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure are also adjusted for short-term air pollution levels.

[c] Additionally adjusted for the storage time of the blood samples.

4

Table S11. Associations of green space, air pollution and traffic noise with waist circumference, blood pressure, cholesterol and HbA1c in adolescents aged 16 years who have lived at their current home address ≥ two years (n=756).[a]

Exposure (increment)	WC (cm)	SBP (mmHg) [b]	DBP (mmHg) [b]	Total cholesterol (mmol/L)	Total/HDL cholesterol ratio	HbA1c (mmol/mol) [c]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.12)	-0.34 (-1.01, 0.33)	0.37 (-0.68, 1.41)	0.24 (-0.49, 0.97)	-0.01 (-0.08, 0.07)	-0.08 (-0.16, 0.01)	**-0.28 (-0.53, -0.04)**
Total percentage of green space in 300m						
Quartile 1 (< 11.82)	ref	ref	ref	ref	ref	ref
Quartile 2 (11.82 - 19.88)	0.69 (-0.62, 2.00)	0.26 (-1.75, 2.27)	0.90 (-0.51, 2.30)	-0.06 (-0.20, 0.09)	-0.03 (-0.20, 0.15)	0.12 (-0.36, 0.61)
Quartile 3 (19.88 - 35.13)	0.75 (-0.58, 2.08)	-0.42 (-2.48, 1.63)	1.04 (-0.40, 2.48)	-0.12 (-0.27, 0.03)	0.00 (-0.17, 0.18)	0.15 (-0.34, 0.64)
Quartile 4 (≥ 35.13)	-0.16 (-1.52, 1.21)	1.48 (-0.63, 3.58)	0.87 (-0.60, 2.34)	-0.03 (-0.18, 0.13)	-0.11 (-0.30, 0.07)	-0.31 (-0.82, 0.19)
Urban green in 300m (11.24)	-0.24 (-0.95, 0.47)	-0.40 (-1.48, 0.69)	0.61 (-0.15, 1.37)	-0.05 (-0.12, 0.03)	0.00 (-0.10, 0.09)	0.00 (-0.26, 0.26)
Agricultural green in 300m (17.69)	-0.16 (-0.70, 0.38)	0.56 (-0.27, 1.39)	0.44 (-0.15, 1.02)	0.00 (-0.06, 0.06)	-0.02 (-0.09, 0.05)	-0.19 (-0.39, 0.01)
Natural green in 300m (yes vs. no)	-0.15 (-1.24, 0.93)	-0.39 (-2.08, 1.30)	-0.41 (-1.59, 0.78)	0.01 (-0.11, 0.13)	-0.10 (-0.24, 0.05)	0.08 (-0.32, 0.49)
Average NDVI in 3000m (0.09)	0.08 (-0.55, 0.70)	0.07 (-0.92, 1.05)	-0.41 (-1.10, 0.28)	-0.04 (-0.11, 0.03)	-0.01 (-0.09, 0.07)	-0.19 (-0.42, 0.04)
Total percentage of green space in 3000m						
Quartile 1 (< 48.88)	ref	ref	ref	ref	ref	ref
Quartile 2 (48.88 - 58.78)	0.01 (-1.31, 1.36)	0.16 (-1.92, 2.24)	0.20 (-1.26, 1.65)	0.02 (-0.13, 0.17)	0.10 (-0.07, 0.28)	-0.21 (-0.71, 0.28)
Quartile 3 (58.78 - 68.32)	0.54 (-0.81, 1.90)	-0.06 (-2.16, 2.04)	0.85 (-0.62, 2.32)	-0.02 (-0.17, 0.12)	0.14 (-0.04, 0.32)	-0.05 (-0.55, 0.45)
Quartile 4 (≥ 68.32)	0.10 (-1.32, 1.52)	0.77 (-1.44, 2.98)	-0.18 (-1.72, 1.36)	0.12 (-0.04, 0.27)	0.07 (-0.12, 0.26)	**-0.56 (-1.08, -0.03)**
Urban green in 3000m (7.10)	-0.71 (-2.48, 1.05)	-1.10 (-3.80, 1.60)	0.49 (-1.39, 2.37)	0.06 (-0.13, 0.25)	0.17 (-0.06, 0.41)	-0.04 (-0.69, 0.60)
Agricultural green in 3000m						
Quartile 1 (< 25.37)	ref	ref	ref	ref	ref	ref
Quartile 2 (25.37 - 42.68)	-0.89 (-2.60, 0.82)	0.46 (-2.18, 3.09)	1.10 (-0.74, 2.93)	0.15 (-0.04, 0.34)	**0.25 (0.03, 0.48)**	0.00 (-0.63, 0.63)
Quartile 3 (42.68 - 56.85)	-0.71 (-3.03, 1.60)	-0.52 (-4.07, 3.02)	1.34 (-1.13, 3.81)	0.07 (-0.18, 0.33)	**0.31 (0.01, 0.62)**	-0.44 (-1.29, 0.41)
Quartile 4 (≥ 56.85)	-1.41 (-4.43, 1.60)	-0.64 (-5.26, 3.98)	1.52 (-1.70, 4.73)	0.20 (-0.13, 0.53)	0.37 (-0.03, 0.76)	-0.54 (-1.65, 0.57)
Natural green in 3000m (12.53)	-0.05 (-0.81, 0.71)	-0.50 (-1.67, 0.67)	-0.58 (-1.40, 0.23)	0.01 (-0.07, 0.10)	0.08 (-0.02, 0.18)	0.00 (-0.29, 0.28)
NO_2 (7.92 μg/m^3)	-0.18 (-1.19, 0.82)	-0.49 (-2.06, 1.07)	0.08 (-1.02, 1.17)	-0.07 (-0.18, 0.04)	-0.04 (-0.17, 0.09)	**0.45 (0.08, 0.82)**
$PM_{2.5}$ absorbance (0.31 x 10^{-5}/m)	-0.08 (-1.18, 1.03)	-0.11 (-1.82, 1.59)	-0.15 (-1.34, 1.04)	-0.06 (-0.18, 0.06)	**-0.16 (-0.30, -0.01)**	0.20 (-0.21, 0.60)
PM_{10} (μg/m^3)						
Quartile 1 (<23.99)	ref	ref	ref	ref	ref	ref
Quartile 2 (23.99 - 24.37)	-1.34 (-2.69, 0.01)	-1.82 (-3.91, 0.28)	0.23 (-1.23, 1.70)	-0.14 (-0.29, 0.01)	0.00 (-0.18, 0.18)	0.14 (-0.37, 0.64)
Quartile 3 (24.37 - 24.83)	-0.51 (-1.91, 0.89)	-0.70 (-2.87, 1.46)	0.35 (-1.17, 1.86)	0.05 (-0.11, 0.20)	0.07 (-0.11, 0.26)	0.21 (-0.32, 0.73)
Quartile 4 (≥ 24.83)	-0.21 (-1.66, 1.25)	-1.58 (-3.83, 0.66)	-0.66 (-2.24, 0.91)	-0.14 (-0.30, 0.02)	-0.19 (-0.38, 0.01)	0.29 (-0.25, 0.83)

$PM_{2.5}$ (1.22 µg/m³)	-0.53 (-1.94, 0.88)	0.38 (-1.79, 2.55)	0.42 (-1.10, 1.94)	-0.04 (-0.19, 0.12)	**-0.19 (-0.38, 0.00)**	0.19 (-0.34, 0.71)
OP^{ESR} (269.95 A.U./m³)	-0.87 (-2.22, 0.47)	-0.82 (-2.91, 1.27)	-0.31 (-1.77, 1.15)	-0.05 (-0.20, 0.10)	-0.07 (-0.25, 0.11)	0.27 (-0.23, 0.77)
OP^{DTT} (0.25 nmol DTT/min/m³)	-0.21 (-0.88, 0.46)	-0.67 (-1.70, 0.35)	0.30 (-0.42, 1.02)	-0.03 (-0.11, 0.04)	0.03 (-0.06, 0.12)	0.14 (-0.10, 0.39)
Road traffic noise (dB(A))						
Quartile 1 (<49.00)	ref	ref	ref	ref	ref	ref
Quartile 2 (49.00 - 52.10)	0.36 (-0.97, 1.69)	-1.03 (-3.09, 1.03)	-1.25 (-2.69, 0.19)	-0.07 (-0.22, 0.08)	0.15 (-0.02, 0.33)	0.37 (-0.12, 0.87)
Quartile 3 (52.10 - 55.70)	0.00 (-1.33, 1.32)	-0.83 (-2.88, 1.22)	-1.20 (-2.63, 0.23)	-0.03 (-0.18, 0.12)	0.17 (0.00, 0.35)	0.34 (-0.15, 0.84)
Quartile 4 (≥ 55.70)	-0.40 (-1.75, 0.96)	-0.29 (-2.39, 1.81)	-0.56 (-2.03, 0.90)	-0.06 (-0.21, 0.10)	0.01 (-0.17, 0.20)	0.05 (-0.46, 0.56)
Railway noise (7.60 dB(A))	-0.24 (-0.76, 0.29)	-0.19 (-1.00, 0.62)	0.08 (-0.49, 0.64)	0.01 (-0.05, 0.07)	-0.02 (-0.09, 0.05)	0.09 (-0.11, 0.28)

Abbreviations: WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure or quartiles of exposure, except for natural green in a buffer of 300m.

Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-c).

Statistically significant results are highlighted in bold (p <0.05).

[a] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.

[b] Additionally adjusted for cuff size, the room temperature during the medical examination and the average of the ambient temperature on the seven days preceding the blood pressure measurements. Associations of air pollution with blood pressure are also adjusted for short-term air pollution levels.

[c] Additionally adjusted for the storage time of the blood samples.

Waist circumference

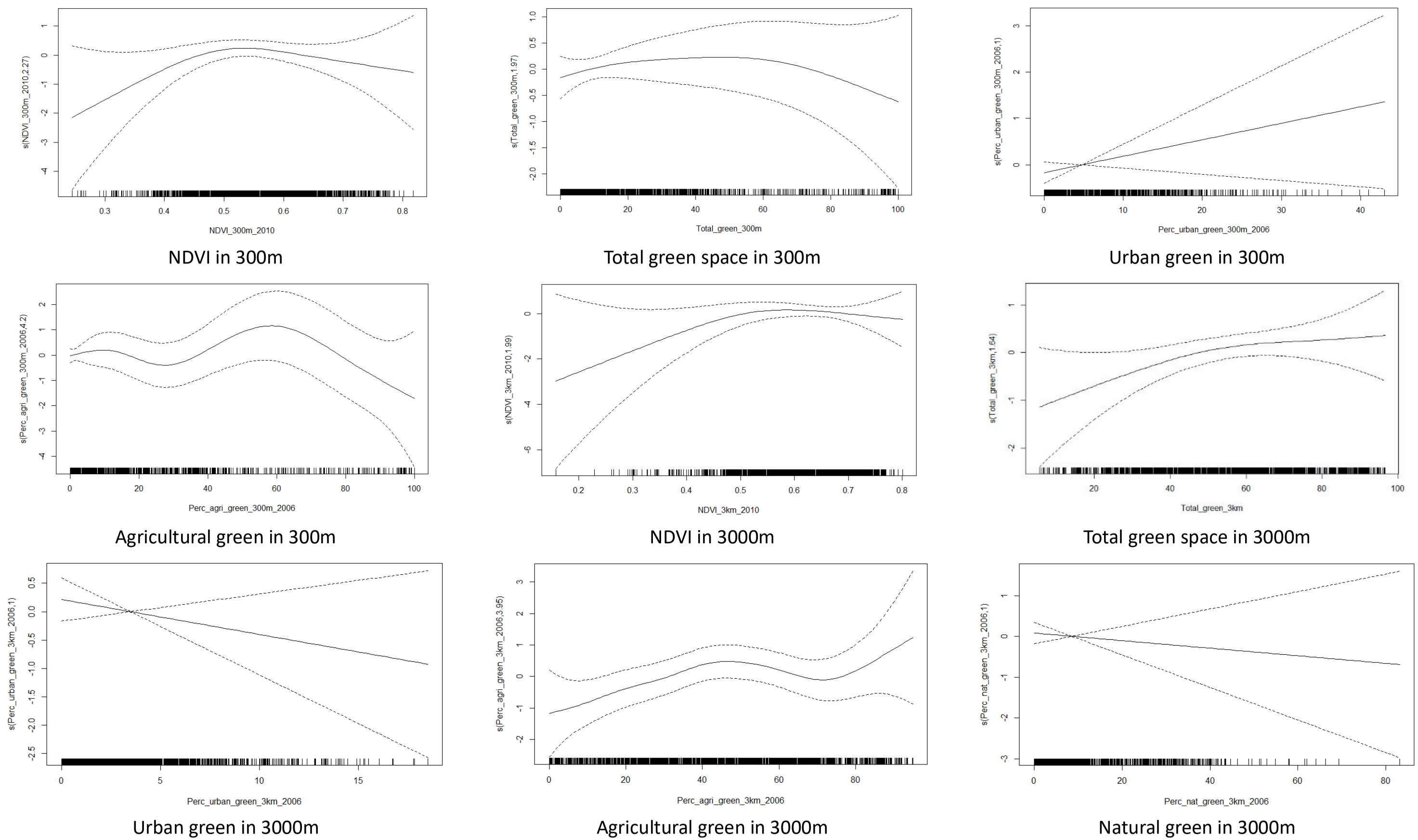


Figure S1. Exposure-response curves for the associations of green space, air pollution and traffic noise with cardiometabolic health at age 12.

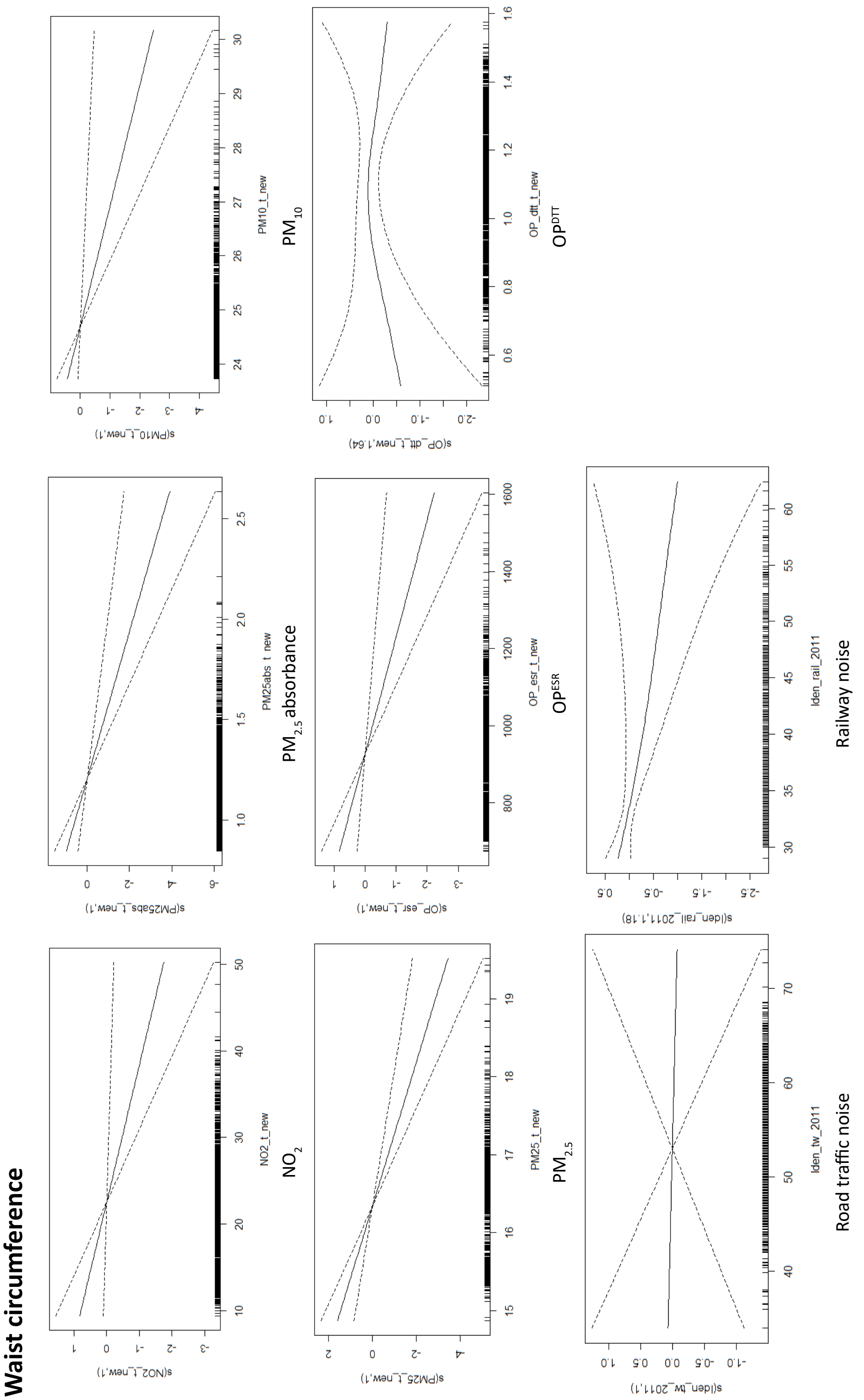
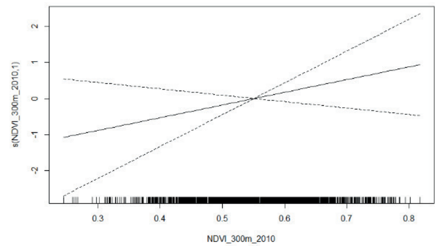
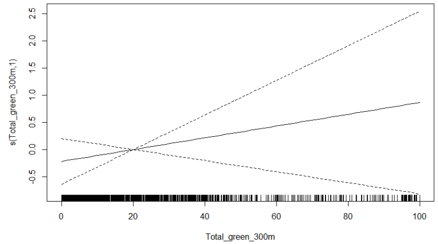


Figure S1 (continued).

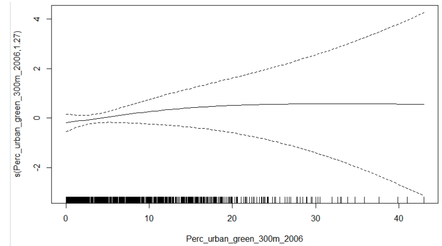
Systolic blood pressure



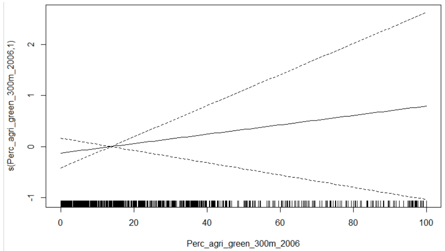
NDVI in 300m



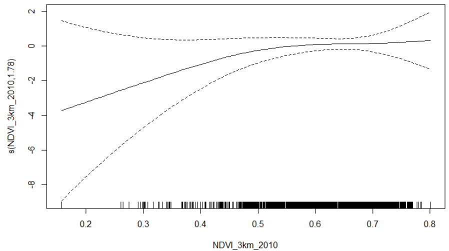
Total green space in 300m



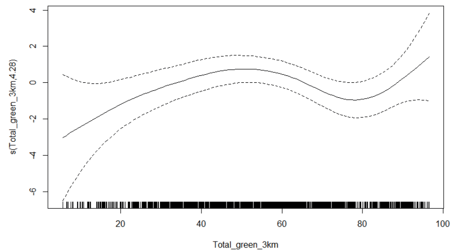
Urban green in 300m



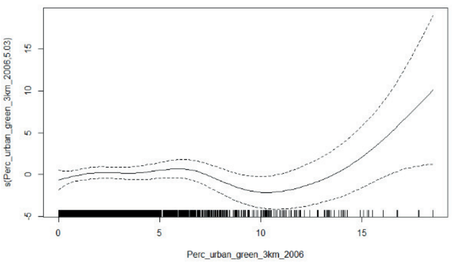
Agricultural green in 300m



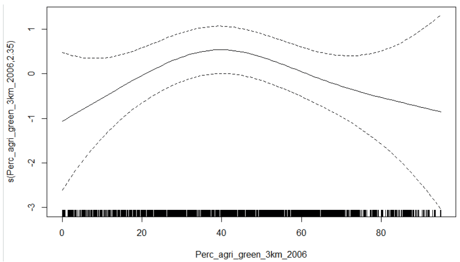
NDVI in 3000m



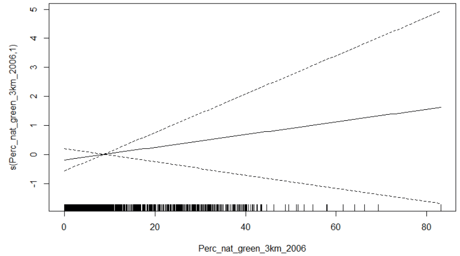
Total green space in 3000m



Urban green in 3000m



Agricultural green in 3000m



Natural green in 3000m

Figure S1 (continued).

Systolic blood pressure

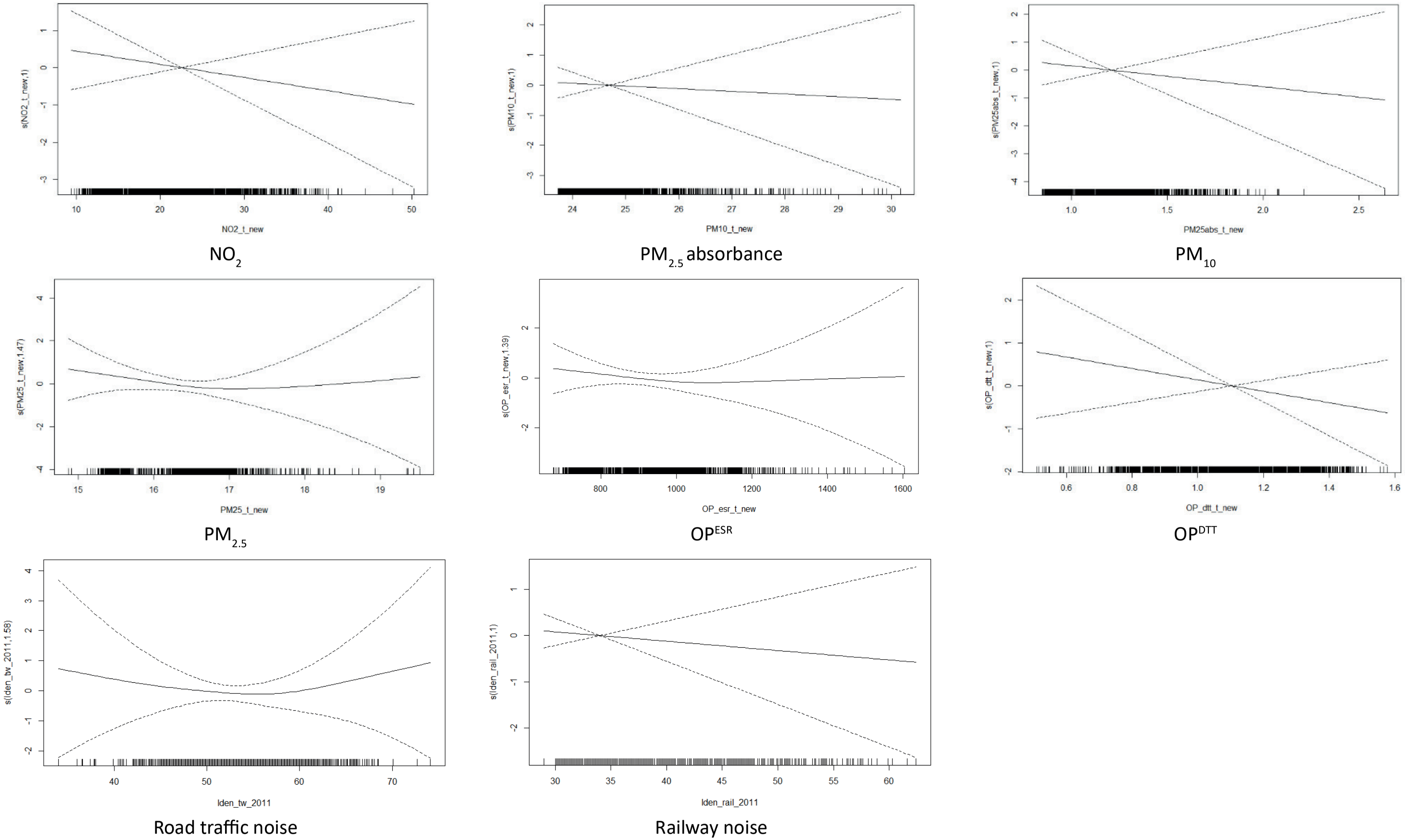


Figure S1 (continued).

Diastolic blood pressure

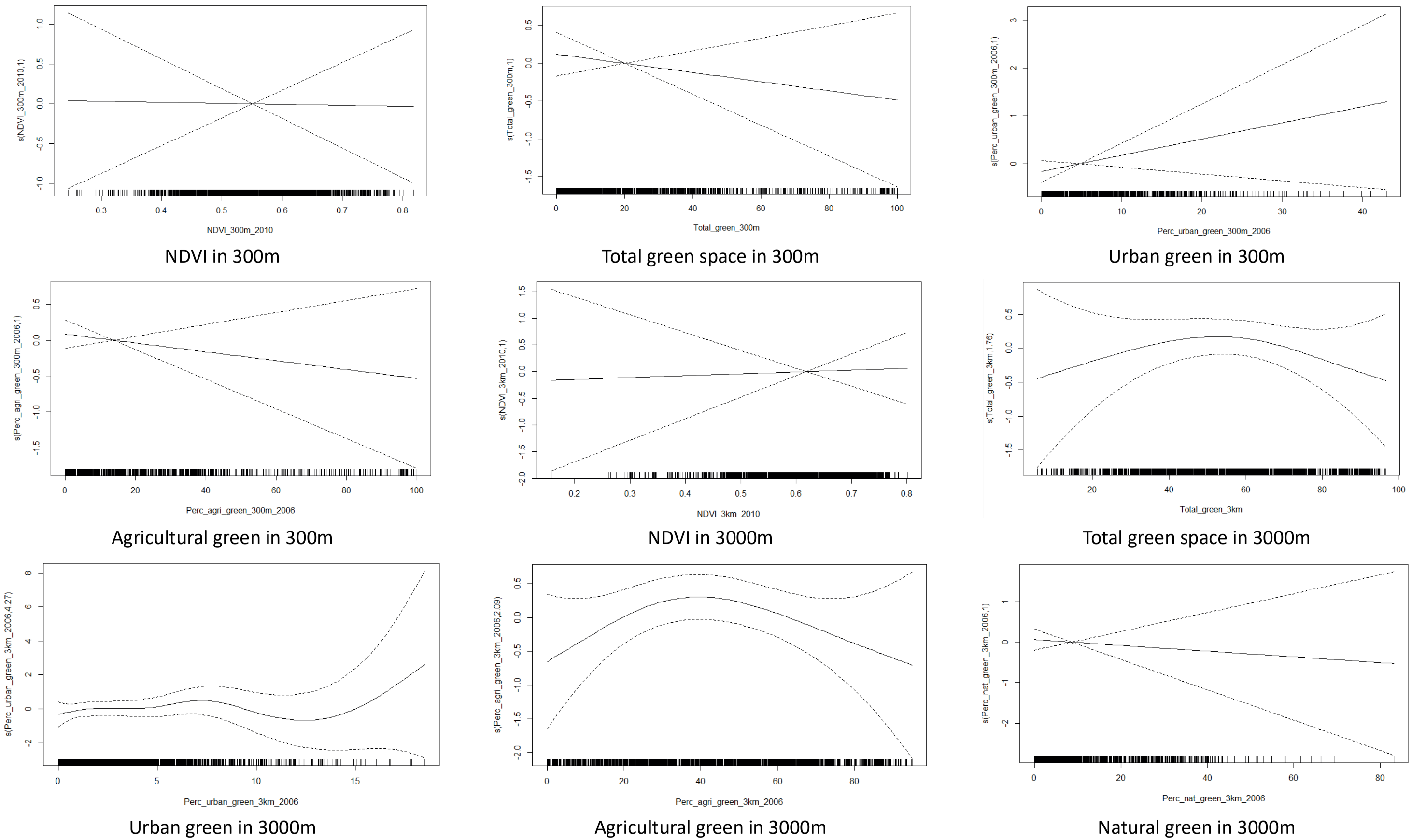


Figure S1 (continued).

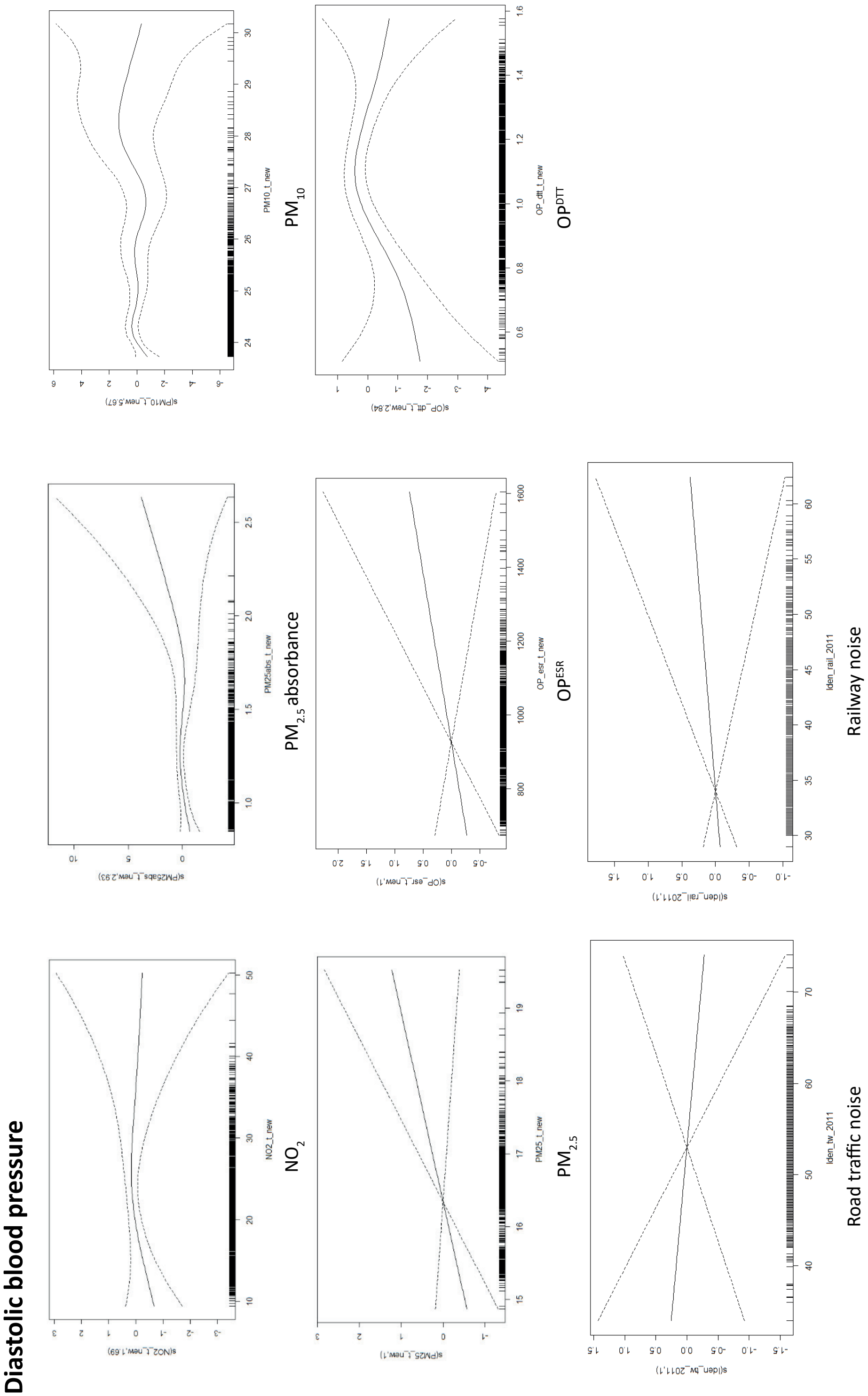


Figure S1 (continued).

Total cholesterol

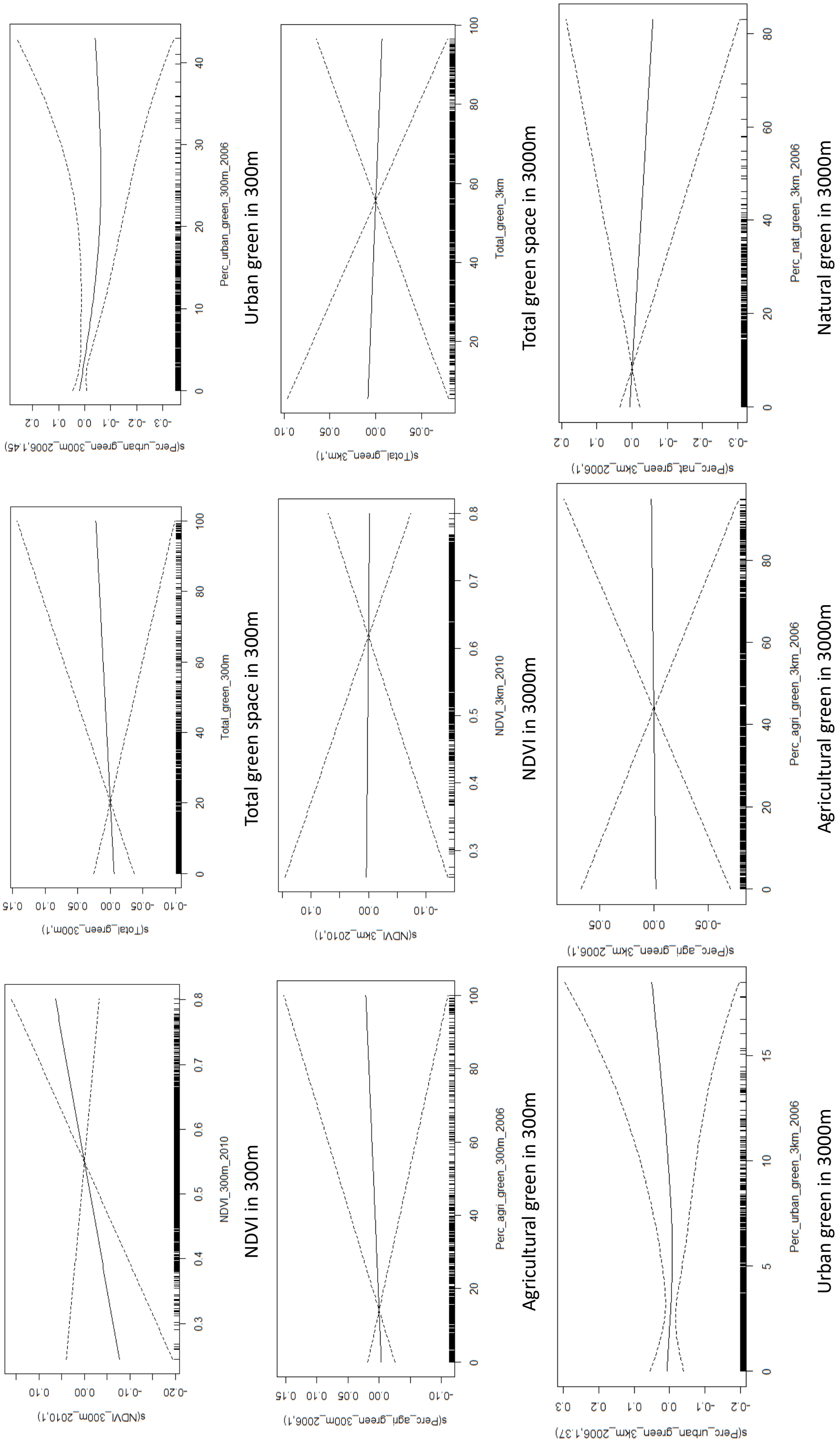


Figure S1 (continued).

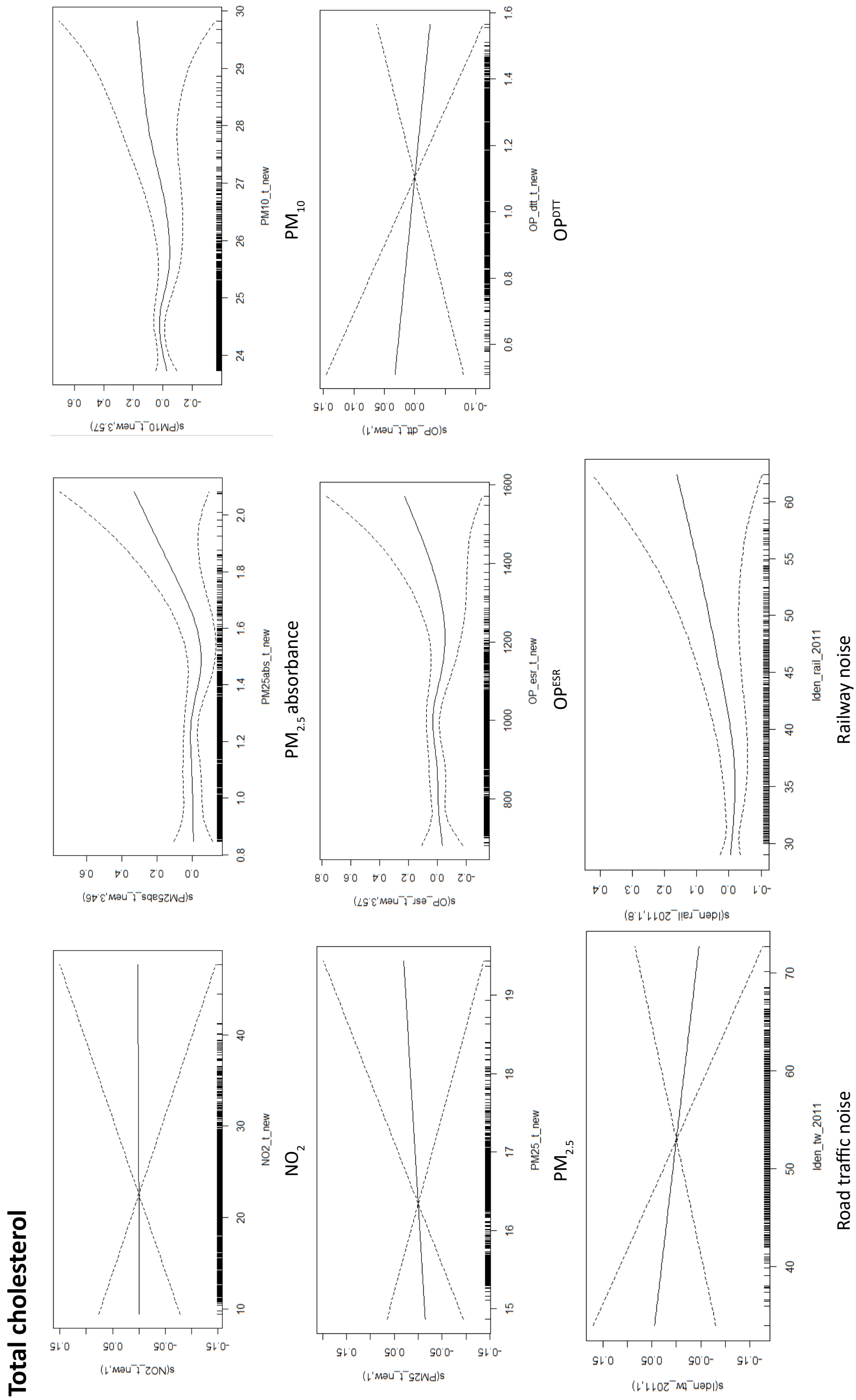


Figure S1 (continued).

Total/HDL cholesterol ratio

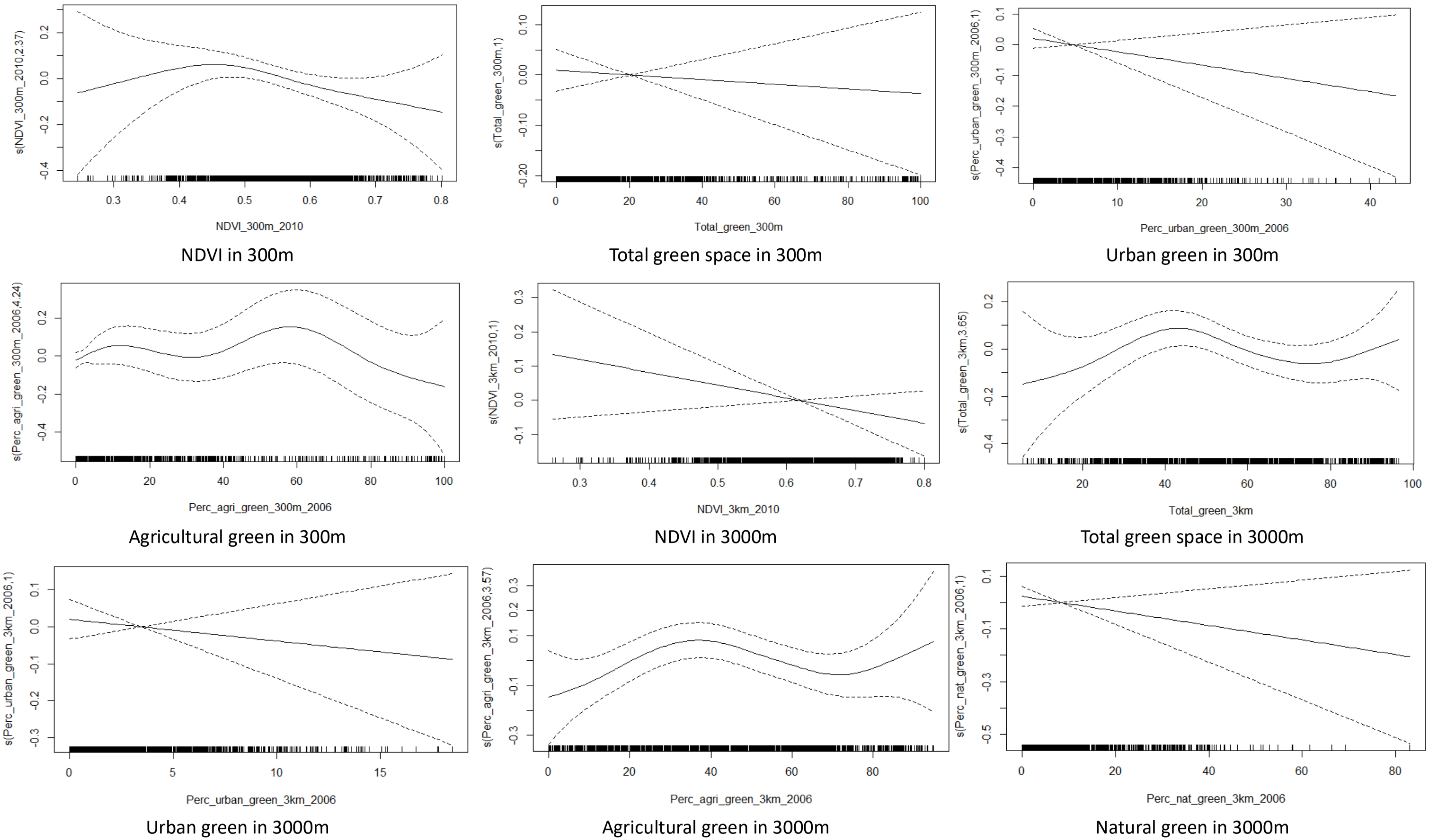


Figure S1 (continued).

Total/HDL cholesterol ratio

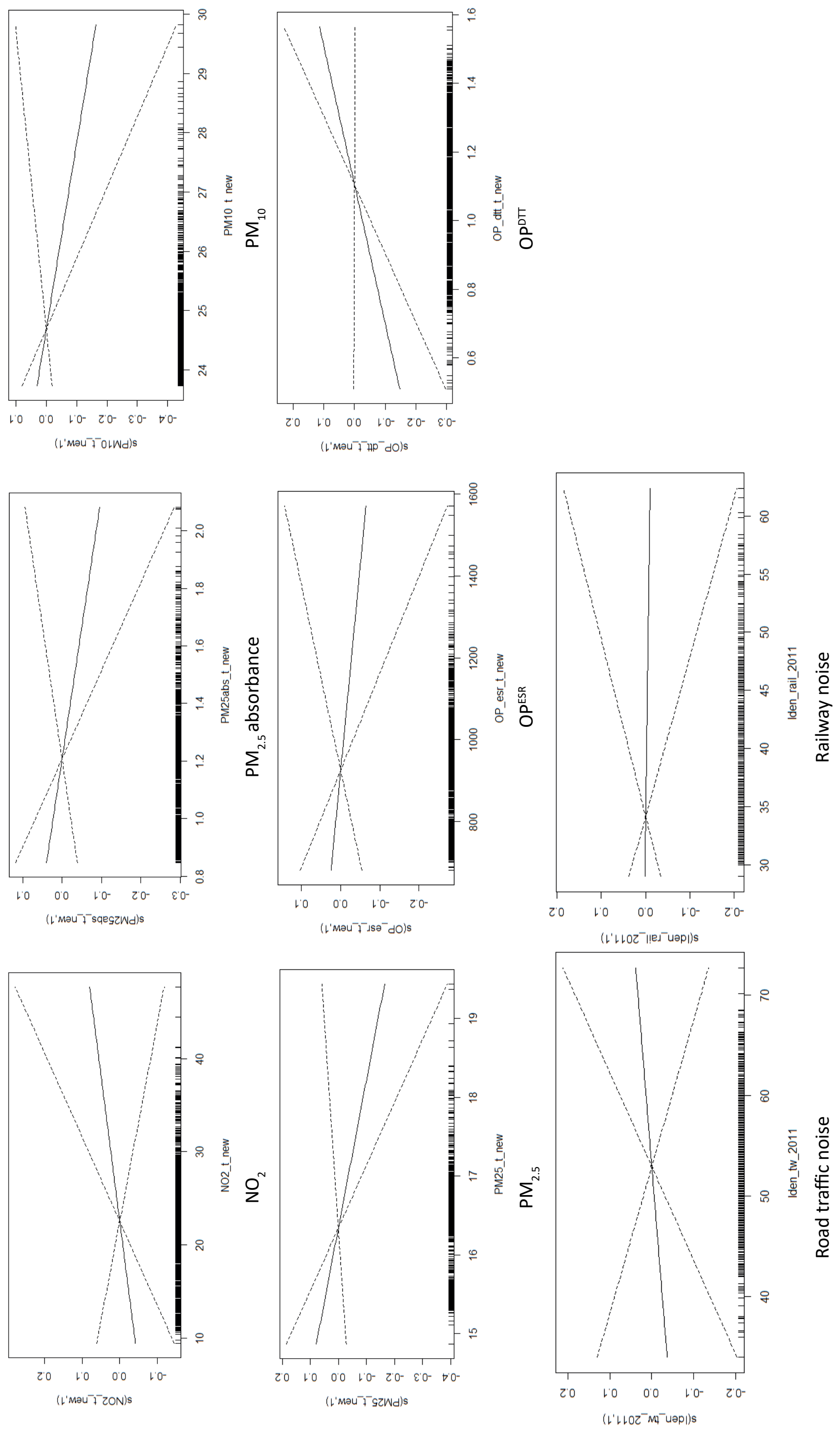


Figure S1 (continued).

HbA1c

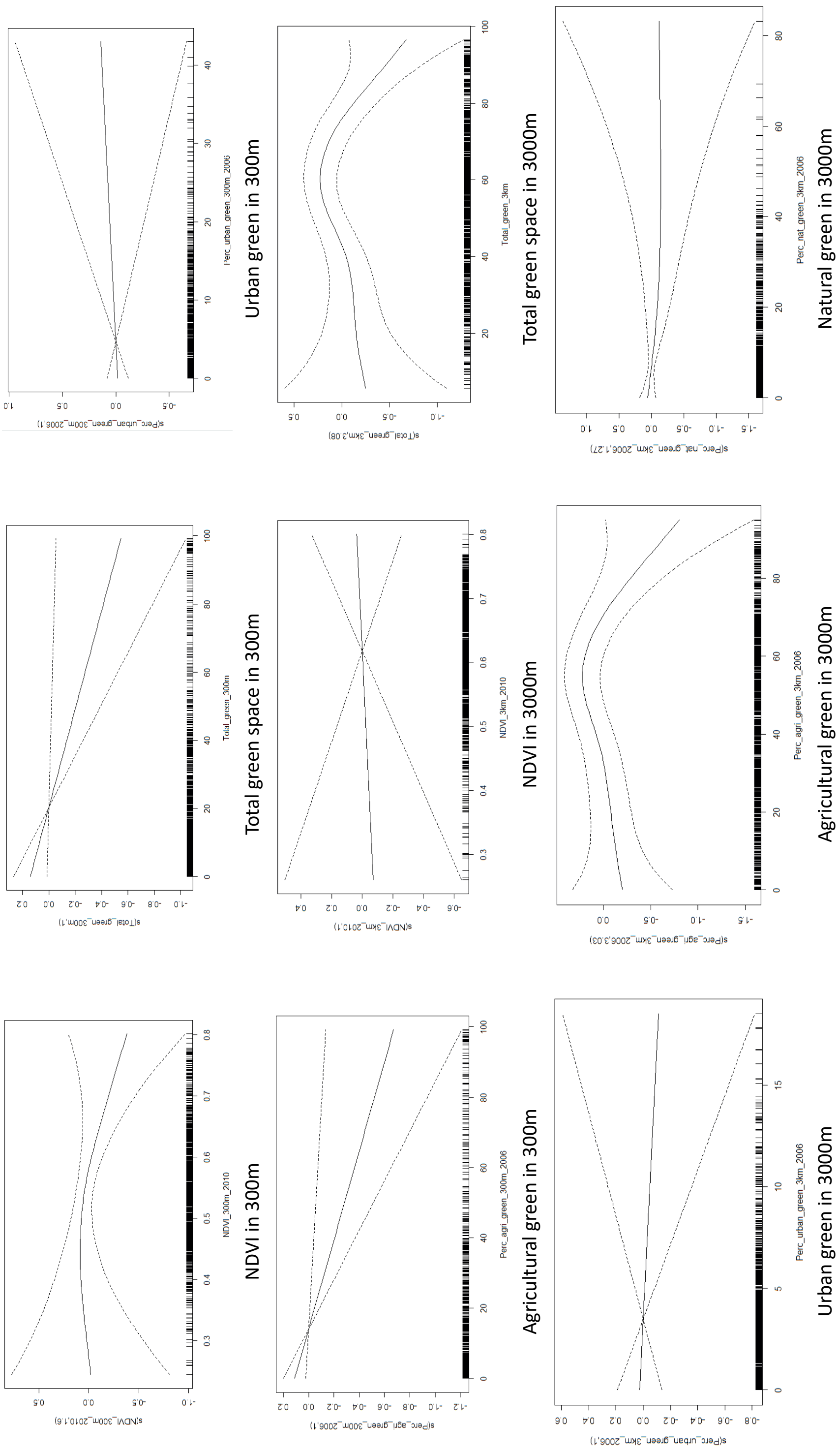


Figure S1 (continued).

HbA1c

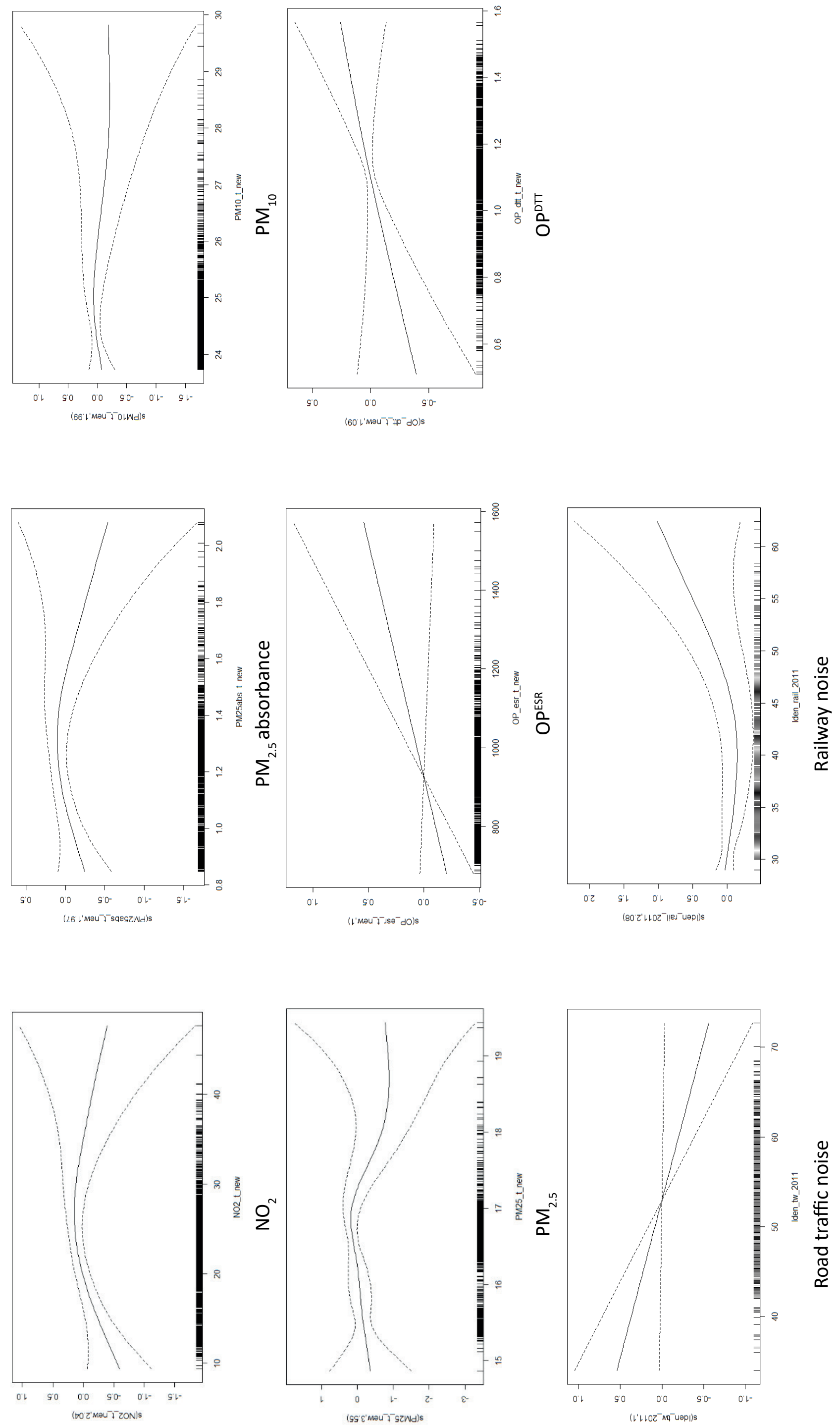


Figure S1 (continued).

Waist circumference

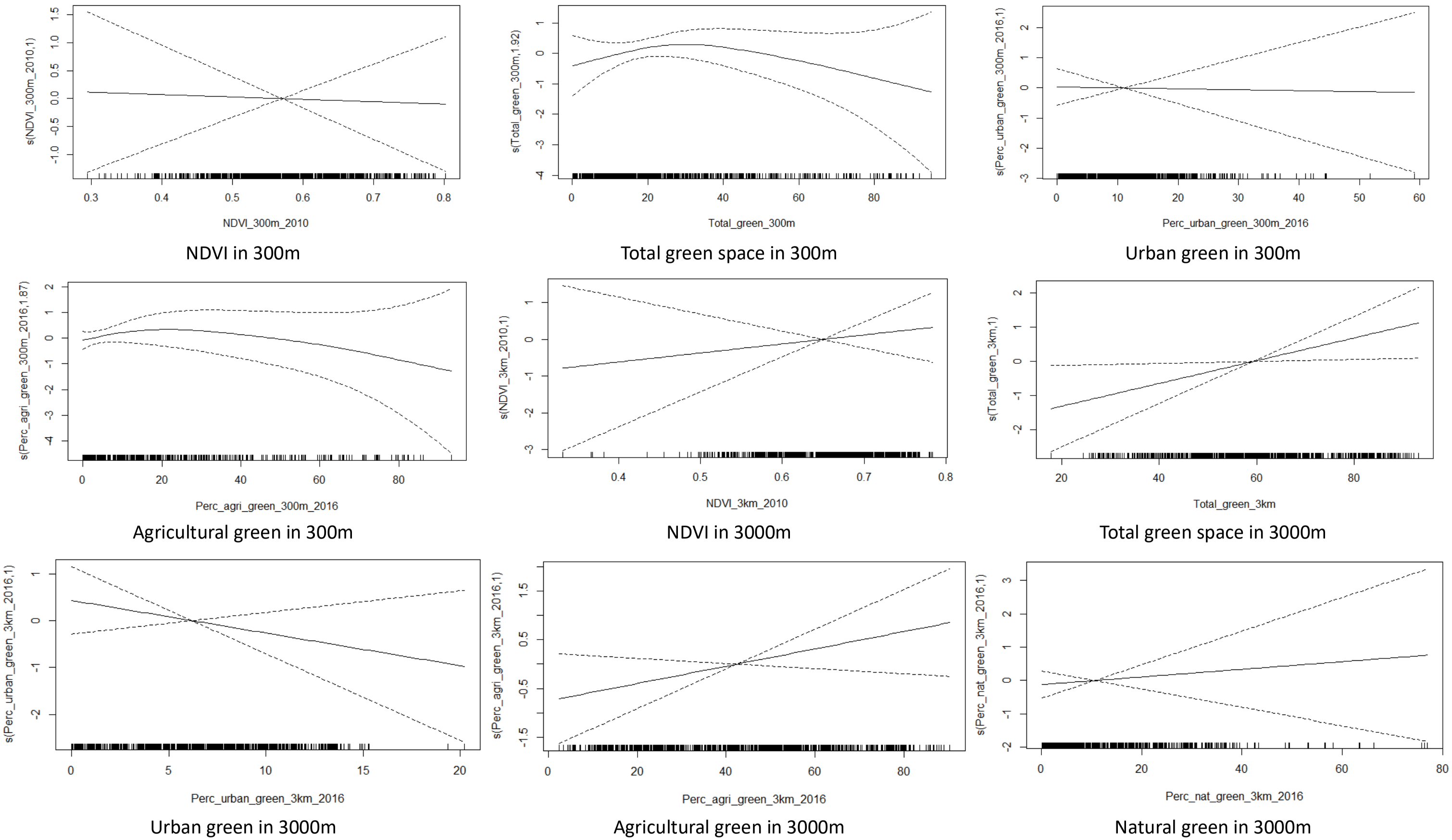


Figure S2. Exposure-response curves for the associations of green space, air pollution and traffic noise with cardiometabolic health at age 16.

Waist circumference

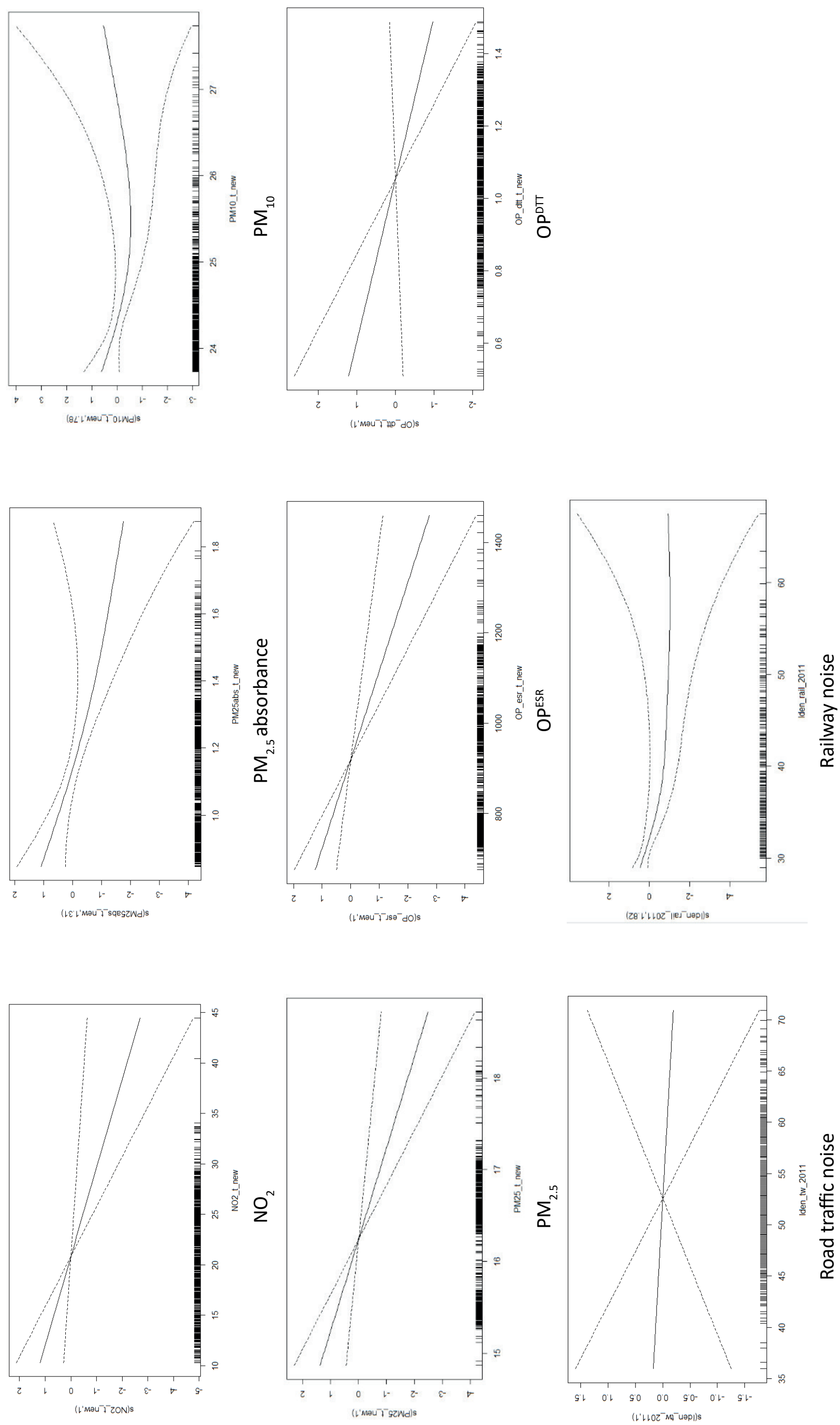


Figure S2 (continued).

Systolic blood pressure

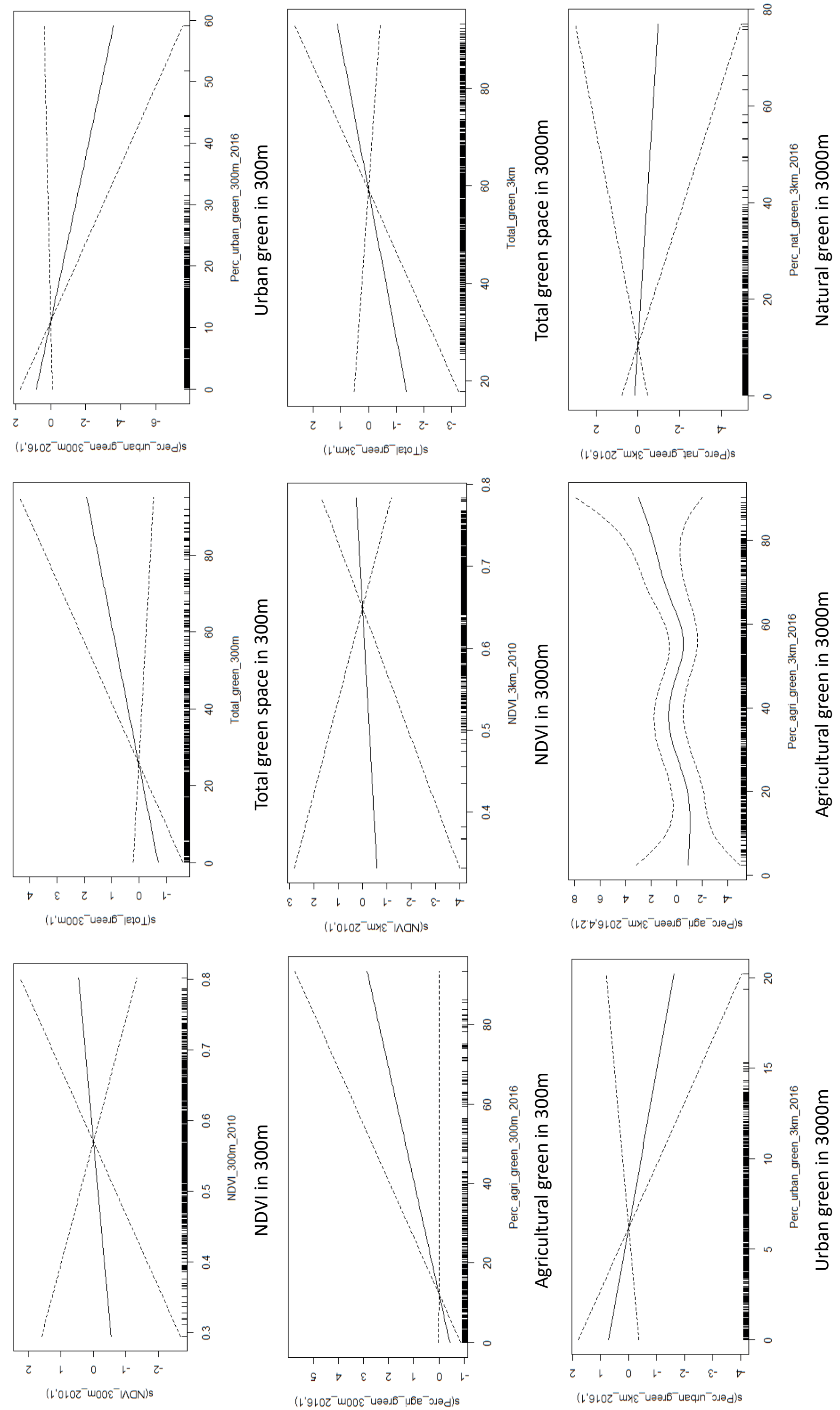


Figure S2 (continued).

Systolic blood pressure

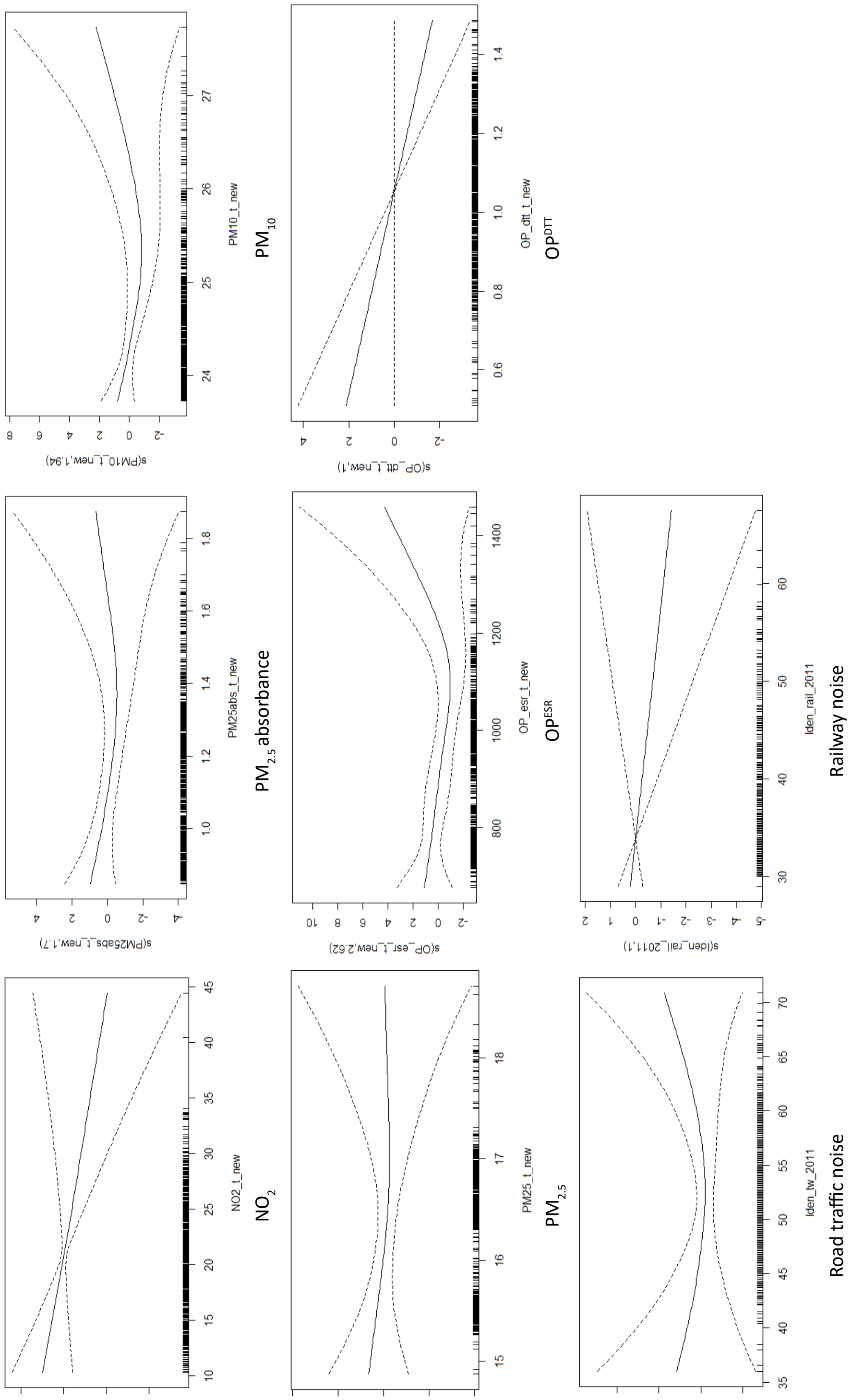
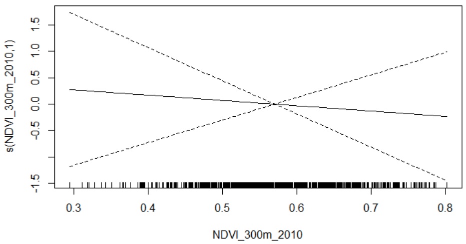
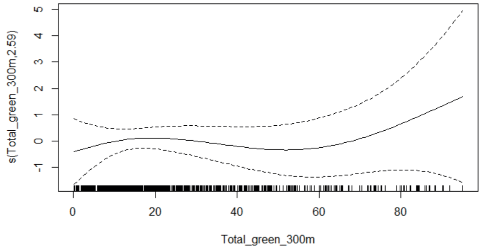


Figure S2 (continued).

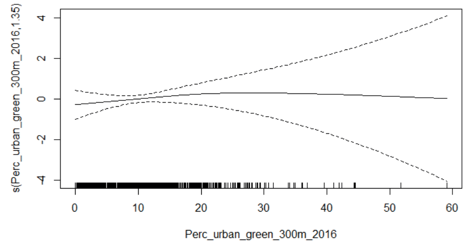
Diastolic blood pressure



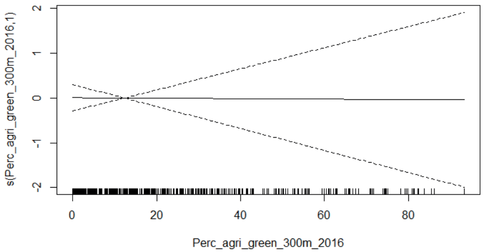
NDVI in 300m



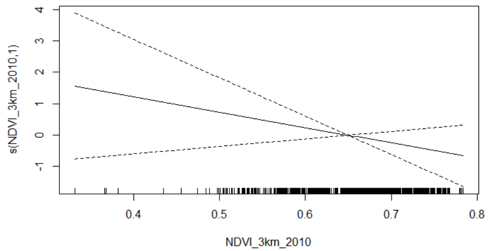
Total green space in 300m



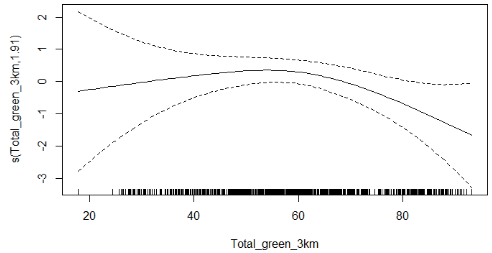
Urban green in 300m



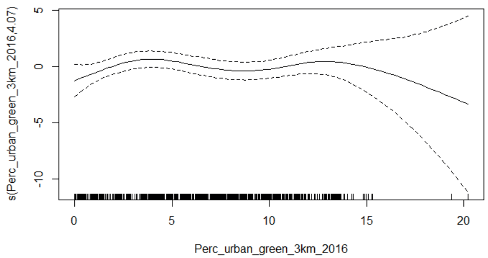
Agricultural green in 300m



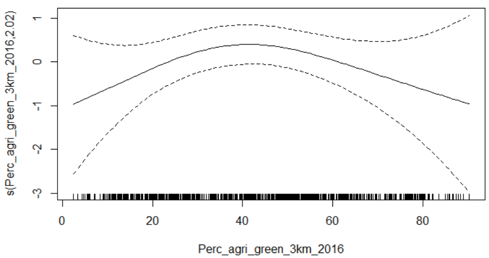
NDVI in 3000m



Total green space in 3000m



Urban green in 3000m



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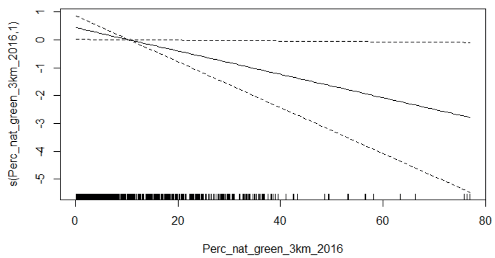
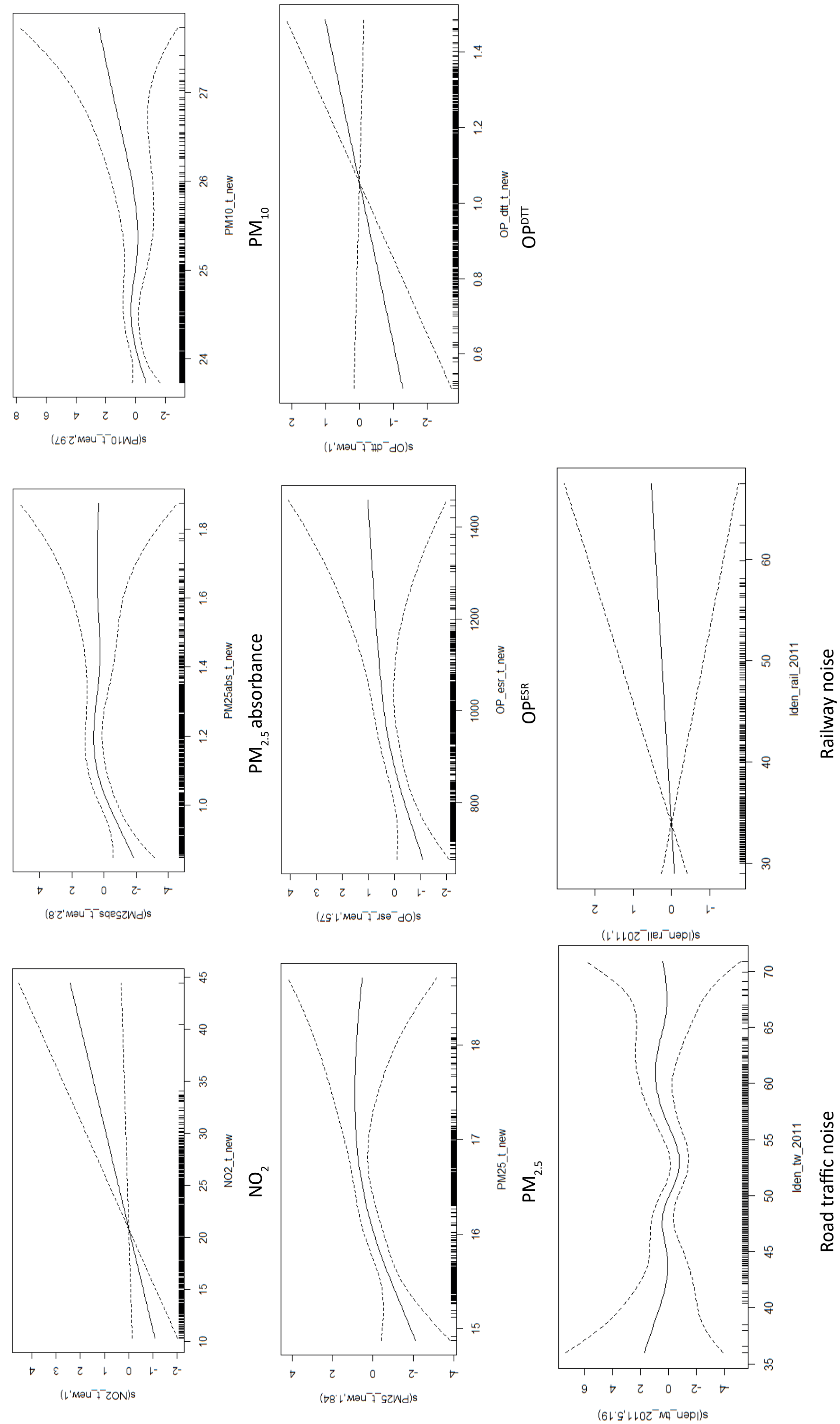


Natural green in 3000m

Figure S2 (continued).

Diastolic blood pressure



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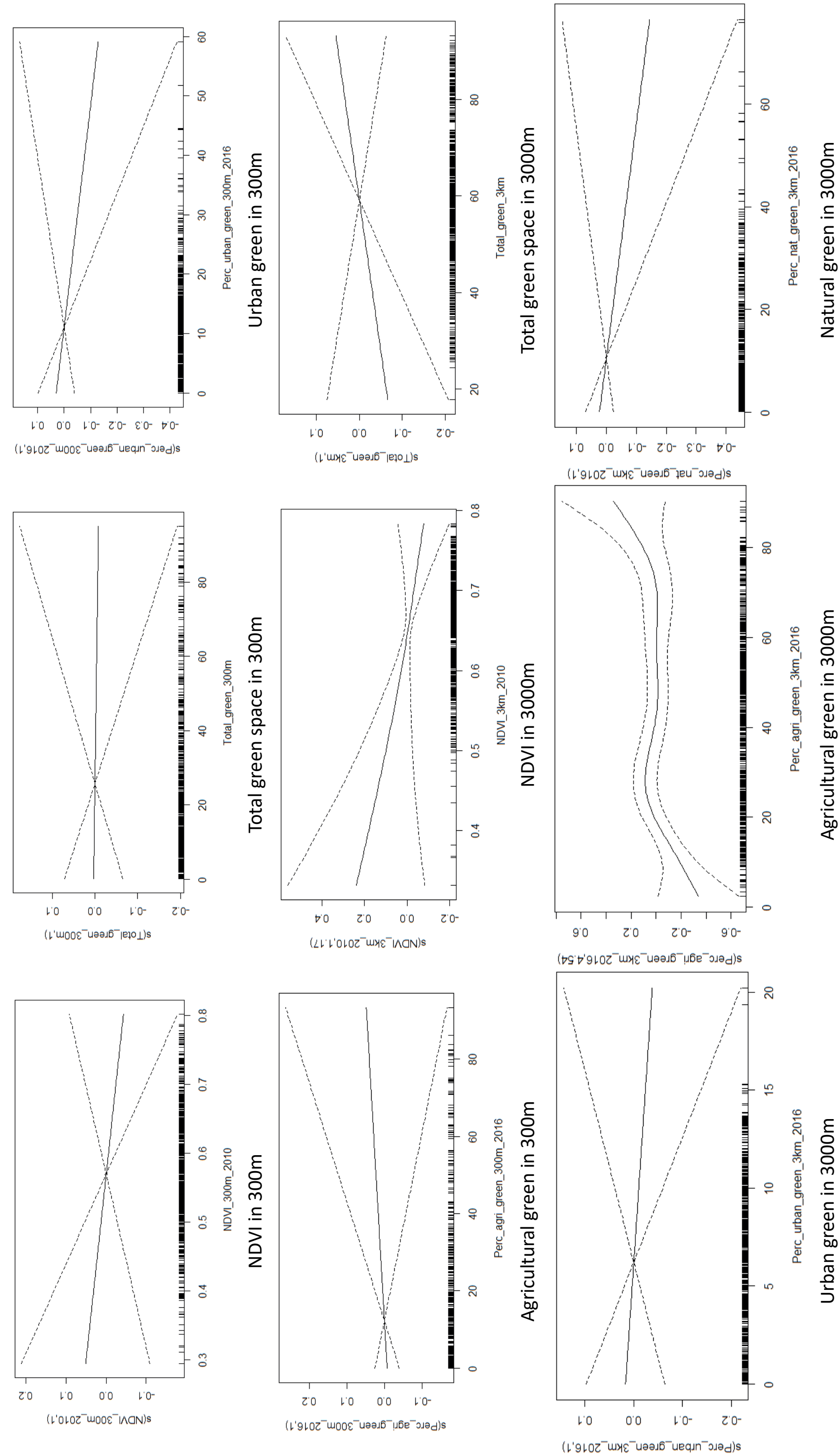
Total cholesterol



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Total cholesterol

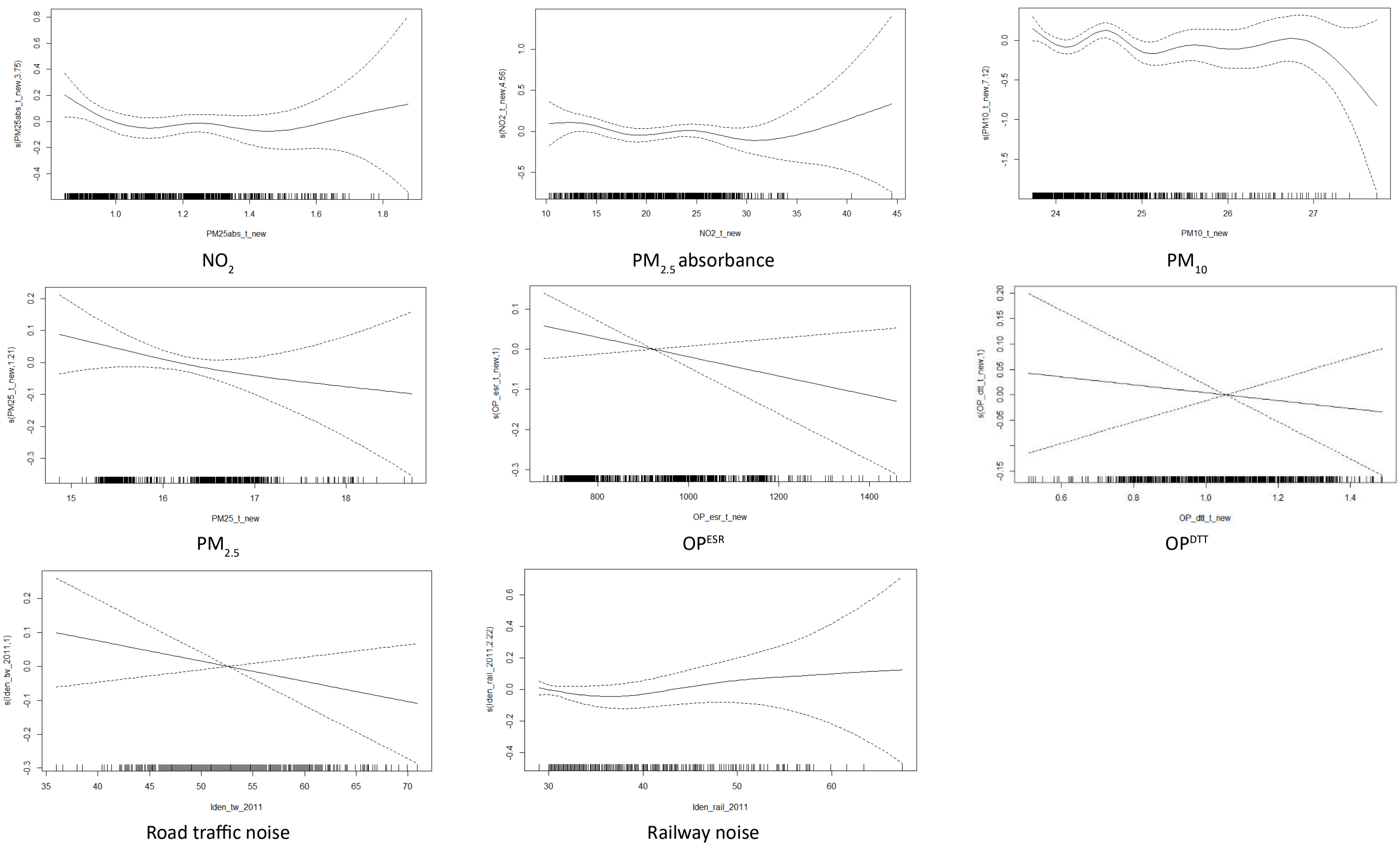

Figure S2 (continued).

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Total/HDL cholesterol ratio

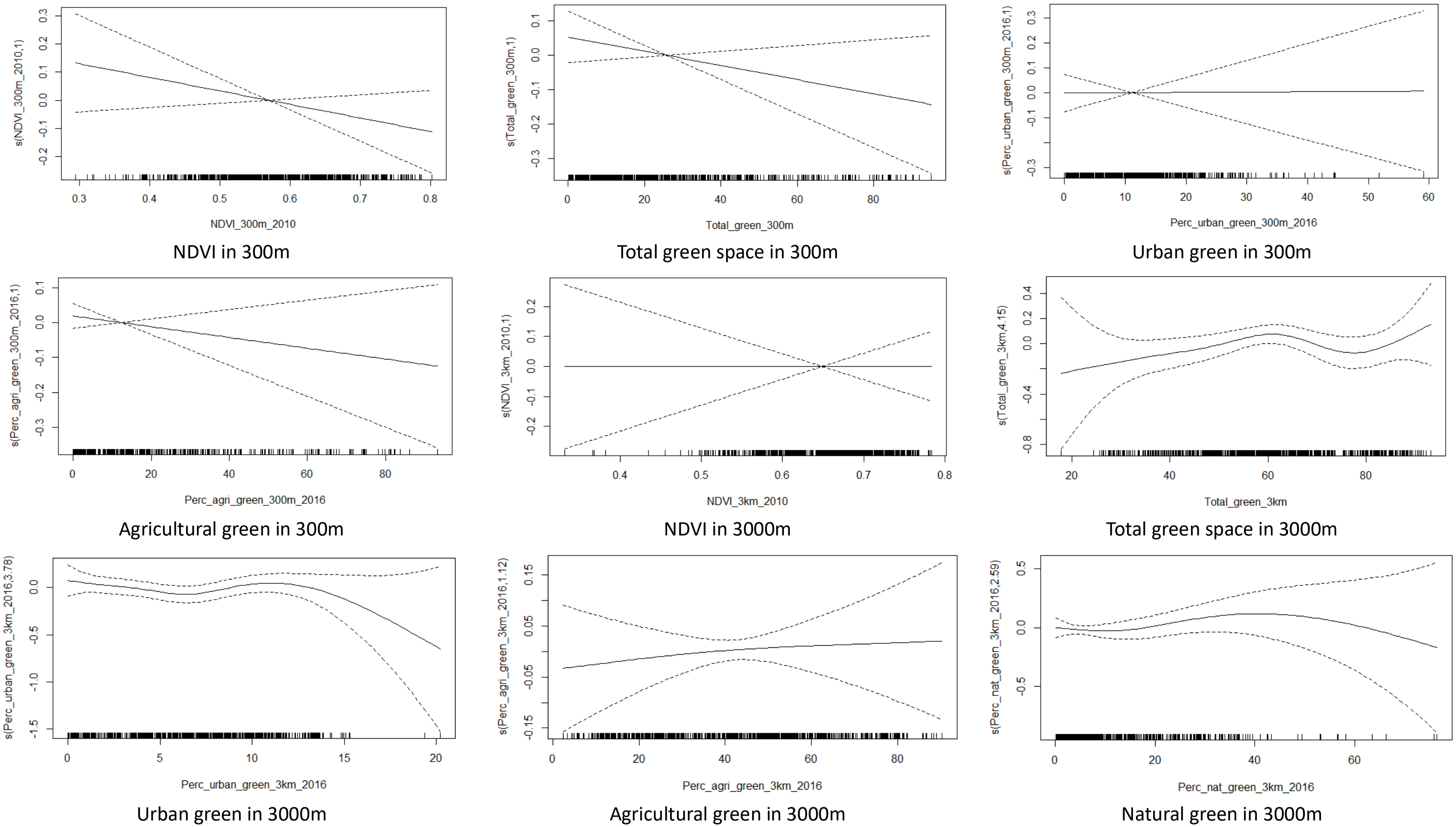


Figure S2 (continued).

Total/HDL cholesterol ratio

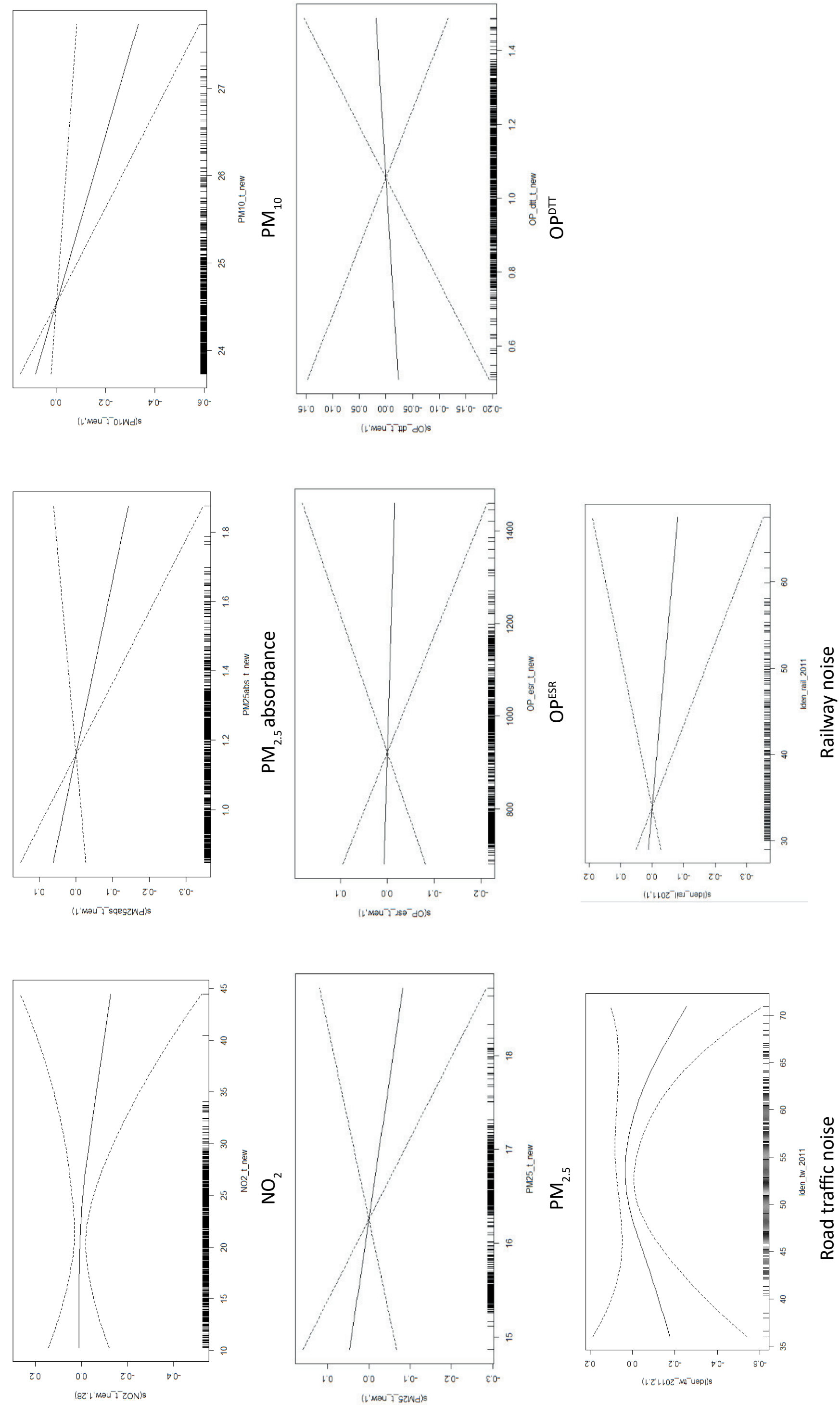
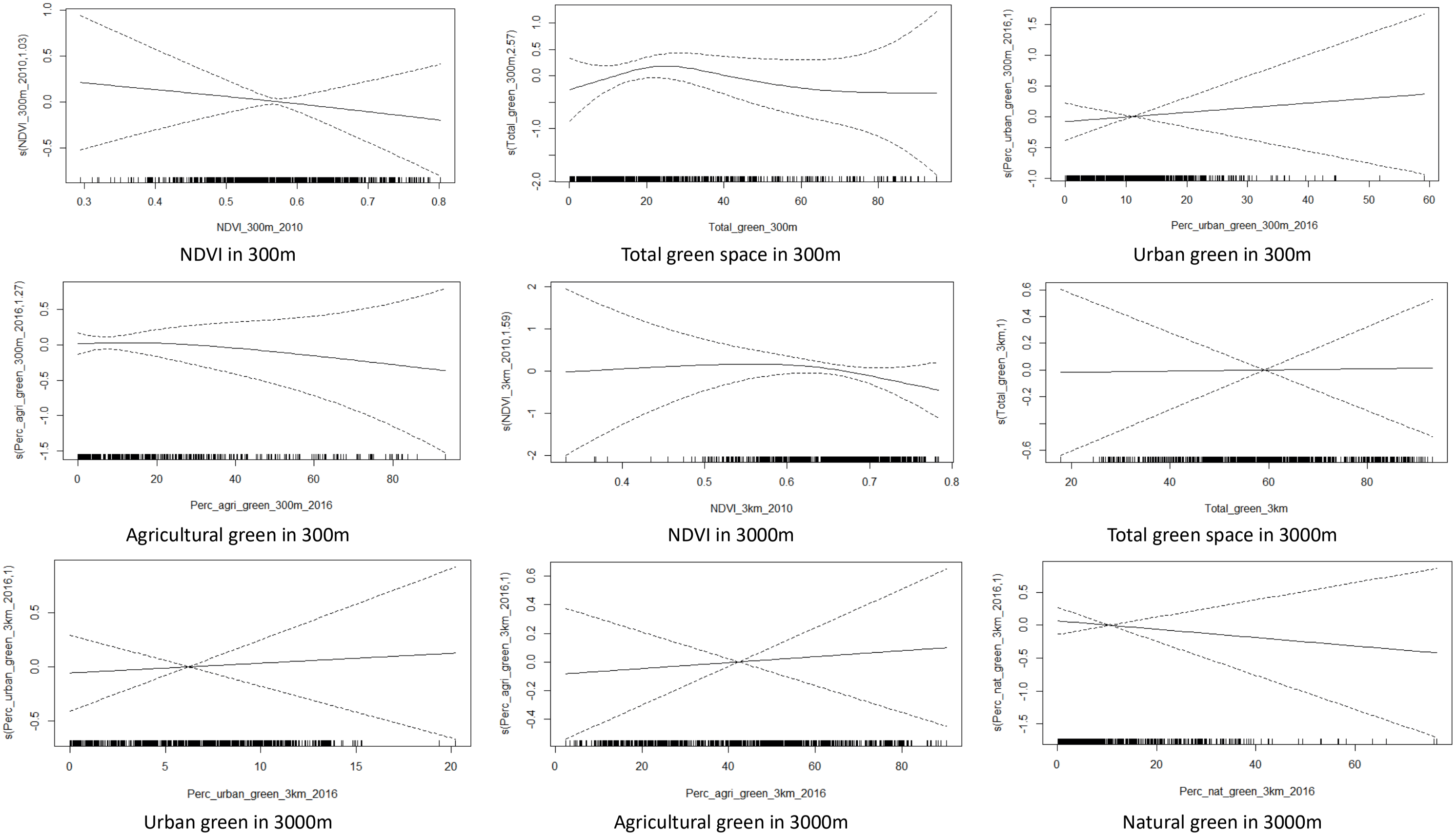


Figure S2 (continued).

HbA1c



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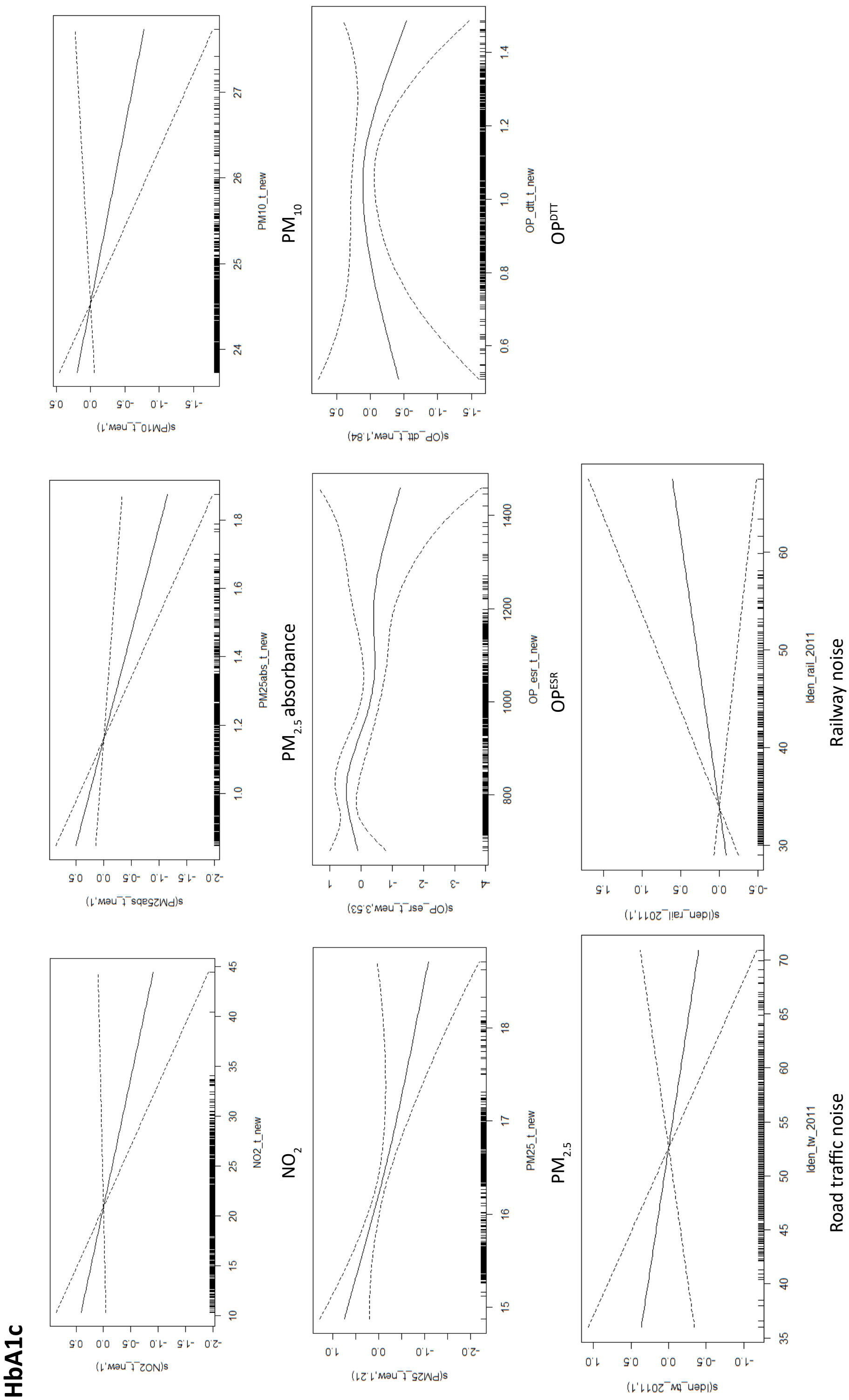

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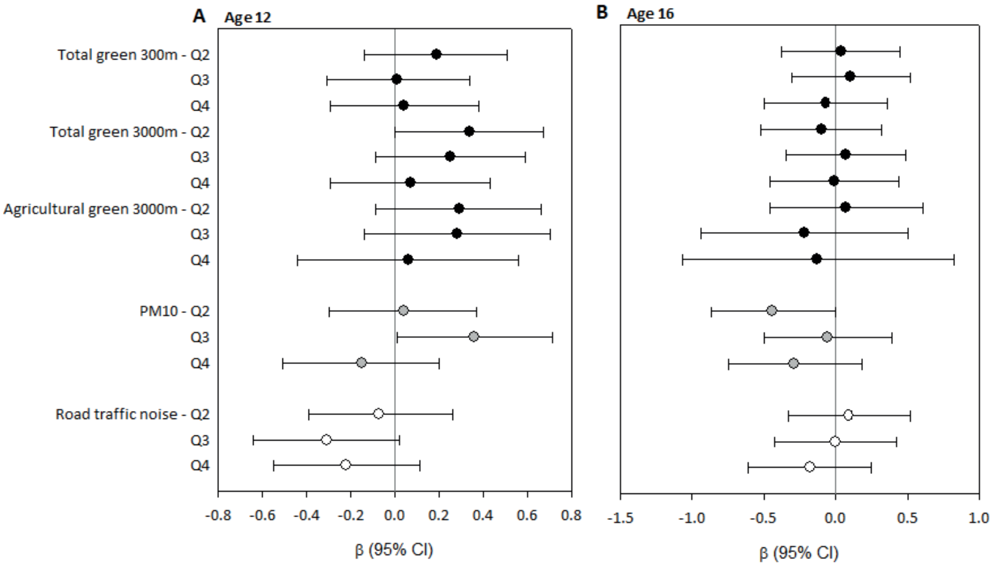

Figure S3. Associations of green space, air pollution and traffic noise with the cardiometabolic risk score for quartiles of exposure at age 12 and 16. Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, pubertal development, neighborhood socioeconomic status and region.

Chapter 5

Green space, air pollution, traffic noise and saliva cortisol in children: The PIAMA study

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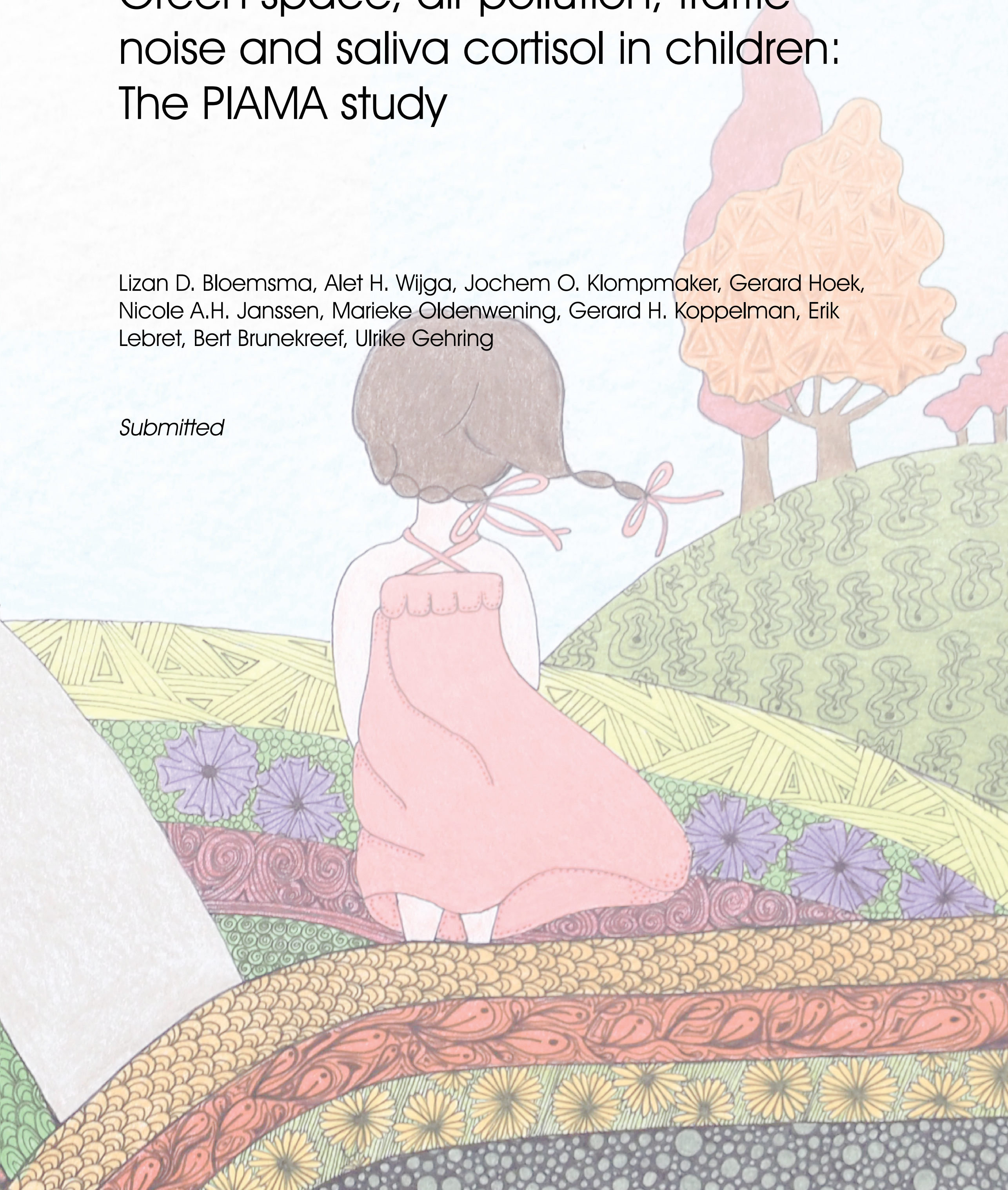
Submitted



Abstract

Background: Green space, air pollution and traffic noise exposure may be associated with stress levels in children. A flattened diurnal cortisol slope (the decline in cortisol concentrations from awakening to evening) is an indicator of chronic stress. We examined associations of green space, air pollution and traffic noise with the diurnal cortisol slope in children aged 12 years.

Methods: At age 12 years, 1027 participants of the Dutch PIAMA birth cohort collected three saliva samples during one day. We defined the diurnal cortisol slope as the change in saliva cortisol concentrations from the post-awakening peak to 8.00pm (in nmol/L per hour). We estimated residential exposure to green space (i.e. the average Normalized Difference Vegetation Index (NDVI) and percentages of green space in circular buffers of 300m and 3000m), air pollution and traffic noise. Associations of these exposures with the diurnal cortisol slope were assessed by multiple linear regression, adjusting for potential confounders.

Results: Higher average NDVI and total percentage of green space in a 3000m buffer were associated with a larger diurnal decrease in cortisol levels (adjusted difference [95% confidence interval] -0.11nmol/L/hr [-0.21, 0.00nmol/L/hr] per IQR increase in the average NDVI; -0.13nmol/L/hr [-0.26, 0.00nmol/L/hr] per IQR increase in the total percentage of green space). These associations remained after adjustment for air pollution and road traffic noise. Moreover, road traffic noise tended to be related to a larger diurnal decrease in cortisol levels.

Conclusions: Residential exposure to green space may be associated with lower stress levels in children aged 12 years.

Introduction

Green space may improve health by reducing stress, promoting physical activity, increasing social cohesion and reduced exposure to environmental stressors, including air pollution and noise.[1-3] Previous studies have shown associations between exposure to green space and reduced stress levels, mainly in adults.[4-7] In contrast, exposure to ambient air pollution and traffic noise may be associated with higher stress levels.[8-12]

The secretion of the stress hormone cortisol follows a circadian rhythm, characterized by high levels upon awakening, a substantial increase in cortisol concentrations in the 30-45 minutes after awakening (the cortisol awakening response (CAR)), followed by declining cortisol concentrations until reaching its minimum around bedtime.[13,14] The diurnal slope is the change in cortisol concentration from the post-awakening peak to its lowest point. Stress activates the hypothalamic–pituitary–adrenal (HPA) axis and the subsequent release of cortisol. With repeated stress exposure, the HPA axis becomes less flexible, which results in smaller differences between morning and evening cortisol concentrations.[15] Several studies have shown relationships between long-term stress exposure and a flattened diurnal cortisol slope.[13,16] Additionally, it has been suggested that the diurnal cortisol slope is a superior predictor of both chronic stress and potential HPA axis dysregulation compared to other measures of cortisol, such as the total daily cortisol output.[13]

The associations of green space, air pollution and traffic noise with cortisol levels in children and adolescents are not clear as the few epidemiological studies so far have reported inconsistent results. Van Aart et al. found no relationship between residential greenness and hair cortisol concentrations, an indicator of stress exposure during the last three months, in 153 children in Belgium.[17] Few studies found higher urinary or saliva cortisol concentrations in children exposed to high levels of road traffic noise.[9] A recent study, however, found no associations between residential exposure to road traffic noise and saliva cortisol concentrations in 1751 adolescents in Stockholm County.[18] One study found that higher exposure to nitrogen dioxide (NO_2) was associated with a decrease in the diurnal cortisol slope in 140 adolescents in California.[19] No previous epidemiological studies have assessed relationships between green space or traffic noise and the diurnal cortisol slope in children or adolescents.

Exposures to green space, air pollution and traffic noise are generally spatially correlated. Road traffic is a major source of both air pollution and noise, while higher levels of green space are associated with lower levels of air pollution and noise.[20-23] It is therefore important to assess both the individual and joint associations of these exposures with health outcomes in children. The aim of this study was to examine the individual and joint associations of green space, air pollution and traffic noise with the diurnal cortisol slope, an indicator of chronic stress, in children aged 12 years.

Methods

Study design and population

This study was performed within the ongoing Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. Detailed descriptions of the PIAMA study have been published previously.[24,25] Briefly, pregnant women were recruited in 1996/1997 from the general population in three different parts of the Netherlands. The baseline study population consisted of 3963 children. Participating parents completed questionnaires during pregnancy, three months after their child was born, when the child was one year old, and yearly thereafter until the child was eight. When the children were 11, 14 and 17 years old, both parents and children completed questionnaires.

Additionally, 1094 children (27.6% of the baseline study population) collected saliva samples as part of a medical examination at age 12 years. For 24 children, at least one sample did not contain enough saliva to determine saliva cortisol concentrations. Furthermore, we excluded three participants from the present analysis because their samples were unintentionally mixed during analysis or their tubes did not have a cap. In addition, we excluded three children with diabetes, five children with extremely high cortisol concentrations (>3 standard deviations (SDs) above the maximum of all other measured cortisol concentrations) and 32 children who used (inhaled) corticosteroids on the day of the saliva collection. Our study population consisted of 1027 children. The study protocol has been approved by the ethical review boards of the participating institutes and all parents and children gave written informed consent.

Saliva cortisol

Children were asked to collect three saliva samples during one day as part of a medical examination at age 12 years: immediately after awakening, thirty minutes after awakening (when cortisol levels are usually highest) and at 8.00pm (in the evening). Children were not allowed to eat, drink or brush their teeth between the collection of the first and second sample. Participants were instructed to store the saliva samples in a refrigerator until a research assistant collected them, typically within a few days. The samples were then stored at -20°C for eight to ten years, until they were analyzed using the DEMEDITEC Cortisol free in Saliva ELISA kit from Demeditec Diagnostics GmbH (Kiel, Germany).

We defined the diurnal cortisol slope as the difference between the evening cortisol concentration and the cortisol concentration thirty minutes after awakening. Researchers have argued for excluding the CAR when calculating the cortisol slope, because the CAR is influenced by different biological mechanisms than the rest of the diurnal cortisol rhythm.[14] The cortisol concentrations immediately after awakening were therefore not included in the present analysis. Except for the CAR, the diurnal cortisol rhythm is characterized by a gradual decline throughout the day.[13] The time interval between the collection of the second and third saliva sample differed between participants. We therefore calculated the diurnal cortisol slope in nmol/L *per hour* as follows: (cortisol concentration at 8.00pm - cortisol concentration 30 minutes after awakening)/number of hours between the collection of the two saliva samples.

Exposure assessment

We estimated exposure to green space, air pollution and traffic noise at the children's current home addresses at the time of the saliva collection at age 12 years. More details of the exposure assessment have been described elsewhere.[22,23]

Green space. The Normalized Difference Vegetation Index (NDVI) was used to assess greenness levels surrounding the children's homes. The NDVI was derived from Landsat 5 Thematic Mapper data at a spatial resolution of 30m x 30m. NDVI values range from -1 to +1, with higher values indicating more greenness.[26] We combined cloud free images of the summer of 2010 to create a map of the Netherlands. We quantified residential surrounding greenness as the average NDVI in circular buffers of 100m, 300m, 500m, 1000m and 3000m around each participant's home address. Since we observed high correlations between the average NDVI in different buffer sizes, we only included the average NDVI in buffers of 300m and 3000m in the present study.

We additionally used Bestand Bodemgebruik of 2006, a detailed land-use map of the Netherlands, to assess the total percentage of green space and percentages of urban, agricultural and natural green space in buffers of 300m and 3000m around the children's homes.[27] In contrast to the NDVI, Bestand Bodemgebruik does not include private green property (such as gardens) and street greenery. We assessed surrounding greenness and the percentages of green space in ArcGIS 10.2.2 (Esri, Redlands, CA, USA).

Air pollution. We estimated annual average concentrations of particulate matter with diameters of <10 µm (PM_{10}) and <2.5 µm ($PM_{2.5}$), $PM_{2.5}$ absorbance, NO_2 and the oxidative potential of $PM_{2.5}$ (electron spin resonance (OP^{ESR}) and dithiothreitol (OP^{DTT})) at the children's homes with land-use regression (LUR) models that were developed within the ESCAPE project. Details of the LUR model development have been published previously.[28-30] The performance of the LUR models was evaluated using leave-one-out cross validation (R^2_{LOOCV}) and ranged from 0.47 for OP^{DTT} to 0.89 for $PM_{2.5}$ absorbance.[28-30]

Traffic noise. We used the Standard Model Instrumentation for Noise Assessments (STAMINA), developed at the Dutch National Institute for Public Health and the Environment, to estimate annual average road traffic and railway noise exposure.[31] Daily average (L_{den}) and nighttime average (L_{night}) road traffic and railway noise exposure at the children's home addresses were estimated for 2011. L_{den} is the A-weighted noise level over a whole day weighted with 5dB(A) extra in the evening (19.00 - 23.00) and 10dB(A) extra at night (23.00 - 7.00). We only included L_{den} in our analyses, because L_{den} and L_{night} were highly correlated (r = 0.99 for road traffic noise; r = 0.95 for railway noise).

Potential confounding variables

We obtained information on parental level of education, maternal smoking during pregnancy (yes/no) and any smoking in the child's home at age 11 years (yes/no) from parental questionnaires. We defined parental level of education as the maximum of the father's and mother's educational level (categorized as low/intermediate and high). A child had a high level of parental education if either his/her mother or father was highly educated. Children's height (in cm) was measured by trained staff during the medical examinations at age 12 years. Pubertal development (using the puberty development scale: 1 = not yet started; 2 = barely started; 3 = definitely started; and 4 = seems complete) was reported by the children in a questionnaire administered at age 11 years.[32] We used the status scores of the 4-digit postal code areas from the Netherlands Institute for Social Research (SCP) of 2010 as an indicator of neighborhood socio-economic status (SES). Status scores comprise the average income, the percentage of residents with a low income, percentage unemployed persons and the percentage of low educated residents in a postal code area. A lower status score indicates a lower neighborhood SES.[33] The degree of urbanization of the 4-digit postal code areas was obtained from Statistics Netherlands (CBS). We included the degree of urbanization in two categories in our analyses: ≥1500 addresses/km^2; <1500 addresses/km^2.

Statistical methods

We assessed the shapes of the unadjusted associations of the continuous exposures and potential confounders with the diurnal cortisol slope by generalized additive models with integrated smoothness estimation and an identity link (GAM function; The R Project for Statistical Computing 2.8.0, www.r-project.org). The associations of green space, air pollution and traffic noise with the diurnal cortisol slope were linear or almost linear (Figure S1). We therefore included all exposures as continuous variables in our multiple linear regression analyses with the diurnal cortisol slope (in nmol/L/hr) as dependent variable and expressed the associations per interquartile range increase (IQR) in exposure. Since 82.7% of the children had no natural green space in a buffer of 300m around their homes, we created a binary variable: natural green space in a buffer of 300m yes/no. We mutually adjusted the associations with the percentages of agricultural, natural and urban green space in all analyses. Finally, we explored confounding of associations with one exposure by the other exposures of interest with two- and three-exposure models.

We specified several regression models with increasing degree of adjustment for potential confounders. Model 1 was the unadjusted model. Model 2 was adjusted for age, sex, parental level of education, maternal smoking during pregnancy, any smoking in the child's home, pubertal development, height and season. We then explored potential confounding by neighborhood SES (Model 3) and degree of urbanization (Model 4), by additionally adjusting for these variables. We included the degree of urbanization in our analyses to account for the fact that people living in urban areas may experience more stress (for reasons other than air pollution, traffic noise or lack of green space) than people living in non-urban areas.[34] This could, however, lead to over-adjustment because the degree of urbanization is also a determinant of the exposures of interest, i.e. green space, air pollution and traffic noise. We therefore included the degree of urbanization in a separate model.

As a sensitivity analysis, we excluded children whose saliva samples had not been stored according to protocol (n = 106): 1) samples that were stored at room temperature for a few days, 2) samples that had not been stored in the freezer within seven days and 3) samples that were unintentionally removed from the freezer for 24 hours. We performed the statistical analyses, except the GAM analyses of the linearity of the associations, with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

The median age of the study participants was 12.6 years (Table 1). A higher proportion of our study participants had at least one highly educated parent (58.3% vs. 50.6%) and a lower proportion of mothers had smoked during pregnancy (13.3% vs. 17.9%) compared to the baseline study population (n = 3963). The distributions of the diurnal cortisol slope and morning and evening saliva cortisol levels in our study population are shown in Figures 1 and S2. The median saliva cortisol concentration thirty minutes after awakening was 24.7 nmol/L (25th and 75th percentiles: 17.7, 33.4 nmol/L, Table 1). Evening cortisol concentrations were considerably lower with a median of 2.0 nmol/L (25th and 75th percentiles: 1.4, 2.8 nmol/L). The median diurnal cortisol slope was -1.8 nmol/L/hr (25th and 75th percentiles: -2.5, -1.3 nmol/L/hr).

The Spearman correlations between the green space indicators, air pollutants and traffic noise are shown in Table S1. Road traffic noise levels were moderately positively correlated with the various air pollutants, with the highest correlations for $PM_{2.5}$ absorbance (r = 0.46) and PM_{10} (r = 0.47). Correlations between the green space indicators and traffic noise ranged from -0.36 to -0.17 and the correlations between the green space indicators and air pollutants ranged from -0.72 to -0.17.

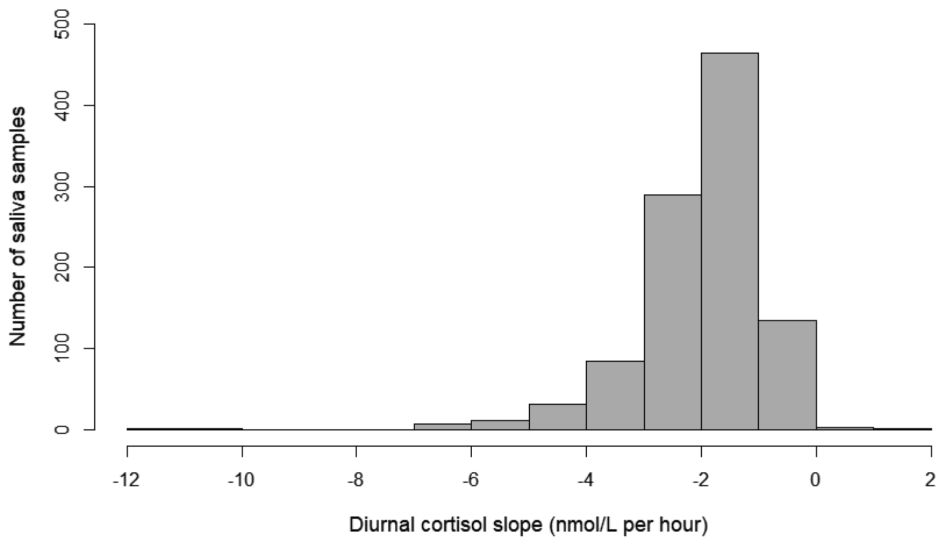


Figure 1. Distribution of the diurnal cortisol slope (in nmol/L per hour) in 1027 children aged 12 years.

Table 1. Characteristics of the study population and the distribution of green space, air pollution and traffic noise levels.

Characteristic	**n (%) or median (25th - 75th percentiles)**
N	1027
Saliva cortisol at waking (nmol/L)	16.4 (12.3 - 21.5)
Saliva cortisol 30 min post waking (nmol/L)	24.7 (17.7 - 33.4)
Saliva cortisol at 8.00pm (nmol/L)	2.0 (1.4 - 2.8)
Diurnal cortisol slope (nmol/L/hr)	-1.8 (-2.5, -1.3)
Boys	504 (49.1)
Age (years)	12.6 (12.4 - 12.8)
Parental level of education	
Low/intermediate	426 (41.7)
High	596 (58.3)
Maternal smoking during pregnancy (yes)	135 (13.3)
Smoking in child's home (yes)	111 (11.0)
Puberty development scale	1.4 (1.0 - 1.8)
Neighborhood SES [a]	0.29 (-0.38 - 1.09)
Degree of urbanization	
≥1500 addresses/km^2	418 (40.8)
<1500 addresses/km^2	607 (59.2)
Average NDVI in 300m	0.55 (0.49 - 0.62)
Total percentage of green space in 300m	12.4 (2.4 - 29.6)
Percentage urban green in 300m	0.7 (0.0 - 7.4)
Percentage agricultural green in 300m	0.2 (0.0 - 21.4)
Percentage natural green in 300m	0.0 (0.0 - 0.0)
Buffers that have no natural green	846 (82.7)
Average NDVI in 3000m	0.63 (0.56 - 0.69)
Total percentage of green space in 3000m	56.3 (40.0 - 71.3)
Percentage urban green in 3000m	2.7 (0.9 - 4.7)
Percentage agricultural green in 3000m	44.1 (25.1 - 61.9)
Percentage natural green in 3000m	3.7 (1.5 - 10.4)
NO_2 (µg/m^3)	22.8 (18.1 - 26.6)
$PM_{2.5}$ absorbance (10^{-5}/m)	1.2 (1.0 - 1.3)
PM_{10} (µg/m^3)	24.5 (24.0 - 25.0)
$PM_{2.5}$ (µg/m^3)	16.5 (15.6 - 16.7)
OP^{ESR} (A.U./m^3)	932.8 (780.2 - 1026.4)
OP^{DTT} (nmol DTT/min/m^3)	1.1 (1.0 - 1.2)
Road traffic noise (L_{den} dB(A))	52.2 (49.2 - 56.1)
Railway noise (L_{den} dB(A))	30.3 (29.0 - 37.6)

Abbreviations: SES = socioeconomic status; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol; NDVI = Normalized Difference Vegetation Index.

[a] A higher score indicates a higher SES.

The effect estimates from the single-exposure models were similar across the four regression models, i.e. the adjustment for potential confounders hardly changed the associations (Table 2). A higher average NDVI in a buffer of 3000m was associated with a larger diurnal decrease in cortisol concentrations (adjusted difference -0.11 nmol/L/hr [95% confidence interval (CI) -0.21, 0.00 nmol/L/hr] per IQR increase in Model 4). Similarly, we found relationships between the total percentage of green space in a buffer of 3000m and a larger diurnal decrease in cortisol levels (adjusted difference -0.13 nmol/L/hr [95% CI -0.26, 0.00 nmol/L/hr] per IQR increase). The associations with the total percentage of green space in a buffer of 3000m were driven by associations with the percentage of agricultural green space (adjusted difference -0.16 nmol/L/hr [95% CI -0.35, 0.04 nmol/L/hr] per IQR increase in model 4). The average NDVI in a buffer of 300m was also related to a larger diurnal decrease in cortisol concentrations (Table 2). This relationship, however, was weaker than the relationships with green space in a buffer of 3000m. We did not find associations with the percentages of green space, based on a land-use map, in a buffer of 300m.

We also observed a non-significant association between higher road traffic noise exposure and a larger diurnal decrease in saliva cortisol concentrations (adjusted difference -0.08 nmol/L/hr [95% CI -0.16, 0.01 nmol/L/hr] per IQR increase in model 4). We found no associations of air pollutants with the diurnal cortisol slope (Table 2).

Associations of the total percentage of green space in a buffer of 3000m with the diurnal cortisol slope were slightly stronger in two- and three-exposure models (for example, adjusted difference -0.19 nmol/L/hr [95% CI -0.34, -0.04 nmol/L/hr] per IQR increase after additional adjustment for OP^{DTT} and road traffic noise, Table 3). Associations with the average NDVI in a buffer of 3000m hardly changed after adjustment for air pollution and road traffic noise.

After the exclusion of children whose saliva samples had not been stored according to protocol, the associations of green space with the diurnal cortisol slope remained (Table S2). However, the relationship between road traffic noise and a larger diurnal decrease in cortisol levels was weaker in this subgroup of children (adjusted difference -0.05 nmol/L/hr [95% CI -0.14, 0.04 nmol/L/hr] per IQR increase in model 4).

Table 2. Associations of green space, air pollution and traffic noise with the diurnal cortisol slope (in nmol/L per hour) at age 12 years.

Exposure (increment)	Model 1 [a]	Model 2 [b]	Model 3 [c]	Model 4 [d]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.13)	-0.07 (-0.16, 0.03)	-0.09 (-0.18, 0.01)	-0.08 (-0.18, 0.01)	-0.07 (-0.18, 0.03)
Total percentage of green space in 300m (27.23)	-0.01 (-0.08, 0.07)	-0.02 (-0.10, 0.06)	-0.02 (-0.10, 0.06)	-0.01 (-0.09, 0.08)
Urban green in 300m (7.40)	-0.02 (-0.10, 0.05)	-0.03 (-0.10, 0.05)	-0.03 (-0.10, 0.05)	-0.03 (-0.10, 0.05)
Agricultural green in 300m (21.41)	-0.01 (-0.08, 0.05)	-0.03 (-0.09, 0.04)	-0.02 (-0.09, 0.04)	-0.01 (-0.08, 0.06)
Natural green in 300m (yes vs. no)	0.08 (-0.10, 0.27)	0.06 (-0.13, 0.24)	0.06 (-0.13, 0.25)	0.06 (-0.12, 0.25)
Average NDVI in 3000m (0.13)	**-0.10 (-0.20, -0.01)**	**-0.11 (-0.21, -0.02)**	**-0.12 (-0.21, -0.02)**	**-0.11 (-0.21, 0.00)**
Total percentage of green space in 3000m (31.29)	**-0.11 (-0.21, 0.00)**	**-0.12 (-0.22, -0.01)**	**-0.12 (-0.22, -0.02)**	-0.13 (-0.26, 0.00)
Urban green in 3000m (3.84)	-0.03 (-0.16, 0.10)	-0.01 (-0.14, 0.12)	0.00 (-0.14, 0.13)	-0.01 (-0.14, 0.12)
Agricultural green in 3000m (36.74)	-0.14 (-0.31, 0.03)	-0.14 (-0.31, 0.04)	-0.14 (-0.31, 0.04)	-0.16 (-0.35, 0.04)
Natural green in 3000m (8.88)	-0.02 (-0.09, 0.04)	-0.02 (-0.09, 0.04)	-0.02 (-0.09, 0.04)	-0.03 (-0.09, 0.04)
NO_2 (8.49 μg/m^3)	0.03 (-0.06, 0.12)	0.05 (-0.04, 0.14)	0.05 (-0.05, 0.15)	0.02 (-0.10, 0.14)
$PM_{2.5}$ absorbance (0.27 x 10^{-5}/m)	0.00 (-0.08, 0.09)	0.03 (-0.05, 0.12)	0.03 (-0.05, 0.12)	0.00 (-0.10, 0.10)
PM_{10} (0.96 μg/m^3)	0.01 (-0.06, 0.08)	0.03 (-0.04, 0.10)	0.03 (-0.04, 0.10)	0.01 (-0.07, 0.09)
$PM_{2.5}$ (1.13 μg/m^3)	-0.06 (-0.18, 0.06)	-0.02 (-0.14, 0.10)	-0.03 (-0.15, 0.09)	-0.06 (-0.19, 0.07)
OP^{ESR} (246.21 A.U./m^3)	-0.04 (-0.15, 0.07)	-0.03 (-0.14, 0.09)	-0.03 (-0.15, 0.08)	-0.06 (-0.19, 0.06)
OP^{DTT} (0.26 nmol DTT/min/m^3)	0.00 (-0.10, 0.09)	0.00 (-0.09, 0.10)	0.00 (-0.09, 0.10)	-0.02 (-0.13, 0.08)
Road traffic noise (6.90 dB(A))	-0.08 (-0.16, 0.00)	-0.06 (-0.14, 0.03)	-0.05 (-0.14, 0.03)	-0.08 (-0.16, 0.01)
Railway noise (8.60 dB(A))	0.01 (-0.07, 0.09)	0.01 (-0.07, 0.09)	0.01 (-0.08, 0.09)	0.00 (-0.08, 0.08)

Abbreviations: CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-d).

Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Unadjusted model.
[b] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the child's home, pubertal development, height and season.
[c] Includes model II and neighborhood SES.
[d] Includes model II and degree of urbanization (in two categories: ≥1500 addresses/km^2; <1500 addresses/km^2).

Table 3. Associations of green space in a 3000m buffer with the diurnal cortisol slope (in nmol/L per hour) at age 12 years, adjusted for air pollution and road traffic noise.

	Average NDVI in 3000m	Total percentage of green space in 3000m
Adjusted for [a]	β (95% CI)	β (95% CI)
NO_2 + road traffic noise	**-0.12 (-0.24, 0.00)**	-0.15 (-0.32, 0.01)
$PM_{2.5}$ absorbance + road traffic noise	**-0.11 (-0.23, 0.00)**	-0.15 (-0.30, 0.00)
PM_{10} + road traffic noise	**-0.11 (-0.22, 0.00)**	-0.14 (-0.29, 0.01)
$PM_{2.5}$ + road traffic noise	**-0.12 (-0.22, -0.01)**	**-0.15 (-0.29, -0.01)**
OP^{ESR} + road traffic noise	**-0.12 (-0.22, -0.01)**	**-0.15 (-0.29, -0.02)**
OP^{DTT} + road traffic noise	**-0.15 (-0.27, -0.04)**	**-0.19 (-0.34, -0.04)**

Abbreviations: CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure.

Statistically significant results are highlighted in bold (p <0.05).

[a] Additionally adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the child's home, pubertal development, height, season and degree of urbanization (in two categories: ≥1500 addresses/km^2; <1500 addresses/km^2).

5

Discussion

Main findings

We found that higher exposure to residential green space in a buffer of 3000m was associated with a larger diurnal decrease in saliva cortisol concentrations in children aged 12 years. These relationships remained after adjustment for ambient air pollution and road traffic noise. Moreover, road traffic noise tended to be related to a larger diurnal decrease in cortisol concentrations. We observed no associations of ambient air pollution with the diurnal cortisol slope.

Comparison with previous epidemiological studies and interpretation of our findings

The findings of the present study are in line with several epidemiological studies showing that higher exposure to green space is related to lower self-reported stress levels in children and adolescents.[6,7,17] Only one previous study has examined associations of green space with cortisol concentrations in children. This study by Van Aart et al. found no relation between residential greenness (defined as the percentage of semi-natural and forested area in a buffer of 2000m and the percentage of agricultural area in a buffer of 300m) and hair cortisol concentrations, an indicator of stress exposure during the last three months, in children aged 9 to 15 years in Belgium.[17]

We found a more consistent association of a larger diurnal decrease in cortisol concentrations with green space in a buffer of 3000m than with green space in a buffer of 300m. This implies that the availability of green space in a greater area surrounding the children's homes, rather than green space closer to home, is related to lower stress levels in our study population. In the Netherlands, children aged 12 years generally have a high level of independence (i.e. they are allowed to visit places further away from home) and cycle to school independently. This may explain why green space in a buffer of 3000m was more closely related to the diurnal cortisol slope than green space in a buffer of 300m in this study.

The associations of green space in a buffer of 3000m with a larger diurnal cortisol slope remained after adjustment for ambient air pollution and road traffic noise. This indicates that the relationships between green space and the diurnal cortisol slope are not explained by lower air pollution or road traffic noise levels (as a result of fewer air pollution and noise sources in green areas). Van Aart et al. found associations of residential greenness with lower self-reported psychosocial stress independent of ambient concentrations of black carbon and $PM_{2.5}$ and traffic noise levels, which is consistent with the findings from our study.[17] We observed that associations of green space in a buffer of 3000m were driven by associations with the percentage of agricultural green space. There is a possibility that these associations partly reflect urban-rural differences in chronic stress levels (for reasons other than air pollution, traffic noise or lack of green space), which we did not adequately capture by including the degree of urbanization as a categorical variable in our analyses. In other words: the associations of (agricultural) green space with the diurnal cortisol slope could be partly attributed to residual confounding by degree of urbanization.

We did not observe associations between ambient air pollution and the diurnal cortisol slope in children aged 12 years. A previous study found that ambient NO_2 exposure, but not $PM_{2.5}$ exposure, was associated with a decrease in the diurnal cortisol slope in 140 adolescents in Los Angeles.[19] NO_2 concentrations and the variability in NO_2 concentrations were higher in the study in Los Angeles than in our study (mean (IQR) 44.2 (10.0) μg/m^3 versus 22.5 (8.5) μg/m^3 in our study), which may explain the discrepancy between the two studies.

In this study, road traffic noise tended to be related to a larger diurnal decrease in cortisol levels, an indicator of lower chronic stress levels. This is an unexpected finding, since we hypothesized that exposure to traffic noise may be associated with higher stress levels in children. This association, however, weakened when we excluded children whose saliva samples had not been stored according to protocol. No previous studies have examined relationships between road traffic or railway noise exposure and the diurnal cortisol slope in children or adolescents. However, three small cross-sectional studies (sample sizes from 43 to 115) showed significantly higher urinary or saliva cortisol levels in children with high road traffic noise exposure.[9] Residential road traffic noise exposure was not associated with morning or evening saliva cortisol concentrations in adolescents aged 16 years in a recent study in Stockholm County.[18] In the same study, noise annoyance (mainly due to noise from neighbors or road traffic at the residence) was related to higher morning cortisol levels.[18] This suggests that individual perception of noise from different sources, rather than estimated road traffic noise levels, may influence cortisol concentrations in children. We do not have reasonable explanations for our observed association of road traffic noise with a larger diurnal decrease in cortisol levels and future studies are needed that examine relationships between exposure to traffic noise and biomarkers of chronic stress in children.

Strengths and limitations

This study has several strengths. We have measured a commonly used biomarker of chronic stress in a large population of children aged 12 years. We estimated exposure to multiple spatially correlated environmental factors that may be associated with stress levels in children. Furthermore, we included detailed and specific indicators of residential exposure to green space. Most previous epidemiological studies only used the total percentage of green space or average NDVI in several buffers around participants' home addresses to assess exposure to green space.[2] We additionally examined associations of specific types of green space (urban, agricultural and natural) with the diurnal cortisol slope in children.

This study also has some limitations. As in most previous studies, saliva samples were only collected during one day. Since we only had access to one day of saliva cortisol data, we had to assume that the collection day represented a typical circadian cycle for the participants and that the observed associations reflected long-term effects rather than acute HPA-axis modifications. One study showed that, of the cortisol features, total daily cortisol output may be most stable over time, followed by the diurnal cortisol slope and the CAR.[35] However, stability estimates were generally quite modest.[35] Rotenberg et al. found that the diurnal cortisol profile was relatively stable in children and adolescents in Montreal, but also reported that at least three to seven days of saliva collections are needed to minimize within-subject variance in the diurnal cortisol slope.[36]

Like the majority of previous epidemiological studies, we only had information on traffic noise levels outside the homes of our study participants. We lacked information on window type, orientation of the bedroom and indoor insulation, which may affect a child's actual exposure to traffic noise. This may have led to misclassification of individual traffic noise exposure. Another limitation is that we did not know if and how often our study participants used the green spaces in the specified buffers around their homes. Finally, information on the quality of green spaces was not available in this study. Quality characteristics of green spaces, such as safety, walkability and sport/play facilities, may affect the use of green spaces.[3,37]

Implications and future research directions

High levels of stress during childhood have been linked to impaired emotional and behavioral development as well as adverse health consequences later in life, including depression, cardiovascular disease and diabetes.[38] It is therefore important to assess the impact of modifiable determinants on chronic stress levels in children. The results of this study suggest that protecting or increasing green spaces may be effective public health interventions to reduce stress levels in children in the Netherlands. However, more epidemiological studies are needed that assess associations of green space with both subjective stress and cortisol concentrations in children in order to design and implement effective public health interventions. Future studies should examine associations of green space, air pollution and traffic noise with saliva cortisol concentrations, and other (physiological) markers of chronic stress, that are collected during multiple days in children and adolescents, taking other sources of acute and chronic stress into account as potential confounders.

Conclusion

Residential exposure to green space was associated with a larger diurnal decrease in saliva cortisol concentrations, an indicator of lower chronic stress levels, in children aged 12 years. Ambient air pollution and traffic noise were not significantly related to the diurnal cortisol slope in children.

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Supplemental Material

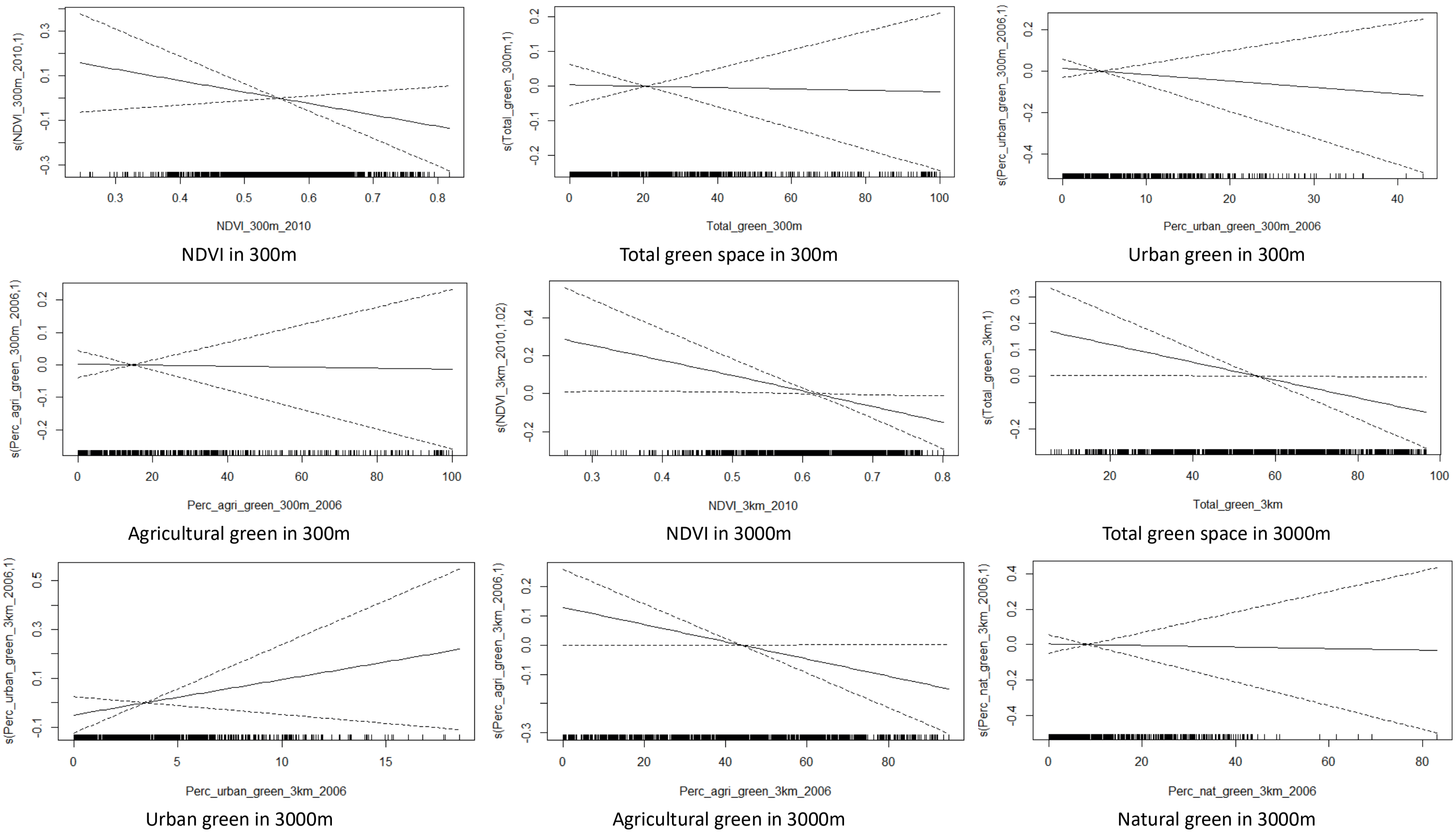

Figure S1. Exposure-response curves for the associations of green space, air pollution and traffic noise with the diurnal cortisol slope at age 12 years.

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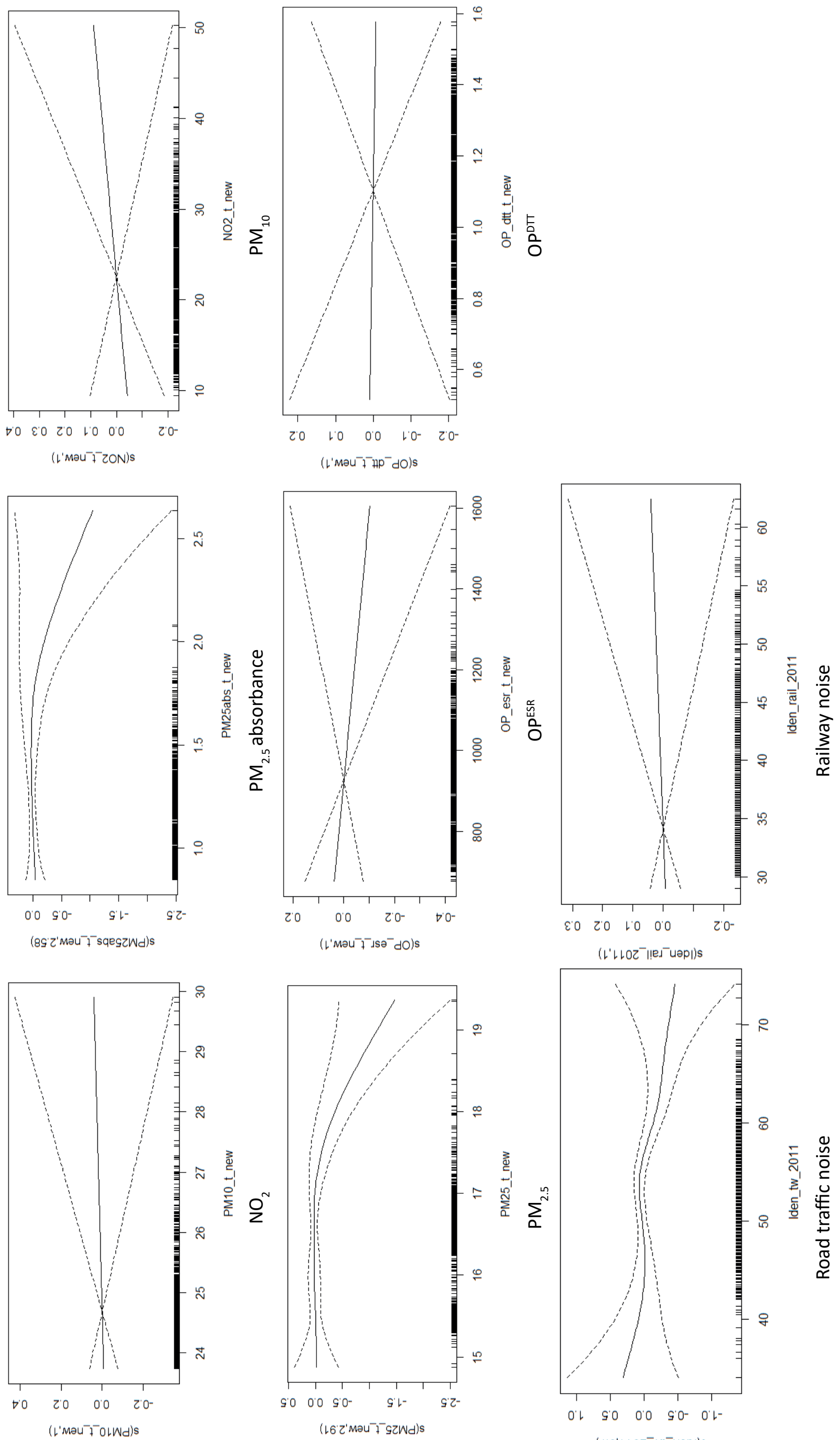

Figure S1 (continued).

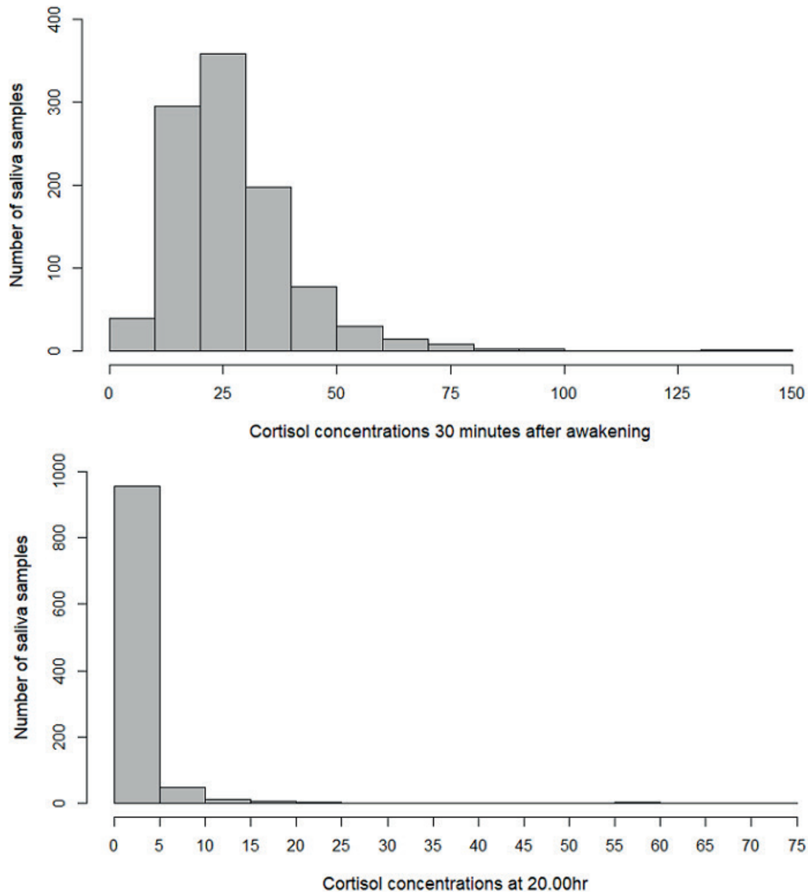

Figure S2. Distributions of saliva cortisol concentrations (in nmol/L) 30 minutes after awakening and at 8.00pm in 1027 children aged 12 years.

Table S1. Spearman correlations between green space, ambient air pollution and traffic noise at age 12 years.

		NDVI		Total percentage of green space		Air pollutants						Noise	
		300m	3000m	300m	3000m	NO_2	$PM_{2.5}$ abs	PM_{10}	$PM_{2.5}$	OP^{ESR}	OP^{DTT}	Road traffic	Railway
NDVI	300m		0.59	0.64	0.53	-0.60	-0.47	-0.41	-0.32	-0.27	-0.67	-0.26	-0.20
	3000m			0.30	0.83	-0.64	-0.50	-0.52	-0.22	-0.17	-0.56	-0.21	-0.28
Total percentage green space	300m				0.46	-0.46	-0.38	-0.38	-0.28	-0.33	-0.53	-0.21	-0.17
	3000m					-0.72	-0.64	-0.70	-0.34	-0.38	-0.57	-0.26	-0.36
Air pollutants	NO_2						0.89	0.76	0.65	0.63	0.73	0.39	0.34
	$PM_{2.5}$ abs							0.87	0.81	0.72	0.55	0.46	0.34
	PM_{10}								0.63	0.53	0.49	0.47	0.31
	$PM_{2.5}$									0.80	0.37	0.41	0.29
	OP^{ESR}										0.30	0.36	0.30
	OP^{DTT}											0.25	0.19
Noise	Road traffic												0.16
	Railway												

Abbreviations: NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Table S2. Associations of green space, air pollution and traffic noise with the diurnal cortisol slope (in nmol/L/hr) in children whose samples have been stored according to protocol (n = 921).*

Exposure (increment)	Model 1 [a]	Model 2 [b]	Model 3 [c]	Model 4 [d]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Average NDVI in 300m (0.13)	-0.07 (-0.17, 0.03)	-0.09 (-0.19, 0.01)	-0.09 (-0.19, 0.01)	-0.07 (-0.18, 0.05)
Total percentage of green space in 300m (27.19)	0.00 (-0.08, 0.08)	-0.02 (-0.10, 0.07)	-0.02 (-0.10, 0.07)	0.01 (-0.08, 0.10)
Urban green in 300m (7.40)	-0.02 (-0.09, 0.06)	-0.02 (-0.10, 0.06)	-0.02 (-0.10, 0.06)	-0.02 (-0.10, 0.06)
Agricultural green in 300m (21.29)	-0.01 (-0.08, 0.06)	-0.02 (-0.09, 0.05)	-0.02 (-0.09, 0.05)	0.00 (-0.08, 0.07)
Natural green in 300m (yes vs. no)	0.08 (-0.12, 0.27)	0.07 (-0.13, 0.27)	0.07 (-0.13, 0.27)	0.07 (-0.13, 0.27)
Average NDVI in 3000m (0.13)	**-0.13 (-0.23, -0.03)**	**-0.13 (-0.23, -0.03)**	**-0.14 (-0.24, -0.03)**	**-0.12 (-0.23, -0.01)**
Total percentage of green space in 3000m (31.38)	**-0.14 (-0.25, -0.03)**	**-0.15 (-0.26, -0.04)**	**-0.15 (-0.26, -0.04)**	**-0.15 (-0.30, -0.01)**
Urban green in 3000m (3.84)	-0.02 (-0.16, 0.13)	0.01 (-0.14, 0.15)	0.01 (-0.14, 0.16)	0.01 (-0.14, 0.15)
Agricultural green in 3000m (36.81)	-0.17 (-0.35, 0.02)	-0.15 (-0.34, 0.04)	-0.15 (-0.34, 0.04)	-0.16 (-0.38, 0.05)
Natural green in 3000m (8.87)	-0.04 (-0.10, 0.03)	-0.03 (-0.10, 0.04)	-0.03 (-0.10, 0.04)	-0.03 (-0.10, 0.04)
NO_2 (8.50 µg/m^3)	0.06 (-0.04, 0.16)	0.08 (-0.02, 0.18)	0.08 (-0.02, 0.19)	0.05 (-0.08, 0.18)
$PM_{2.5}$ absorbance (0.27 x 10^{-5}/m)	0.05 (-0.04, 0.14)	0.07 (-0.02, 0.16)	0.07 (-0.02, 0.16)	0.04 (-0.07, 0.15)
PM_{10} (0.97 µg/m^3)	0.05 (-0.02, 0.13)	0.07 (-0.01, 0.15)	0.07 (-0.01, 0.15)	0.05 (-0.04, 0.14)
$PM_{2.5}$ (1.13 µg/m^3)	-0.02 (-0.15, 0.11)	0.00 (-0.13, 0.13)	-0.00 (-0.14, 0.13)	-0.04 (-0.18, 0.10)
OP^{ESR} (245.50 A.U./m^3)	0.00 (-0.12, 0.12)	0.00 (-0.12, 0.13)	-0.00 (-0.13, 0.13)	-0.04 (-0.17, 0.09)
OP^{DTT} (0.26 nmol DTT/min/m^3)	0.02 (-0.08, 0.12)	0.02 (-0.08, 0.12)	0.01 (-0.09, 0.12)	-0.02 (-0.13, 0.09)
Road traffic noise (6.90 dB(A))	-0.04 (-0.13, 0.05)	-0.03 (-0.12, 0.06)	-0.02 (-0.11, 0.07)	-0.05 (-0.14, 0.04)
Railway noise (8.60 dB(A))	0.03 (-0.06, 0.11)	0.01 (-0.07, 0.10)	0.01 (-0.08, 0.10)	0.00 (-0.08, 0.09)

Abbreviations: CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.
Associations with the percentages of urban, agricultural and natural green space are adjusted for the other types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-d).
* Children whose saliva samples were not stored in a refrigerator for a few days, children whose samples were removed from the freezer for 24 hours and children whose samples have not been stored in the freezer within seven days were excluded.

Statistically significant results are highlighted in bold ($p < 0.05$).

[a] Unadjusted model.
[b] Adjusted for sex, age, parental level of education, maternal smoking during pregnancy, smoking in the child's home, pubertal development, height and season.
[c] Includes model 2 and neighborhood SES.
[d] Includes model 2 and degree of urbanization (in two categories: ≥1500 addresses/km^2; <1500 addresses/km^2).

Chapter 6

Green space, air pollution, traffic noise and mental wellbeing throughout adolescence: findings from the PIAMA study

Lizan D. Bloemsma, Ulrike Gehring, Jochem O. Klompmaker, Gerard Hoek, Nicole A.H. Janssen, Erik Lebret, Bert Brunekreef, Alet H. Wijga

Abstract

Background: Green space, air pollution and traffic noise exposure may be associated with mental health in adolescents. We assessed the individual and joint associations of residential green space, air pollution and traffic noise with mental wellbeing from age 11 to 20 years.

Methods: We included 3059 participants of the Dutch PIAMA birth cohort who completed the five-item Mental Health Inventory (MHI-5) at ages 11, 14, 17 and/or 20 years. MHI-5 scores ranged from 0 to 100, with scores ≤60 indicating a poor mental wellbeing. We estimated exposure to green space (the average Normalized Difference Vegetation Index (NDVI) and percentages of green space in circular buffers of 300m and 3000m), ambient air pollution and traffic noise at the adolescents' home addresses at the times of completing the MHI-5. Associations with poor mental wellbeing were assessed by generalized linear mixed models, adjusting for potential confounders.

Results: The odds of poor mental wellbeing at age 11 to 20 years decreased with increasing exposure to green space in a 3000m buffer (adjusted odds ratio (OR) 0.78 [95%CI 0.68-0.88] per IQR increase in the average NDVI; adjusted OR 0.77 [95%CI 0.67-0.88] per IQR increase in the total percentage of green space). Higher air pollution exposure was associated with a higher odds of poor mental wellbeing, but associations attenuated after adjustment for green space and traffic noise. Traffic noise was not related to mental wellbeing throughout adolescence.

Conclusions: Residential exposure to green space may be associated with a better mental wellbeing in adolescents. Future studies assessing relationships between air pollution and mental wellbeing in adolescence should account for green space levels.

Introduction

It has been estimated that 10-20% of adolescents globally experience mental health problems.[1] Mental health conditions account for 16% of the global burden of disease and injury in persons aged 10 to 19 years.[1] Studies suggest that a substantial proportion of mental health conditions in adults originate in early life, indicating that poor mental wellbeing in childhood and adolescence may have long-lasting consequences.[2] The identification of risk factors for poor mental wellbeing in adolescents may therefore contribute to the development of interventions to prevent later adult mental health problems.

It is increasingly recognized that mental wellbeing is affected both by personal characteristics, such as genetic factors and lifestyle habits, and by environmental exposures.[3] Recent epidemiological studies have assessed associations of green space, air pollution or traffic noise with mental health outcomes in adults and children. Several studies have shown that exposure to green space is related to improved mental wellbeing in children and adolescents.[4,5] In contrast, Dzhambov et al. found no associations between residential green space and self-reported mental health in adolescents in Bulgaria.[6] Another study found no relationships between school surrounding greenness and psychological distress, self-rated mental health, suicide ideation and suicide attempt in students in Canada.[7] A recent review has shown that exposure to increased concentrations of several air pollutants, including particulate matter, nitrogen dioxide (NO_2) and sulfur dioxide (SO_2), may be associated with poor mental health.[8] However, only few studies have assessed relationships between ambient air pollution and mental health outcomes in adolescents.[9-11] Several epidemiological studies showed no associations between exposure to aircraft or traffic noise and mental wellbeing in children.[12] Similarly, two studies conducted in Bulgaria and the United States found no associations of noise exposure with self-reported mental health or mental health disorders in adolescents.[13,14]

In daily life, people are exposed to multiple environmental risks and amenities. Exposures to green space, air pollution and traffic noise are generally spatially correlated. Higher levels of green space are associated with lower levels of ambient air pollution and noise, while air pollution and noise share road traffic as a major common source.[15-19] However, none of the epidemiological studies that have been performed so far has assessed the combined associations of these three environmental exposures with mental health in adolescents. The aim of this study is therefore to examine the individual and joint associations of residential green space, air pollution and traffic noise with mental wellbeing from age 11 to 20 years.

Methods

Study design and population

This study was conducted within the ongoing Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. The design of the PIAMA study has been described elsewhere.[20,21] In brief, pregnant women were recruited in 1996/1997 from the general population in three different regions of the Netherlands during their second trimester of pregnancy. The baseline study population consisted of 3963 children. Data on socio-demographic and lifestyle characteristics, growth and development were collected through parental questionnaires during pregnancy, at the child's ages of three months and one year, and yearly thereafter until the child was eight years old. When the adolescents were 11, 14, and 17 years old, both parents and adolescents were requested to complete questionnaires. At age 20 years, only the adolescents themselves filled in a questionnaire. The study protocol has been approved by the institutional review boards of the participating institutes and written informed consent was obtained from all parents and children. In this study, we included 3059 adolescents (77.2% of the baseline study population) who have completed the five-item Mental Health Inventory (MHI-5) at least once at ages 11, 14, 17 or 20 years.

Mental wellbeing

At ages 11, 14, 17 and 20 years, participants of the PIAMA study were requested to complete the MHI-5.[22,23] The MHI-5 is a validated brief questionnaire that has been widely used internationally to assess mental wellbeing and consists of the following five questions: "How much of the time, during the last month, have you 1) been a very nervous person?; 2) felt calm and peaceful?; 3) felt downhearted and blue?; 4) been a happy person?; and 5) felt so down in the dumps that nothing could cheer you up?".[22] Response options ranged from 1 (constantly) to 5 (never). We calculated the MHI-5 score as follows: (the sum of the 5 items - 5) / 20 x 100. This resulted in scores ranging from 0 to 100, with higher scores indicating a better mental wellbeing. Adolescents with a MHI-5 score ≤60 were classified as adolescents with a poor mental wellbeing.[23]

Residential exposures

We estimated green space, ambient air pollution and traffic noise levels at the adolescents' current home addresses at the times of completing the MHI-5 (i.e. recent exposures). Details of the exposure assessment have been published previously.[18,19]

Green space. We used multiple indicators to assess residential exposure to green space. The Normalized Difference Vegetation Index (NDVI) was used to assess greenness levels around the adolescents' homes.[24] The NDVI was derived from Landsat 5 Thematic Mapper data at 30m x 30m resolution. NDVI values range from -1 to 1, with higher values indicating a higher density of green vegetation. We created a map of the Netherlands by combining cloud free images of the summer of 2010. We calculated the average NDVI in circular buffers of 300m and 3000m around the adolescents' homes at the times of completing the MHI-5.

We additionally assessed the total percentage of green space and percentages of urban, agricultural and natural green space in buffers of 300m and 3000m around the adolescents' homes by using Bestand Bodemgebruik of 2006 and TOP10NL of 2016.[25,26] Bestand Bodemgebruik and TOP10NL are detailed land-use maps of the Netherlands that, in contrast to the NVDI, do not include street greenery and private green property (such as gardens). Since TOP10NL is only available from 2012 onwards, we used Bestand Bodemgebruik to assess the percentages of green space when the study participants were 11 years old (around 2008/2009). TOP10NL of 2016 was used to determine the percentages of green space when the adolescents completed the MHI-5 at ages 14, 17 and 20 years. We assessed surrounding greenness and the percentages of green space in ArcGIS 10.2.2 (Esri, Redlands, CA, USA).

Air pollution. We used land-use regression (LUR) models that were based on measurement campaigns performed in 2009 to estimate annual average concentrations of particulate matter with diameters of <10 µm (PM_{10}) and <2.5 µm ($PM_{2.5}$), NO_2, $PM_{2.5}$ absorbance (a marker of black carbon) and the oxidative potential of $PM_{2.5}$ (electron spin resonance (OP^{ESR}) and dithiothreitol (OP^{DTT})) at all ages without back-extrapolation. Detailed descriptions of the LUR model development have been published previously.[27-29] Substantial variability in annual average ambient air pollution concentrations was explained for PM_{10}, $PM_{2.5}$, NO_2, $PM_{2.5}$ absorbance and OP^{ESR} (leave-one-out cross validation (R^2_{LOOCV}) = 0.60 - 0.89) but not for OP^{DTT} (R^2_{LOOCV} = 0.47).[27-29]

Traffic noise. We estimated annual average road traffic and railway noise levels at the adolescents' homes by the Standard Model Instrumentation for Noise Assessments (STAMINA). The STAMINA model has been developed by the Dutch National Institute for Public Health and the Environment and implements the standard Dutch Calculation method for traffic and industrial noise.[30] Daily average (L_{den}) and nighttime average (L_{night}) traffic noise exposure was estimated for 2011. L_{den} is the A-weighted noise level over a 24 hour period with a penalty of 5 dB(A) in the evening (7.00pm - 11.00pm) and a penalty of 10 dB(A) at night (11.00pm - 7.00am). Since L_{den} and L_{night} were highly correlated (r = 0.99 for road traffic noise; r = 0.96 for railway noise), we only included L_{den} in our analyses.

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Potential confounders

Parental level of education as an indicator of family socioeconomic status (SES, defined as the maximum of the mother's and father's educational level and categorized as low/intermediate and high) and information on maternal smoking during pregnancy (yes/no) were obtained from parental questionnaires administered during pregnancy and when the children were one year old. We assessed any smoking in the adolescent's home (at least once a week vs. no) through parental questionnaires from age 11 to 17 years. At age 20 years, study participants reported exposure to secondhand smoke at home themselves. The adolescents also reported active smoking at age 11 to 20 years. We defined active smoking (yes/no) as smoking at least once a month at ages 11 and 14 years and smoking at least once a week at ages 17 and 20 years. We used the status scores of the 4-digit postal code areas from the Netherlands Institute for Social Research (SCP) of 2006 to 2017 to determine neighborhood SES. Status scores comprise the average income, the percentage unemployed persons, percentage of residents with a low income and the percentage of low educated residents in a postal code area. A higher status score indicates a higher neighborhood SES.[31]

Statistical methods

We first assessed the shapes of the unadjusted associations of the continuous exposures and potential confounders with mental wellbeing by generalized additive models with integrated smoothness estimation and a logit link (GAM function; The R Project for Statistical Computing 2.8.0, www.r-project.org). Since there was no evidence of non-linearity (Figure S1), we included all exposures as continuous variables in the analyses and expressed associations per interquartile range increase (IQR) in exposure. Since a large proportion of the adolescents had no natural green space in a buffer of 300m around their homes (between 57.0% and 83.3% in the different age categories), we created a binary variable: natural green space in a buffer of 300m yes/no. We examined the overall associations of green space, air pollution and traffic noise with poor mental wellbeing from age 11 to 20 years with generalized linear mixed models. We included random subject-specific intercepts to account for within-subject correlation across the repeated mental wellbeing measurements. Additionally, age-specific estimates were obtained by including exposure-age interaction terms.

We defined a priori three regression models with increasing degree of adjustment for potential confounders. Model 1 was adjusted for age. Model 2 was adjusted for age, sex, parental level of education, maternal smoking during pregnancy, any smoking in the adolescent's home and active smoking. Model 3 further included neighborhood SES. We always adjusted associations with the percentages of urban, agricultural and natural green space for the other two types of green space in the same buffer size. We additionally examined potential confounding of associations with one exposure by the other exposures of interest with multi-exposure models (i.e. models including green space, air pollution and traffic noise).

People living in urban areas may have a worse mental wellbeing than people living in less urbanized areas.[32,33] However, adjusting for degree of urbanization could lead to over-adjustment in this study, since the degree of urbanization is a source of residential green space, air pollution and traffic noise levels. As a sensitivity analysis, we have therefore additionally adjusted model 2 for degree of urbanization (in two categories: ≥1500 addresses/km^2; <1500 addresses/km^2) for the exposures that were associated with poor mental wellbeing in multi-exposure models. The statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), except the analyses of the linearity of the associations, which were performed with R version 3.4.3.[34]

Results

Characteristics of the study population and the distributions of residential green space, air pollution and traffic noise levels are shown in Table 1. While tobacco smoke exposure at the adolescents' homes declined throughout the study period, the proportion of active smokers increased from 0% at age 11 years to 20.3% at age 20 years. Study participants more often lived in an urban area, had lower levels of residential green space and were exposed to higher levels of ambient air pollution (except for $PM_{2.5}$) and traffic noise at age 20 than at ages 11, 14 and 17 years. The prevalence of poor mental wellbeing ranged from 5.9% at age 11 to 23.7% at age 20 years (Table 1).

Spearman correlations between the green space indicators and estimated concentrations of ambient air pollutants ranged from -0.76 to -0.23 and were highest for the total percentage of green space in a buffer of 3000m (Table S1). Correlations between green space and traffic noise ranged from -0.38 to -0.19 and road traffic noise levels were moderately positively correlated with the various air pollutants (r = 0.30 to 0.51). Correlations between ambient air pollution and the number of addresses per km^2 (as an indicator of the degree of urbanization) ranged from 0.45 to 0.74 (Table S2). The number of addresses per km^2 was negatively correlated with the green space indicators, except for urban green in a buffer of 300m (r = 0.25) and 3000m (r = 0.75) (Table S2).

Table 1. Characteristics of the study population at ages 11, 14, 17 and 20 years and the distribution of green space, air pollution and traffic noise levels.

Characteristic	n (%) or median (25th - 75th percentiles)			
	Age 11 years	**Age 14 years**	**Age 17 years**	**Age 20 years**
N	2624	2506	2085	2189
MHI-5 score	80.0 (75.0 - 85.0)	80.0 (70.0 - 85.0)	75.0 (65.0 - 85.0)	75.0 (65.0 - 85.0)
Poor mental wellbeing	154 (5.9)	302 (12.1)	384 (18.4)	518 (23.7)
Boys	1320 (50.3)	1258 (50.2)	1011 (48.5)	1037 (47.4)
Parental level of education				
Low/intermediate	1178 (45.2)	1107 (44.5)	872 (42.2)	957 (44.1)
High	1427 (54.8)	1379 (55.5)	1197 (57.9)	1211 (55.9)
Maternal smoking during pregnancy (yes)	397 (15.3)	360 (14.5)	261 (12.6)	309 (14.2)
Smoking in adolescent's home (yes)	333 (13.2)	241 (10.7)	155 (8.7)	194 (8.9)
Active smoking (yes) [a]	0 (0.0)	153 (6.1)	277 (13.4)	443 (20.3)
Neighborhood SES [b]	0.36 (-0.25 - 0.96)	0.22 (-0.44 - 1.02)	0.24 (-0.51 - 0.96)	0.11 (-0.69 - 0.82)
Degree of urbanization				
≥1500 addresses/km²	1030 (40.1)	1028 (41.3)	884 (42.7)	1311 (61.7)
<1500 addresses/km²	1538 (59.9)	1463 (58.7)	1188 (57.3)	813 (38.3)
Average NDVI in 300m	0.55 (0.48 - 0.61)	0.55 (0.48 - 0.61)	0.55 (0.48 - 0.61)	0.50 (0.42 - 0.58)
Total percentage of green space in 300m	12.2 (2.4 - 29.1)	19.7 (11.6 - 33.2)	19.7 (11.6 - 33.4)	15.1 (7.3 - 27.2)
Percentage urban green in 300m	0.7 (0.0 - 7.8)	9.8 (4.4 - 15.7)	9.6 (4.3 - 15.5)	8.6 (3.8 - 14.6)
Percentage agricultural green in 300m	0.0 (0.0 - 19.7)	1.1 (0.0 - 16.2)	1.1 (0.0 - 17.0)	0.0 (0.0 - 9.1)
Percentage natural green in 300m	(0.0 - 0.0)	0.0 (0.0 - 1.3)	0.0 (0.0 - 1.3)	0.0 (0.0 - 0.3)
Any natural green within 300m	428 (16.7)	1059 (42.5)	890 (43.0)	636 (30.7)
Average NDVI in 3000m	0.63 (0.55 - 0.68)	0.62 (0.56 - 0.68)	0.62 (0.55 - 0.68)	0.57 (0.50 - 0.66)
Total percentage of green space in 3000m	55.3 (39.4 - 70.2)	56.3 (42.8 - 67.0)	56.2 (42.6 - 66.9)	44.5 (29.7 - 60.3)
Percentage urban green in 3000m	2.8 (1.0 - 5.0)	6.0 (2.7 - 9.6)	5.9 (2.8 - 9.6)	8.3 (4.1 - 12.1)
Percentage agricultural green in 3000m	43.0 (24.9 - 61.5)	40.4 (23.6 - 55.7)	40.2 (23.8 - 55.8)	27.4 (12.3 - 48.7)
Percentage natural green in 3000m	3.5 (1.4 - 10.5)	4.1 (2.1 - 10.3)	4.1 (2.1 - 10.0)	3.1 (1.8 - 6.5)
PM_{10} (µg/m³) [c]	24.5 (24.0 - 25.0)	24.5 (24.0 - 25.0)	24.5 (24.0 - 25.0)	24.9 (24.2 - 25.7)
$PM_{2.5}$ (µg/m³) [c]	16.5 (15.6 - 16.7)	16.5 (15.6 - 16.7)	16.5 (15.6 - 16.7)	16.5 (15.8 - 16.8)
OP^{ESR} (A.U./m³) [c]	934.3 (774.7 - 1020.8)	930.3 (776.1 - 1017.7)	930.6 (776.5 - 1016.2)	955.1 (844.6 - 1049.9)

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Table 1. Continued.

Characteristic	n (%) or median (25^{th} - 75^{th} percentiles)			
	Age 11 years	**Age 14 years**	**Age 17 years**	**Age 20 years**
OP^{DTT} (nmol DTT/min/m^3) [c]	1.1 (1.0 - 1.3)	1.1 (1.0 - 1.2)	1.1 (1.0 - 1.2)	1.2 (1.1 - 1.3)
NO_2 (µg/m^3) [c]	22.8 (17.9 - 27.0)	22.7 (17.7 - 26.9)	22.7 (17.8 - 27.0)	25.0 (20.7 - 29.6)
$PM_{2.5}$ absorbance (10^{-5}/m) [c]	1.2 (1.0 - 1.3)	1.2 (1.0 - 1.3)	1.2 (1.0 - 1.3)	1.3 (1.1 - 1.4)
Road traffic noise (L_{den} dB(A))	52.5 (49.4 - 56.3)	52.4 (49.4 - 56.3)	52.4 (49.3 - 56.5)	54.4 (50.4 - 58.9)
Railway noise (L_{den} dB(A))	30.4 (29.0 - 37.8)	30.3 (29.0 - 37.7)	30.9 (29.0 - 38.0)	32.6 (29.0 - 39.3)

Abbreviations: SES = socioeconomic status; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

[a] At ages 11 and 14 years, adolescents who smoke at least once a month are considered active smokers. At ages 17 and 20 years, adolescents who smoke at least once a week are considered active smokers.

[b] A higher score indicates a higher SES.

[c] Air pollution is modeled based upon 2009 measurements for all age categories.

Table 2. Associations of green space, air pollution and traffic noise with poor mental wellbeing from age 11 to 20 years.

Exposure (increment)	Model 1[a]	Model 2[b]	Model 3[c]
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Average NDVI in 300m (0.13)	**0.87 (0.78 - 0.97)**	**0.88 (0.78 - 0.98)**	**0.88 (0.79 - 0.99)**
Total percentage of green space in 300m (23.01)	0.96 (0.86 - 1.06)	0.97 0.87 - 1.08)	0.97 (0.87 - 1.08)
Urban green in 300m (11.84)	1.10 (0.97 - 1.25)	1.12 (0.99 - 1.28)	1.11 (0.98 - 1.27)
Agricultural green in 300m (15.54)	0.98 (0.90 - 1.06)	1.00 (0.92 - 1.08)	0.99 (0.91 - 1.08)
Natural green in 300m (yes vs. no)	0.94 (0.77 - 1.15)	0.92 (0.75 - 1.13)	0.94 (0.76 - 1.15)
Average NDVI in 3000m (0.14)	**0.75 (0.66 - 0.85)**	**0.76 (0.67 - 0.87)**	**0.78 (0.68 - 0.88)**
Total percentage of green space in 3000m (28.34)	**0.75 (0.66 - 0.86)**	**0.76 (0.67 - 0.87)**	**0.77 (0.67 - 0.88)**
Urban green in 3000m (7.16)	0.95 (0.75 - 1.19)	0.98 (0.77 - 1.24)	0.97 (0.77 - 1.23)
Agricultural green in 3000m (35.14)	**0.72 (0.57 - 0.92)**	**0.75 (0.59 - 0.96)**	**0.75 (0.59 - 0.96)**
Natural green in 3000m (7.52)	**0.91 (0.85 - 0.99)**	**0.92 (0.84 - 0.99)**	**0.92 (0.85 - 1.00)**
PM_{10} (1.15 µg/m^3)	**1.14 (1.05 - 1.25)**	1.07 (0.98 - 1.16)	1.07 (0.98 - 1.17)
$PM_{2.5}$ (1.15 µg/m^3)	1.15 (1.00 - 1.32)	1.15 (1.00 - 1.33)	**1.19 (1.03 - 1.37)**
OP^{ESR} (241.89 A.U./m^3)	1.09 (0.96 - 1.23)	1.08 (0.95 - 1.23)	1.09 (0.96 - 1.25)
OP^{DTT} (0.28 nmol DTT/min/m^3)	**1.19 (1.05 - 1.35)**	**1.22 (1.07 - 1.39)**	**1.22 (1.07 - 1.39)**
NO_2 (9.11 µg/m^3)	**1.21 (1.08 - 1.36)**	**1.21 (1.07 - 1.36)**	**1.22 (1.08 - 1.37)**
$PM_{2.5}$ absorbance (0.29 x 10^{-5}/m)	**1.18 (1.07 - 1.30)**	**1.17 (1.06 - 1.29)**	**1.18 (1.07 - 1.31)**
Road traffic noise (7.40 dB(A))	1.05 (0.94 - 1.16)	1.02 (0.92 - 1.14)	1.04 (0.93 - 1.16)
Railway noise (9.20 dB(A))	1.03 (0.92 - 1.14)	1.04 (0.93 - 1.16)	1.04 (0.93 - 1.16)

Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.

Associations with the percentages of urban, agricultural and natural green space are adjusted for the other two types of green space in the same buffer size (plus additional confounders as detailed in footnotes a-d).

Statistically significant results ($p < 0.05$) are highlighted in bold.

[a] Adjusted for age.

[b] Adjusted for age, sex, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home and active smoking.

[c] Includes model 2 and neighborhood SES.

In single-exposure models, we observed lower odds of poor mental wellbeing from age 11 to 20 years with higher average NDVI in a buffer of 300m (odds ratio (OR) 0.88 [95% confidence interval (CI) 0.79 - 0.99] per 0.13 increase in the average NDVI in model 3, Table 2). The odds of poor mental wellbeing throughout adolescence was also lower with higher average NDVI and total percentage of green space in a buffer of 3000m (OR 0.78 [95% CI 0.68 - 0.88] per 0.14 increase in the average NDVI and OR 0.77 [95% CI 0.67 - 0.88] per 28.3% increase in the total percentage of green space in model 3). The associations with the total percentage of green space in a buffer of 3000m were driven by the percentages of agricultural and natural green space. Higher exposure to $PM_{2.5}$, OP^{DTT}, NO_2 and $PM_{2.5}$ absorbance was associated with a higher odds of poor mental wellbeing from age 11 to 20 years in model 3 (for example, OR 1.22 [95% CI 1.07 - 1.39] per 0.28 nmol DTT/min/m^3 increase in OP^{DTT} and OR 1.22 [95% CI 1.08 - 1.37] per 9.11 μg/m^3 increase in NO_2). We found no relationships between traffic noise and poor mental wellbeing (Table 2).

Table 3 shows the age-specific associations of green space, air pollution and traffic noise with poor mental wellbeing in adolescence. Relationships of the average NDVI and total percentage of green space in a buffer of 3000m with lower odds of poor mental wellbeing were consistent across all ages. Associations between the air pollutants and poor mental wellbeing were positive at all ages and generally strongest at ages 17 and 20 years.

After additional adjustment for ambient air pollution and road traffic noise, associations with the average NDVI and total percentage of green space in a buffer of 3000m hardly changed (for example, OR 0.79 [95% CI 0.67 - 0.92] per 0.14 increase in the average NDVI and OR 0.80 [95% CI 0.68 - 0.96] per 28.3% increase in the total percentage of green space after adjustment for OP^{DTT} and road traffic noise, Table 4). In contrast, relationships with the average NDVI in a buffer of 300m weakened after adjustment for air pollution and traffic noise (Table S3). Associations of the air pollutants with a higher odds of poor mental wellbeing from age 11 to 20 years weakened in three-exposure models (Table 4). However, associations were still positive and strongest for NO_2 and $PM_{2.5}$ absorbance (OR 1.12 [95% CI 0.94 - 1.33] per 9.11 μg/m^3 increase in NO_2 and OR 1.15 [95% CI 1.00 - 1.32] per 0.29 x 10^{-5}/m increase in $PM_{2.5}$ absorbance after adjustment for the average NDVI in 3000m and road traffic noise).

Additional adjustment for degree of urbanization hardly changed association of the average NDVI in a buffer of 3000m with a lower odds of poor mental wellbeing throughout adolescence (Table S4). Relationships with the total percentage of green space in a buffer of 3000m slightly attenuated after adjustment for degree of urbanization.

Table 3. Age-specific associations of green space, air pollution and traffic noise with poor mental wellbeing from age 11 to 20 years.[a]

	Age 11 years	Age 14 years	Age 17 years	Age 20 years
Exposure (increment)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Average NDVI in 300m (0.13)	0.78 (0.59 - 1.03)	0.87 (0.70 - 1.09)	0.94 (0.75 - 1.17)	0.89 (0.76 - 1.05)
Total percentage of green space in 300m (23.01)	0.85 (0.69 - 1.06)	1.01 (0.83 - 1.22)	1.06 (0.87 - 1.29)	0.96 (0.81 - 1.15)
Urban green in 300m (11.84)	1.20 (0.89 - 1.61)	1.15 (0.90 - 1.45)	1.16 (0.91 - 1.47)	1.08 (0.88 - 1.32)
Agricultural green in 300m (15.54)	0.90 (0.77 - 1.06)	1.02 (0.87 - 1.20)	1.07 (0.91 - 1.26)	0.98 (0.84 - 1.15)
Natural green in 300m (yes vs. no)	0.59 (0.32 - 1.09)	0.95 (0.66 - 1.36)	0.92 (0.64 - 1.33)	0.98 (0.69 - 1.38)
Average NDVI in 3000m (0.14)	**0.73 (0.55 - 0.96)**	**0.70 (0.56 - 0.88)**	**0.79 (0.63 - 1.00)**	0.84 (0.70 - 1.00)
Total percentage of green space in 3000m (28.34)	**0.73 (0.56 - 0.95)**	**0.71 (0.55 - 0.91)**	0.79 (0.62 - 1.01)	**0.81 (0.67 - 0.99)**
Urban green in 3000m (7.16)	0.85 (0.44 - 1.61)	0.83 (0.54 - 1.28)	0.87 (0.56 - 1.34)	1.24 (0.86 - 1.78)
Agricultural green in 3000m (35.14)	0.64 (0.40 - 1.03)	**0.61 (0.38 - 0.98)**	0.72 (0.45 - 1.14)	0.97 (0.67 - 1.42)
Natural green in 3000m (7.52)	0.93 (0.79 - 1.08)	0.88 (0.76 - 1.01)	0.90 (0.78 - 1.04)	0.94 (0.82 - 1.08)
PM_{10} (1.15 μg/m^3)	1.10 (0.89 - 1.36)	1.13 (0.94 - 1.34)	1.07 (0.90 - 1.28)	**1.14 (1.02 - 1.28)**
$PM_{2.5}$ (1.15 μg/m^3)	1.06 (0.76 - 1.48)	1.09 (0.83 - 1.44)	**1.33 (1.01 - 1.75)**	1.21 (1.00 - 1.46)
OP^{ESR} (241.89 A.U./m^3)	1.04 (0.77 - 1.41)	1.01 (0.78 - 1.31)	**1.34 (1.05 - 1.72)**	1.05 (0.88 - 1.25)
OP^{DTT} (0.28 nmol DTT/min/m^3)	1.27 (0.95 - 1.69)	1.17 (0.93 - 1.48)	1.15 (0.91 - 1.45)	**1.28 (1.06 - 1.56)**
NO_2 (9.11 μg/m^3)	1.16 (0.89 - 1.52)	**1.27 (1.02 - 1.58)**	1.23 (0.99 - 1.53)	**1.21 (1.02 - 1.42)**
$PM_{2.5}$ absorbance (0.29 x 10^{-5}/m)	1.13 (0.89 - 1.43)	1.18 (0.96 - 1.43)	1.21 (1.00 - 1.47)	**1.19 (1.04 - 1.35)**
Road traffic noise (7.40 dB(A))	0.88 (0.67 - 1.16)	0.93 (0.75 - 1.16)	1.13 (0.91 - 1.39)	1.09 (0.93 - 1.27)
Railway noise (9.20 dB(A))	0.82 (0.62 - 1.09)	1.01 (0.82 - 1.24)	1.17 (0.96 - 1.42)	1.07 (0.91 - 1.26)

Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index.

Associations are shown for an interquartile range increase in exposure, except for natural green in a buffer of 300m.

Statistically significant results ($p < 0.05$) are highlighted in bold.

[a] Adjusted for age, sex, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, active smoking and neighborhood SES. Associations with the percentages of urban, agricultural and natural green space are additionally adjusted for the other two types of green space.

Table 4. Associations of green space in a buffer of 3000m, air pollution and road traffic noise with poor mental wellbeing from age 11 to 20 years from three-exposure models.

Model [a]	**Exposure**	**OR (95% CI)**
PM_{10} + NDVI in 3000m + road traffic noise	PM_{10}	1.04 (0.93 - 1.17)
	NDVI in 3000m	**0.78 (0.67 - 0.91)**
	Road traffic noise	0.94 (0.82 - 1.07)
PM_{10} + total green space in 3000m + road traffic noise	PM_{10}	1.00 (0.88 - 1.14)
	Total green space in 3000m	**0.75 (0.63 - 0.90)**
	Road traffic noise	0.95 (0.83 - 1.08)
$PM_{2.5}$ + NDVI in 3000m + road traffic noise	$PM_{2.5}$	1.09 (0.92 - 1.29)
	NDVI in 3000m	**0.77 (0.67 - 0.88)**
	Road traffic noise	0.92 (0.81 - 1.05)
$PM_{2.5}$ + total green space in 3000m + road traffic noise	$PM_{2.5}$	1.04 (0.88 - 1.24)
	Total green space in 3000m	**0.76 (0.65 - 0.88)**
	Road traffic noise	0.93 (0.82 - 1.06)
OP^{ESR} + NDVI in 3000m + road traffic noise	OP^{ESR}	1.04 (0.90 - 1.20)
	NDVI in 3000m	**0.76 (0.67 - 0.87)**
	Road traffic noise	0.94 (0.83 - 1.07)
OP^{ESR} + total green space in 3000m + road traffic noise	OP^{ESR}	1.00 (0.86 - 1.16)
	Total green space in 3000m	**0.76 (0.65 - 0.88)**
	Road traffic noise	0.96 (0.85 - 1.09)
OP^{DTT} + NDVI in 3000m + road traffic noise	OP^{DTT}	1.08 (0.92 - 1.27)
	NDVI in 3000m	**0.79 (0.67 - 0.92)**
	Road traffic noise	0.94 (0.84 - 1.06)
OP^{DTT} + total green space in 3000m + road traffic noise	OP^{DTT}	1.10 (0.93 - 1.30)
	Total green space in 3000m	**0.80 (0.68 - 0.96)**
	Road traffic noise	0.95 (0.84 - 1.07)
NO_2 + NDVI in 3000m + road traffic noise	NO_2	1.12 (0.94 - 1.33)
	NDVI in 3000m	**0.83 (0.70 - 0.98)**
	Road traffic noise	0.94 (0.83 - 1.06)
NO_2 + total green space in 3000m + road traffic noise	NO_2	1.10 (0.91 - 1.34)
	Total green space in 3000m	**0.82 (0.67 - 1.00)**
	Road traffic noise	0.94 (0.83 - 1.07)
$PM_{2.5}$ absorbance + NDVI in 3000m + road traffic noise	$PM_{2.5}$ absorbance	1.15 (1.00 - 1.32)
	NDVI in 3000m	**0.83 (0.71 - 0.96)**
	Road traffic noise	0.91 (0.79 - 1.04)
$PM_{2.5}$ absorbance + total green space in 3000m + road traffic noise	$PM_{2.5}$ absorbance	1.12 (0.96 - 1.30)
	Total green space in 3000m	**0.82 (0.69 - 0.98)**
	Road traffic noise	0.92 (0.80 - 1.05)

Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure.

Statistically significant results ($p < 0.05$) are highlighted in bold.

[a] Additionally adjusted for age, sex, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, active smoking and neighborhood SES.

Discussion

Main findings

We found that the odds of poor mental wellbeing from age 11 to 20 years was lower with higher average NDVI and total percentage of green space in a buffer of 3000m. These associations were consistent across all ages and remained after adjustment for air pollution, traffic noise and degree of urbanization. Higher ambient air pollution concentrations were associated with a higher odds of poor mental wellbeing throughout adolescence, but these associations weakened after adjustment for green space and traffic noise.

Comparison with previous studies and interpretation of findings

Our findings are in line with several studies that found relationships between exposure to green space and better mental wellbeing in children and adolescents.[4,5] A recent study by Dzhambov et al. found no associations between self-reported mental wellbeing and the average NDVI, Soil Adjusted Vegetation Index and tree cover density in a buffer of 500m surrounding the homes of 399 adolescents in Bulgaria.[6] This is consistent with our finding of no association between green space in a buffer of 300m and mental wellbeing in adolescence, after adjustment for air pollution and road traffic noise. We did not include green space in buffers of 500m surrounding the adolescents' homes in this study, because green space indicators in buffers of 300m and 500m were highly correlated. Associations with mental wellbeing are therefore likely similar for green space in buffers of 300m and 500m in our study. Another study found no associations between the average NDVI in buffers of 500m and 1000m surrounding the schools of 6313 students aged 11-20 years in Canada with self-rated mental health.[7] The inclusion of different types of green space (i.e. residential green space in the present study and school greenness in the study from Canada), different buffer sizes and cultural and climatic differences may explain the discrepancy between the two studies.

We found associations of green space in a buffer of 3000m with better mental wellbeing in adolescents, which were consistent over a period of nearly ten years. No associations with green space in a buffer of 300m were observed. This implies that the availability of green space in a greater area surrounding the adolescents' homes, rather than green space closer to home, is related to a better mental wellbeing in our study population. Green space may improve mental wellbeing by increasing physical activity levels and social cohesion and by reducing stress and exposure to ambient air pollution and noise.[35-37] The associations of green space in a buffer of 3000m with mental wellbeing in this study remained after adjustment for air pollution and road traffic noise, indicating that these associations are not explained by lower air pollution or traffic noise levels (because of fewer air pollution and noise sources in areas with more green space). Future studies are needed that explore the pathways through which green space may impact mental wellbeing of adolescents.

In single-exposure models, we found that higher exposure to ambient air pollution was associated with a higher odds of poor mental wellbeing throughout adolescence. These associations attenuated after adjustment for green space in a buffer of 3000m and road traffic noise, mainly due to adjustment for green space. We observed lower levels of green space in buffers of 3000m in areas with higher concentrations of ambient air pollution (r =

-0.76 to -0.23). This indicates that the associations of air pollution with mental wellbeing in this study are partly explained by lower levels of green space in areas with higher air pollution concentrations. However, associations of $PM_{2.5}$ absorbance and NO_2 were still positive, providing suggestive evidence for a relation between exposure to traffic-related air pollution and poor mental wellbeing in adolescents. Our findings indicate that future studies that assess relationships between ambient air pollution and mental wellbeing in adolescents should account for green space.

To our knowledge, this is the first study that has examined relationships between exposure to air pollution and self-reported mental wellbeing throughout adolescence. One previous study found that higher residential exposure to $PM_{2.5}$ and NO_2 at age 12 years was associated with an increased odds of major depressive disorders at age 18 years in 284 adolescents in London.[9] A study from Sweden showed that children and adolescents under 18 years of age living in areas with higher exposure to PM_{10} and NO_2 were more likely to have a dispensed medication for a psychiatric disorder.[10] Finally, another study found associations of short-term exposure to ambient air pollution and a higher number of emergency department visits for mental health disorders in individuals aged 8 to 24 years in Toronto, Canada.[11] These studies, however, did not take other environmental exposures into account (e.g. green space and traffic noise) and therefore it remains unclear to what extent associations with air pollution were attributable to green space.

In this study, traffic noise was not associated with mental wellbeing throughout adolescence. This is in line with a review showing that multiple epidemiological studies found no relationships between exposure to aircraft or traffic noise and mental wellbeing in children.[12] Consistently, a study from the United States did not observe a higher prevalence of mental health disorders in adolescents with higher exposure to environmental noise.[14] Dzhambov et al. found that residential road traffic noise was only indirectly associated with worse self-reported mental health (through noise annoyance, decreased physical activity and decreased social cohesion) in the same population of 399 adolescents in Bulgaria.[13]

Strengths and limitations

Important strengths of the current study include the repeated measurements of mental wellbeing throughout adolescence and the inclusion of multiple spatially correlated environmental exposures that may be associated with mental wellbeing. Detailed address histories were available for nearly all study participants, which enabled the collection of virtually complete residential exposure data. Moreover, we used multiple indicators to assess residential exposure to green space. Most previous epidemiological studies only used the average NDVI or total percentage of green space in one or several buffers around participants' homes to define exposure to green space.[38] We additionally assessed relationships between different types of green space (i.e. urban, natural and agricultural) and mental wellbeing in adolescents.

We acknowledge some potential limitations of our study. We used LUR models that were based on measurement campaigns performed in 2009 and we only had traffic noise estimates for 2011. We assumed that the spatial contrasts in air pollution and traffic noise levels remained stable throughout the study period (from 2007 to 2018). This assumption is supported by multiple epidemiological studies from Europe that have shown that the spatial variation in air pollution or noise levels remained constant over periods of seven to 12 years.[16,39-41] Nevertheless, by using purely spatial LUR models in our analyses, we did not account for long-term trends in ambient air pollution concentrations. As a result, we may have overestimated exposure contrasts for the more recent years as NO_2 and PM_{10} concentrations have decreased in the Netherlands over the last decades.[42,43] This may have caused some bias in the observed exposure-response relationships.

Another limitation of this study is that we did not have information on the quality of green spaces. Both perceived and objective quality of green spaces (for example, walkability, safety and aesthetics) may be associated with the use of green spaces.[37,44] For green space to improve physical activity and social cohesion (i.e. potential pathways through which green space may improve mental wellbeing), actual green space visits are likely important. We only had information on the frequency of green space visits when the PIAMA study participants were 17 years old. We have previously shown that these 17-year-olds did make use of green spaces, mainly for physical and social activities, but that the quantity of residential green space was not related to the frequency of green space visits.[45] We did not know if and how often our study participants used the green spaces in the specified buffers around their homes when they were 11, 14 and 20 years old. Finally, we were only able to include traffic noise levels outside the adolescents' homes. Like most previous studies, we did not have information on potential individual level noise modifiers such as the orientation of the bedroom, indoor insulation and window type. Therefore, there is a possibility of misclassification of individual exposure to traffic noise.

Conclusions

Residential exposure to green space may be associated with a better mental wellbeing throughout adolescence. Higher exposure to ambient air pollution was related to a worse mental wellbeing in adolescents, but these associations attenuated after adjustment for green space and traffic noise. Future studies assessing relationships between air pollution and mental wellbeing in adolescence should account for green space levels.

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Supplemental Material

Table S1. Spearman correlations between the green space indicators, air pollutants and traffic noise.

		NDVI		Total percentage of green space		Air pollutants						Noise	
		300m	3000m	300m	3000m	NO_2	$PM_{2.5}$ abs	PM_{10}	$PM_{2.5}$	OP^{ESR}	OP^{DTT}	Road traffic	Railway
NDVI	300m		0.63	0.70	0.58	-0.62	-0.49	-0.47	-0.32	-0.31	-0.68	-0.29	-0.20
	3000m			0.36	0.85	-0.67	-0.55	-0.58	-0.27	-0.23	-0.61	-0.26	-0.28
Total percentage green space	300m				0.48	-0.46	-0.37	-0.37	-0.27	-0.33	-0.53	-0.21	-0.19
	3000m					-0.76	-0.68	-0.74	-0.40	-0.44	-0.63	-0.33	-0.38
Air pollutants	NO_2						0.90	0.80	0.67	0.65	0.76	0.44	0.34
	$PM_{2.5}$ abs							0.88	0.82	0.73	0.60	0.49	0.33
	PM_{10}								0.65	0.57	0.56	0.51	0.31
	$PM_{2.5}$									0.81	0.43	0.41	0.26
	OP^{ESR}										0.37	0.39	0.26
	OP^{DTT}											0.30	0.21
Noise	Road traffic												0.17
	Railway												

Abbreviations: NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Table S2. Spearman correlations between green space, air pollution, traffic noise and the number of addresses per km^2.

	Addresses/km^2
Average NDVI in 300m	-0.55
Total percentage of green space in 300m	-0.50
Urban green in 300m	0.25
Agricultural green in 300m	-0.63
Natural green in 300m	-0.38
Average NDVI in 3000m	-0.62
Total percentage of green space in 3000m	-0.80
Urban green in 3000m	0.75
Agricultural green in 3000m	-0.77
Natural green in 3000m	-0.23
PM_{10}	0.73
$PM_{2.5}$	0.45
OP^{ESR}	0.53
OP^{DTT}	0.63
NO_2	0.74
$PM_{2.5}$ absorbance	0.67
Road traffic noise	0.35
Railway noise	0.30

Abbreviations: NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Table S3. Associations of the average NDVI in a buffer of 300m with poor mental wellbeing from age 11 to 20 years, adjusted for air pollution and road traffic noise.

Adjusted for [a]	Average NDVI in 300m
	OR (95% CI)
PM_{10} + road traffic noise	0.90 (0.79 - 1.02)
$PM_{2.5}$ + road traffic noise	**0.88 (0.78 - 1.00)**
OP^{ESR} + road traffic noise	0.89 (0.79 - 1.01)
OP^{DTT} + road traffic noise	0.99 (0.85 - 1.16)
NO_2 + road traffic noise	0.99 (0.86 - 1.14)
$PM_{2.5}$ absorbance + road traffic noise	0.95 (0.84 - 1.08)

Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in the average NDVI in a buffer of 300m (0.13).

Statistically significant results ($p<0.05$) are highlighted in bold.

[a] Additionally adjusted for age, sex, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, active smoking and neighborhood SES.

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Table S4. Associations of green space in a buffer of 3000m with poor mental wellbeing from age 11 to 20 years from three-exposure models, additionally adjusted for degree of urbanization.

Adjusted for [a]	Average NDVI in 3000m	Total percentage of green space in 3000m
	OR (95% CI)	OR (95% CI)
PM_{10} + road traffic noise	**0.80 (0.68 - 0.93)**	**0.80 (0.66 - 0.97)**
$PM_{2.5}$ + road traffic noise	**0.80 (0.69 - 0.93)**	**0.80 (0.67 - 0.96)**
OP^{ESR} + road traffic noise	**0.80 (0.69 - 0.92)**	**0.81 (0.68 - 0.97)**
OP^{DTT} + road traffic noise	**0.80 (0.68 - 0.94)**	0.84 (0.69 - 1.03)
NO_2 + road traffic noise	**0.81 (0.69 - 0.96)**	0.83 (0.67 - 1.03)
$PM_{2.5}$ absorbance + road traffic noise	**0.83 (0.71 - 0.97)**	0.84 (0.70 - 1.03)

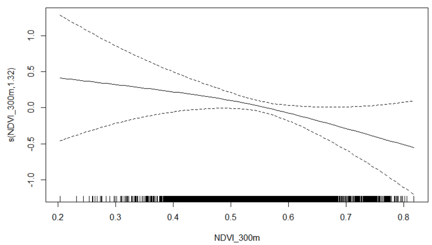
Abbreviations: OR = odds ratio; CI = confidence interval; NDVI = Normalized Difference Vegetation Index; O^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol.

Associations are shown for an interquartile range increase in exposure.

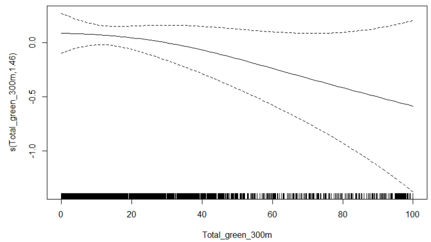
Statistically significant results ($p <0.05$) are highlighted in bold.

[a] Additionally adjusted for age, sex, parental level of education, maternal smoking during pregnancy, smoking in the adolescent's home, active smoking and degree of urbanization (in two categories: ≥1500 addresses/km^2; <1500 addresses/km^2).

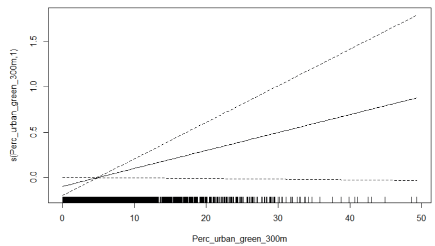
Age 11 years



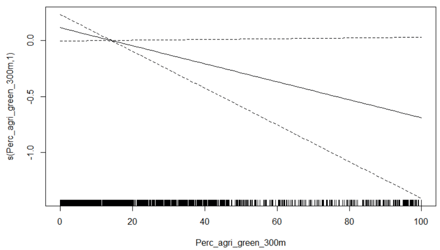
NDVI in 300m



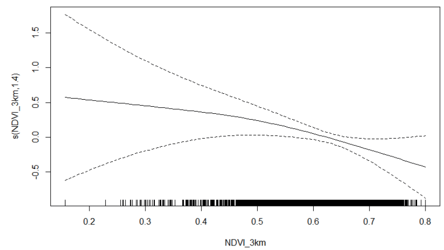
Total green space in 300m



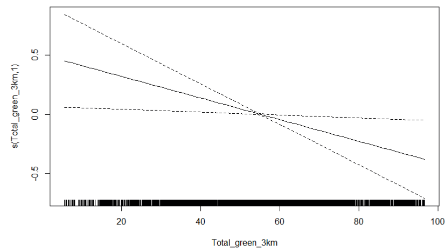
Urban green in 300m



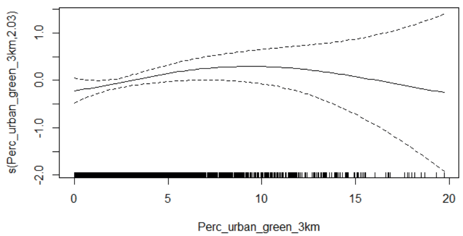
Agricultural green in 300m



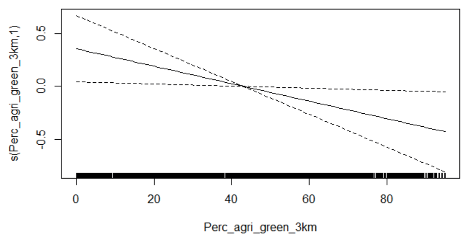
NDVI in 3000m



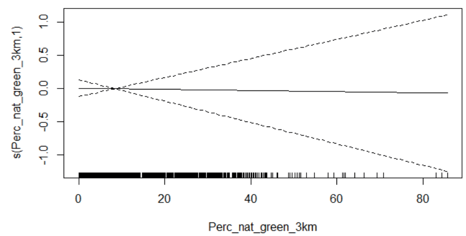
Total green space in 3000m



Urban green in 3000m



Agricultural green in 3000m



Natural green in 3000m

Figure S1. Exposure-response curves for the associations of green space, air pollution and traffic noise with poor mental wellbeing at ages 11, 14, 17 and 20 years.

Age 11 years

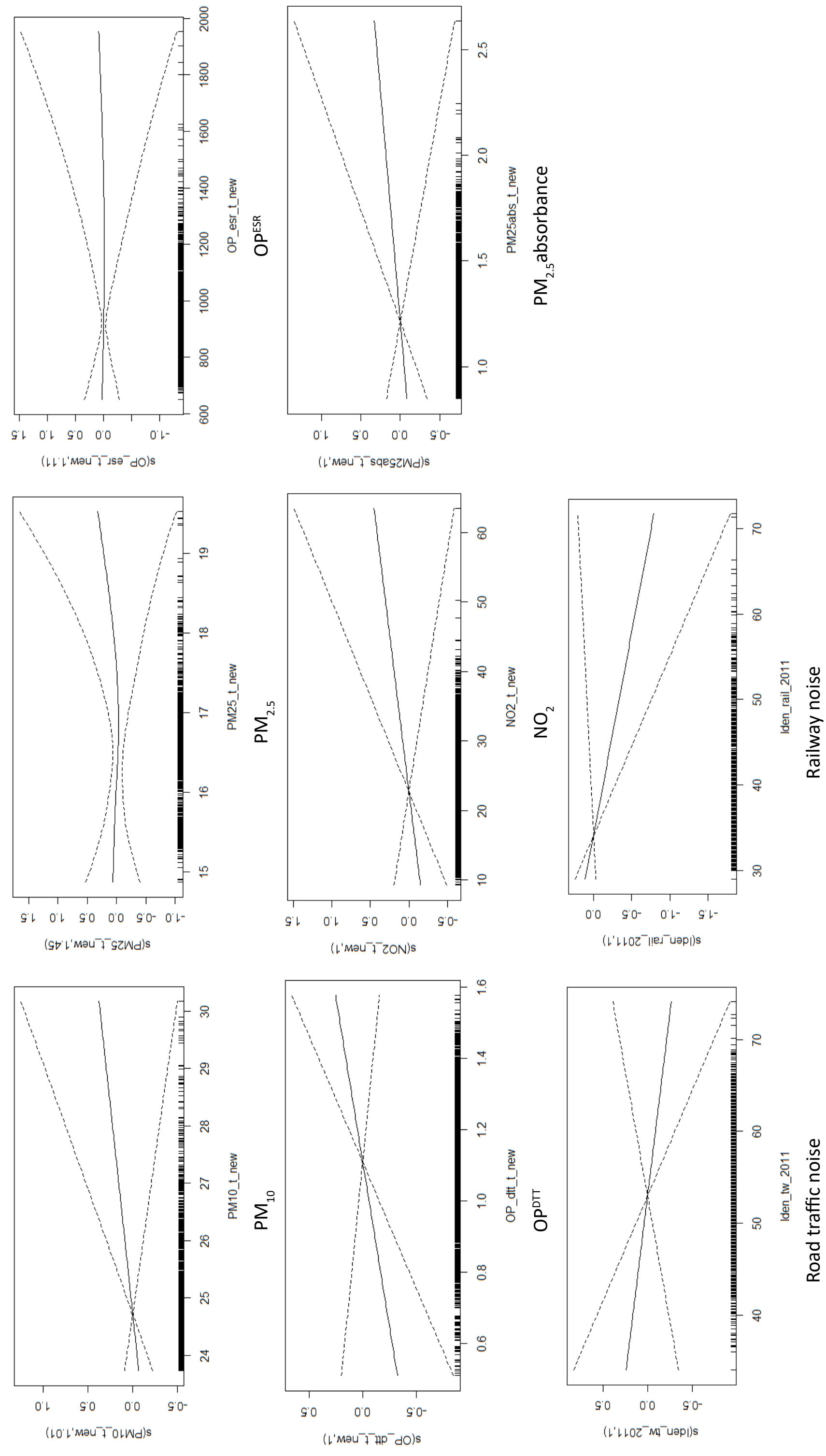


Figure S1 (continued).

Age 14 years

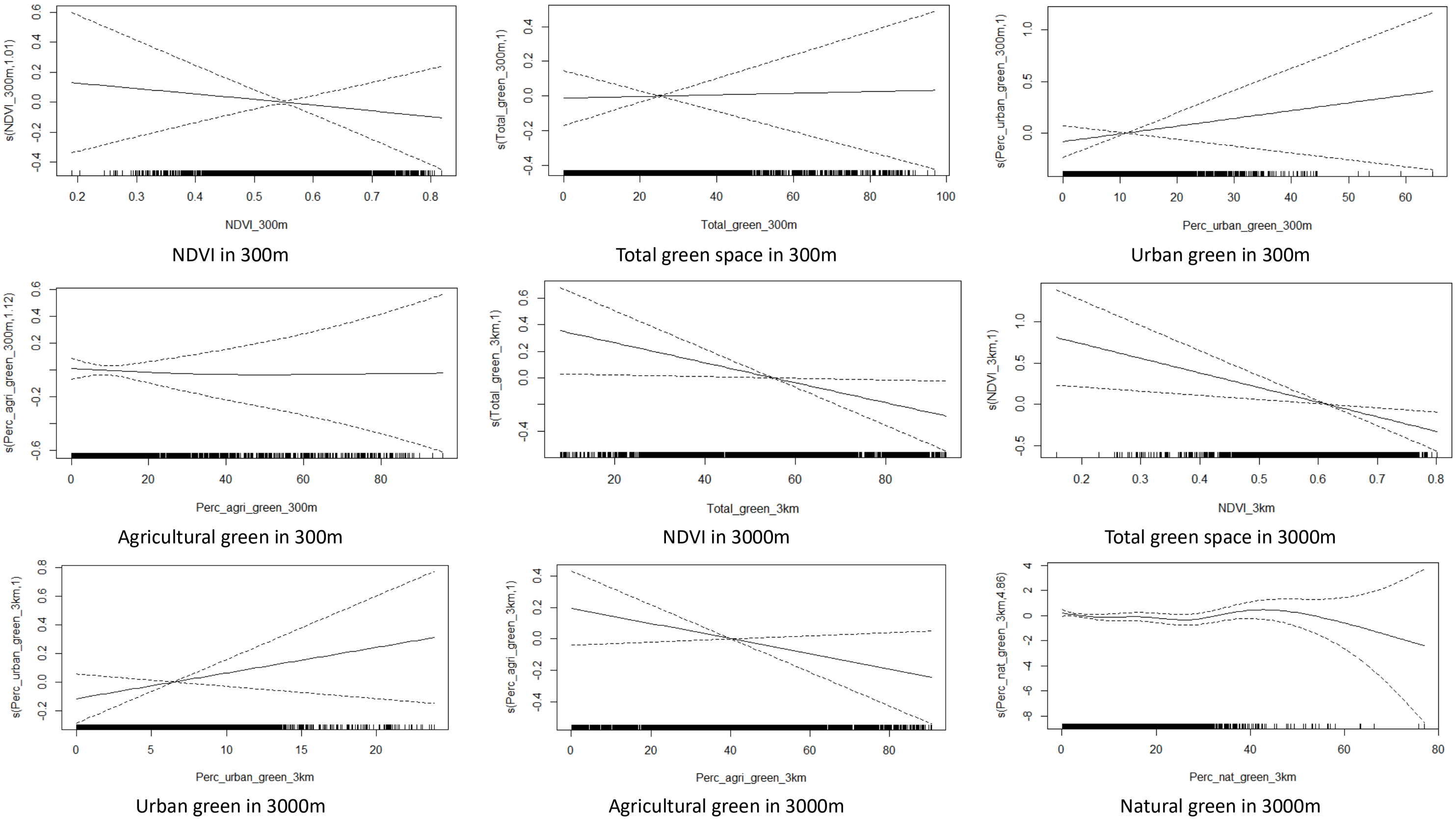


Figure S1 (continued).

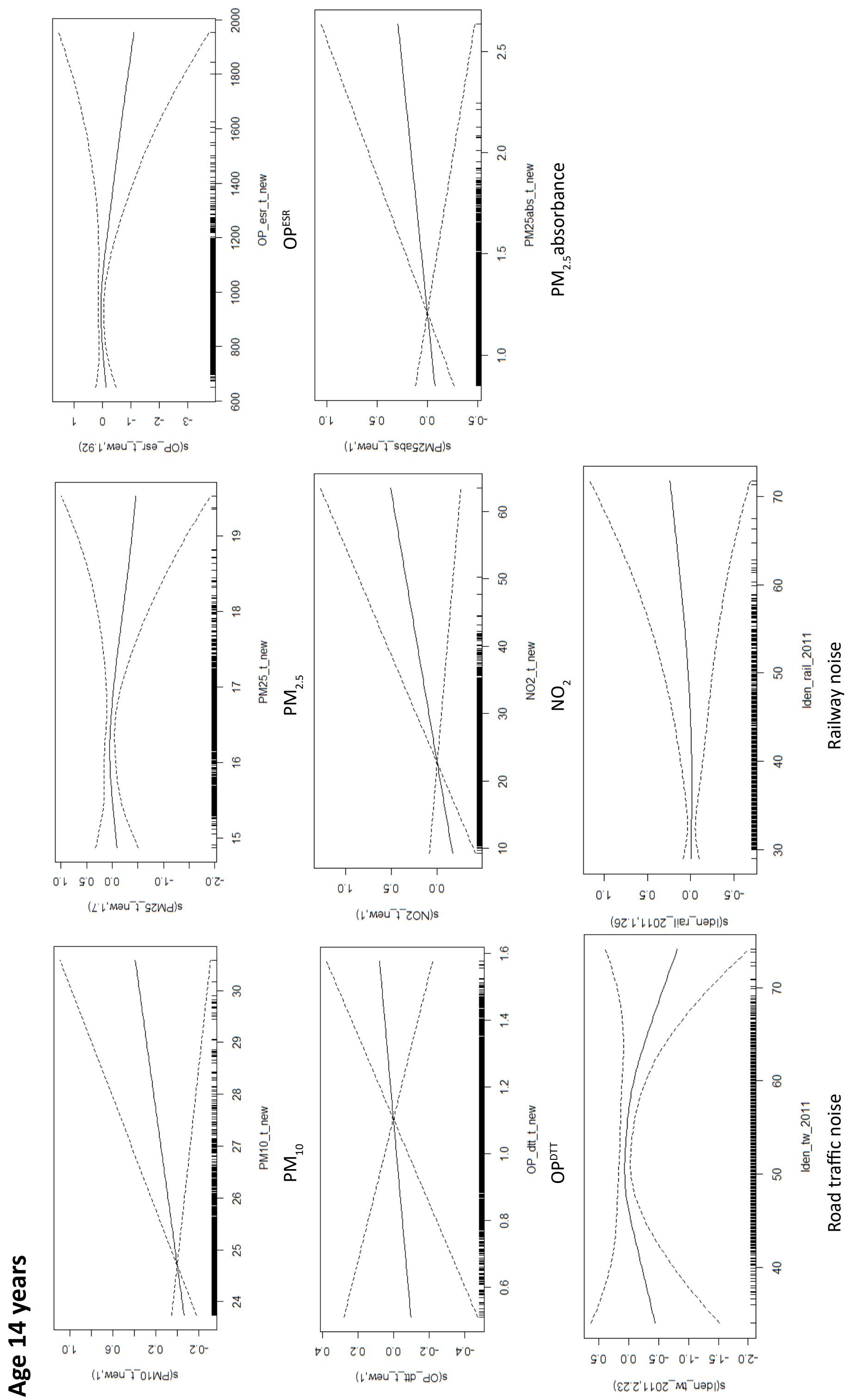


Figure S1 (continued).

Age 17 years

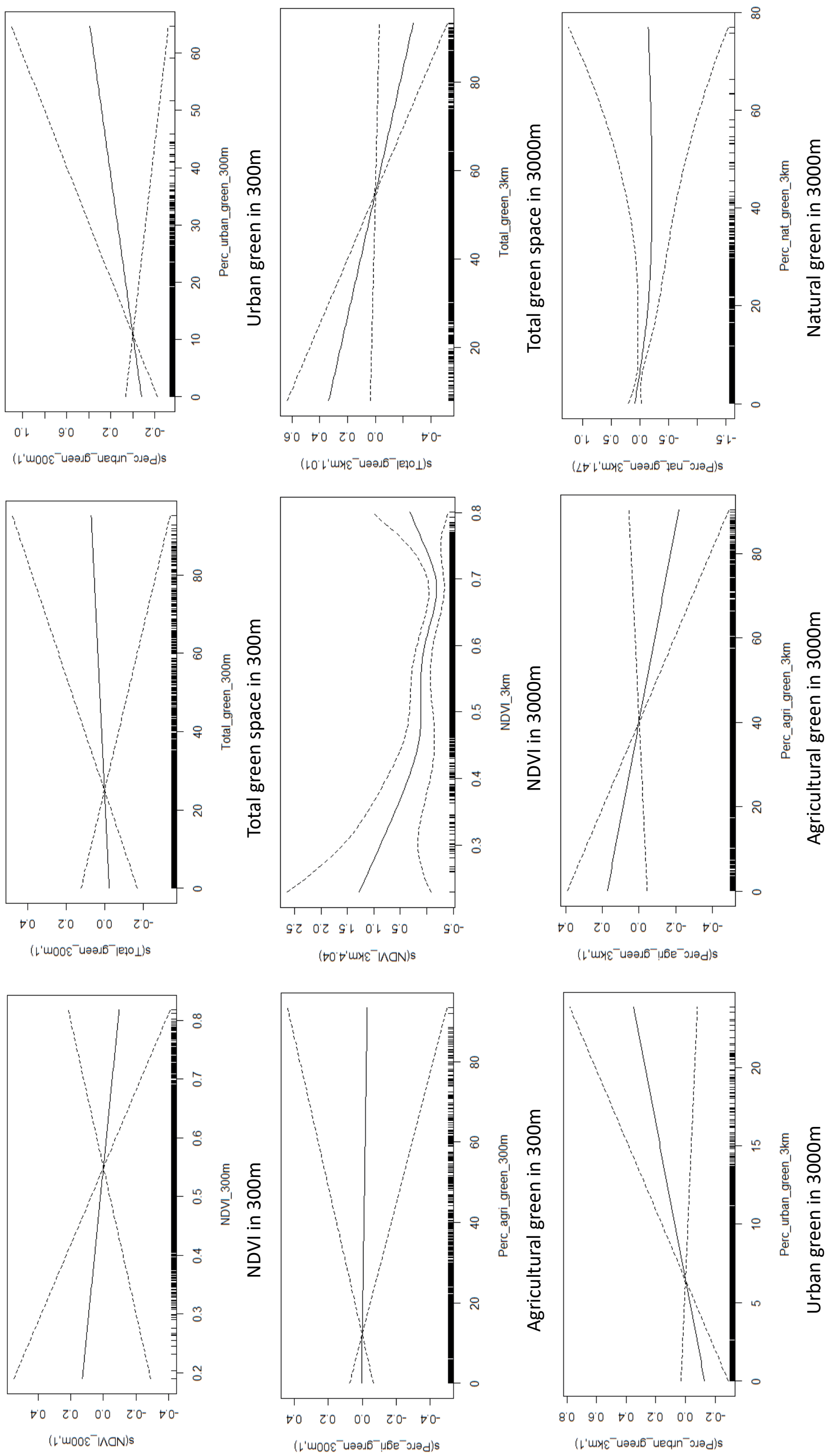


Figure S1 (continued).

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Age 17 years

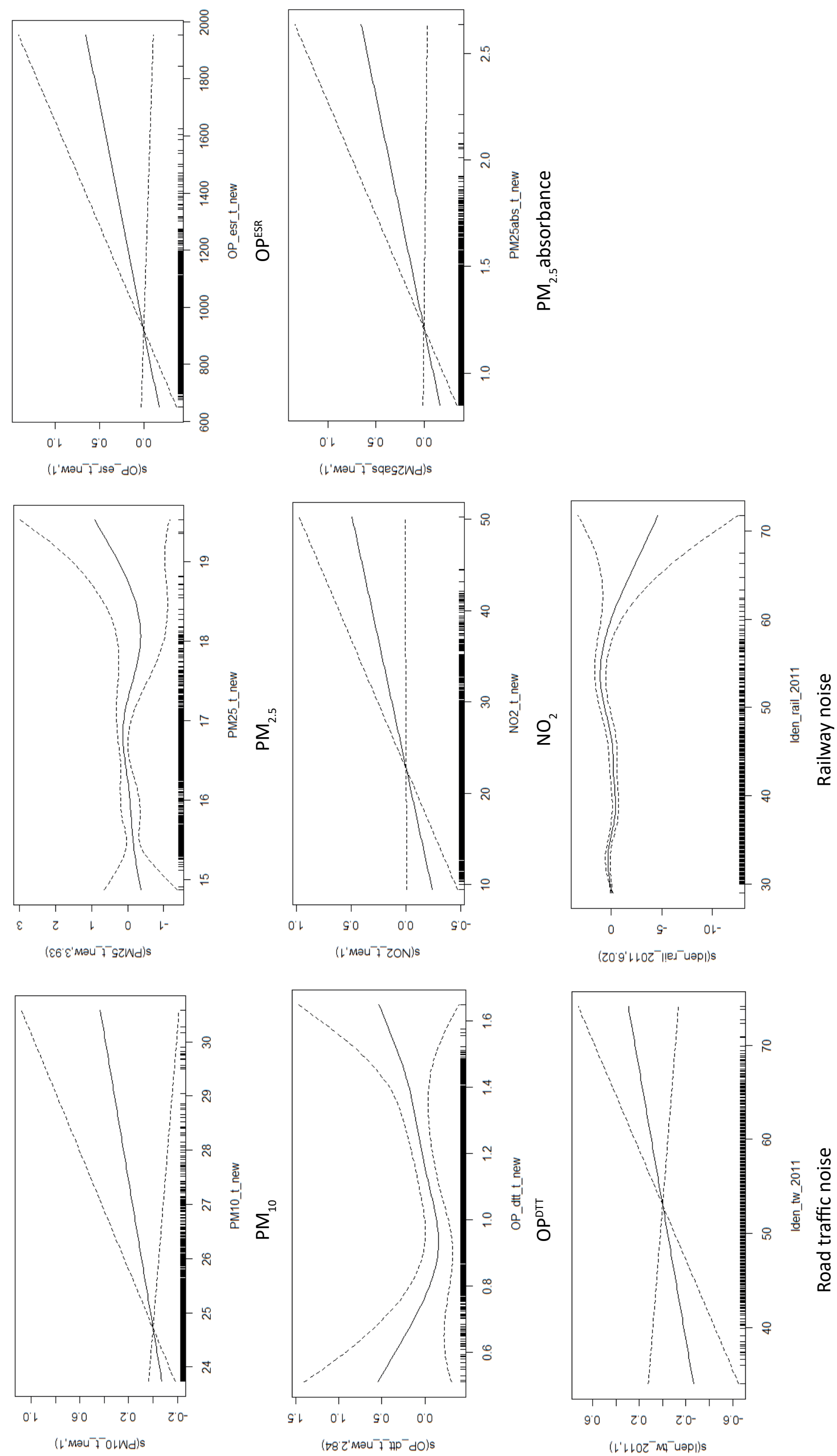

Figure S1 (continued).

Age 20 years

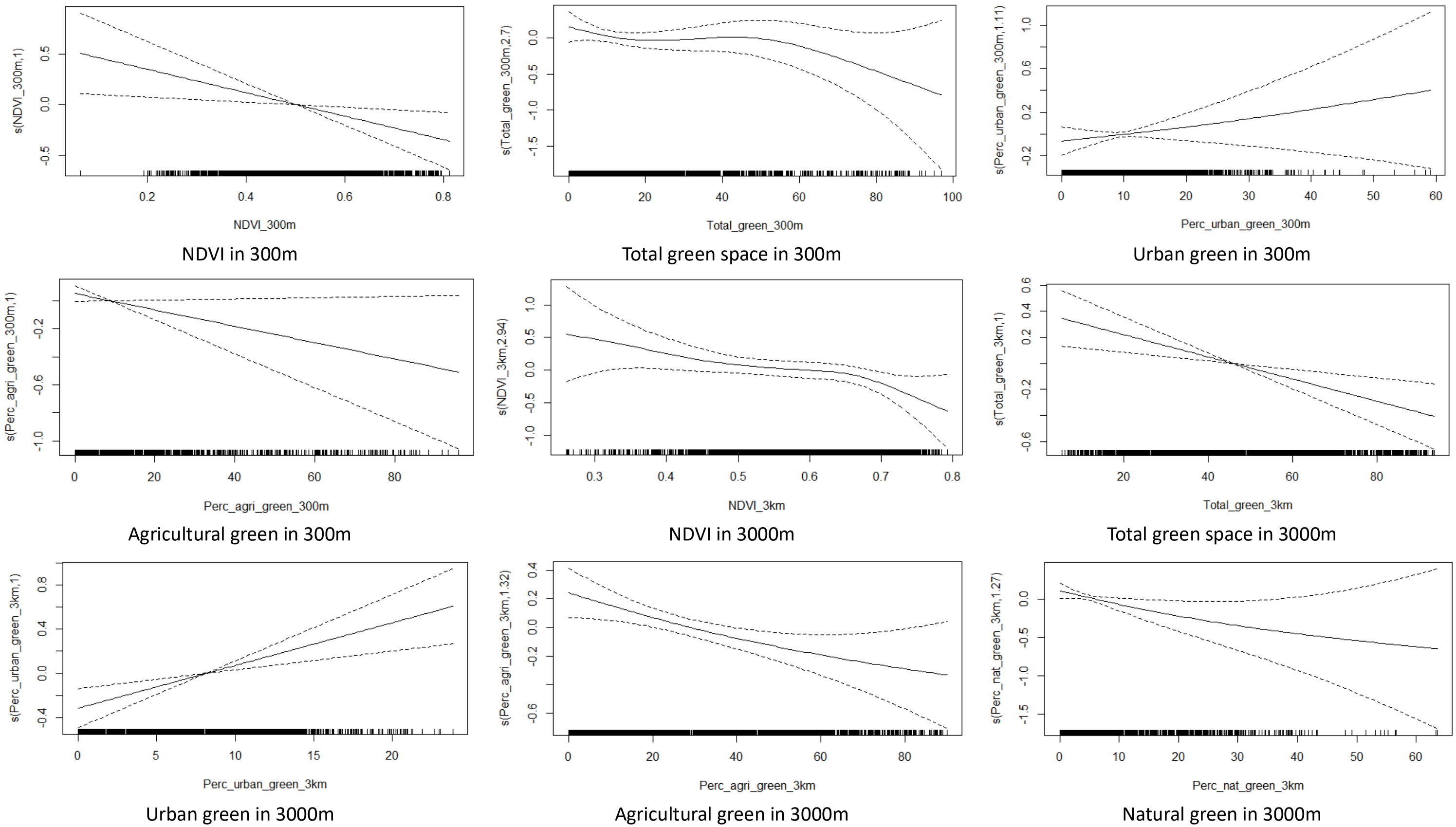

Figure S1 (continued).

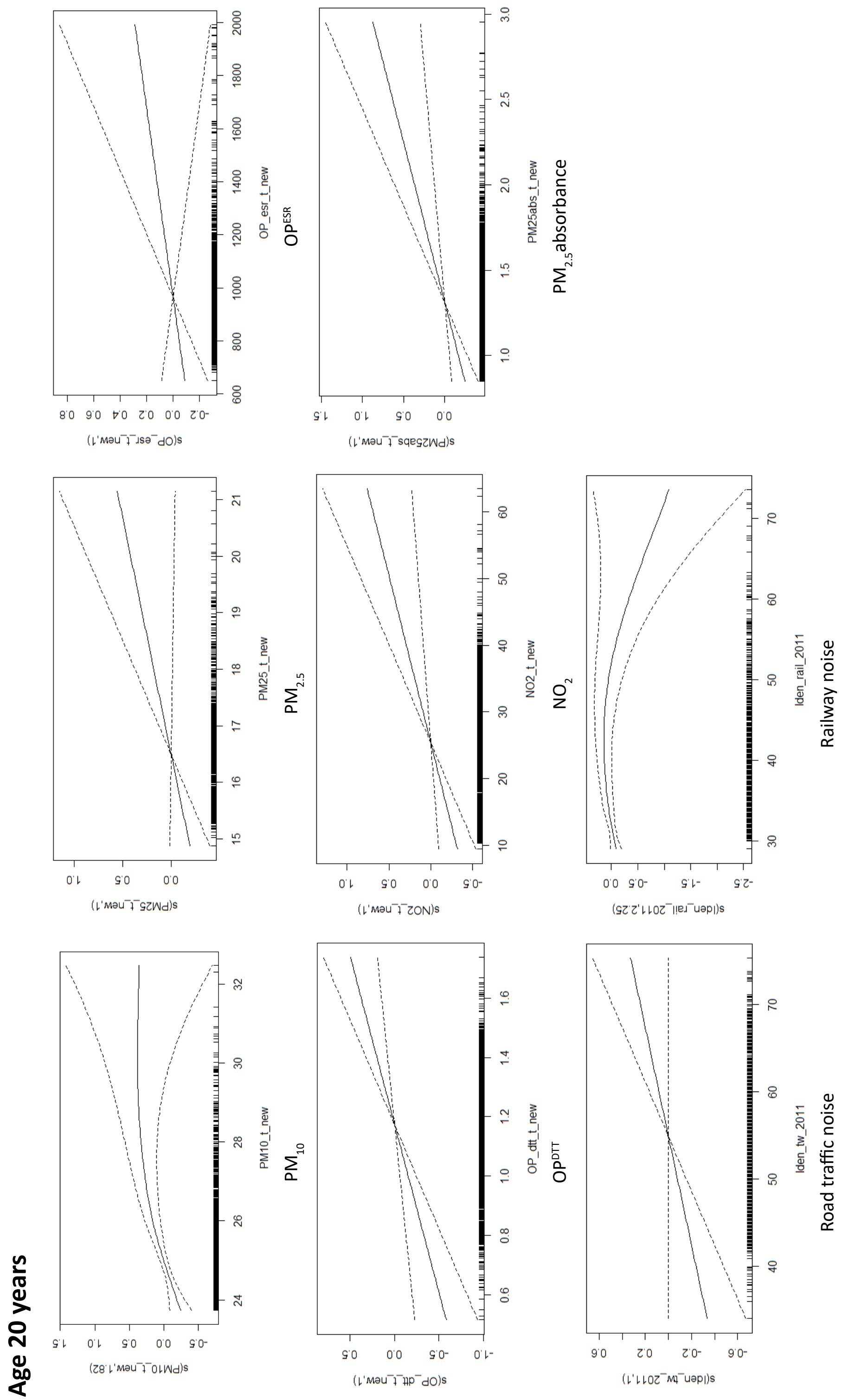

Figure S1 (continued).

Chapter 7

General discussion

The overall aim of this thesis was to examine the individual and combined associations of residential exposure to green space, air pollution and traffic noise with health outcomes in children and adolescents living in the Netherlands. We first examined whether adolescents visit green spaces and for what purposes (chapter 2). In the second part of this thesis, the associations of green space, air pollution and traffic noise exposure with the following health outcomes were studied: overweight (chapter 3), cardiometabolic health (chapter 4), saliva cortisol (chapter 5) and mental wellbeing (chapter 6). The studies in this thesis used data from the ongoing Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study, which followed children from birth until young adulthood.

In this chapter, the main findings and methodological limitations of the studies in this thesis are discussed. Subsequently, this chapter provides recommendations for future research and describes potential implications for public health policy.

Discussion and interpretation of the main findings

This section discusses the main findings for the different environmental exposures studied in this thesis. Table 1 shows the associations of green space, air pollution and traffic noise with health outcomes in children and adolescents observed in this thesis. The statistically significant relationships are displayed in Figure 1. We observed associations of residential green space in a buffer of 3000m with a larger diurnal decrease in cortisol levels, indicating lower chronic stress levels, at age 12 years and a better mental wellbeing throughout adolescence. Nitrogen dioxide (NO_2) was associated with a higher odds of being overweight from age three to 17 years, but not with cardiometabolic health or saliva cortisol. Ambient air pollution was related to a higher odds of poor mental wellbeing in adolescence, but these associations weakened after adjustment for green space. No relationships between exposure to road traffic or railway noise and health outcomes were observed in this thesis.

Green space

Chapter 2 of this thesis shows that 53% of adolescents aged 17 years visited a green space at least once a week in summer, mostly for physical and social activities. Adolescents who reported that a green environment is (very) important to them used green spaces most frequently. The quantity of green space in buffers of 300m and 3000m surrounding the adolescents' homes was not associated with the frequency of green space visits, i.e. adolescents living in neighborhoods with more green space did not visit green spaces more often than their peers living in neighborhoods with less green space. The quantity of green space surrounding the adolescents' homes was generally high, indicating that the majority of our study participants had access to green space. A potential explanation for our finding may therefore be that an increase in the amount of green space will not increase the use of green spaces when the amount of residential green space is already considerable.

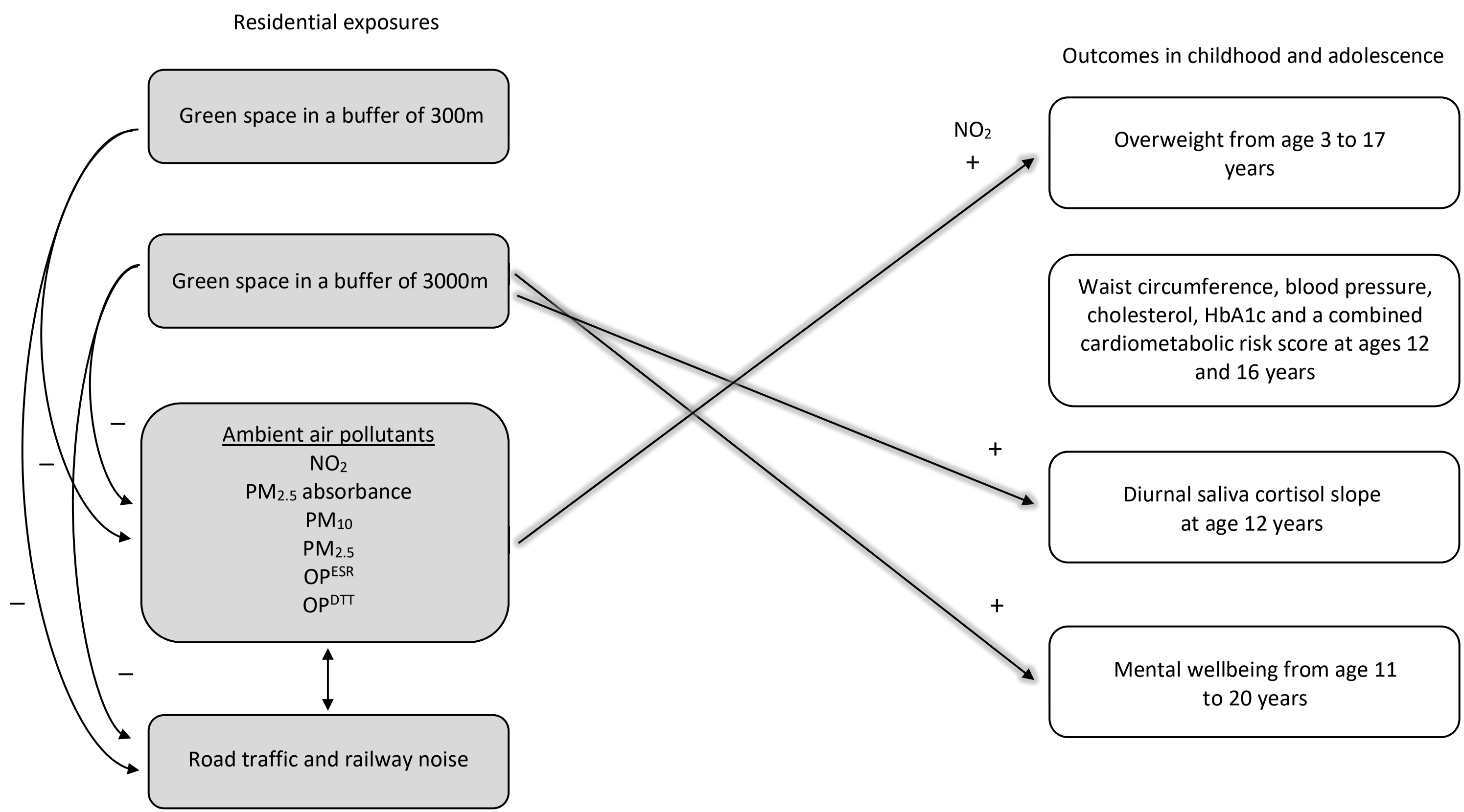

Figure 1. Statistically significant associations of green space, air pollution and traffic noise with health outcomes observed in this thesis. The arrows between the residential exposures represent the observed correlations between green space, air pollution and traffic noise.

Table 1. Associations of green space, air pollution and traffic noise with health outcomes in children and adolescents observed in this thesis.

	Overweight from age 3 to 17 years	Cardiometabolic health at age 12 years	Cardiometabolic health at age 16 years	Diurnal saliva cortisol slope at age 12 years	Mental wellbeing from age 11 to 20 years
Green space					
NDVI in 300m	0	0	0	0	+
Total percentage of green space in 300m	0	0	0	0	0
NDVI in 3000m	0	0	0	++	++
Total percentage of green space in 3000m	0	0	0	++	++
Air pollution					
NO_2	++	0	0	0	0
$PM_{2.5}$ absorbance	+	0	0	0	-
PM_{10}	0	0	0	0	0
$PM_{2.5}$	0	- - WC	0	0	0
OP^{ESR}	NI	0	0	0	0
OP^{DTT}	NI	0	0	0	0
Traffic noise					
Road traffic noise	0	0	0	+	0
Railway noise	0	0	0	0	0

Abbreviations: NDVI = Normalized Difference Vegetation Index; NO_2 = nitrogen dioxide; PM_{10} = particulate matter with a diameter <10 µm; $PM_{2.5}$ = particulate matter with a diameter <2.5 µm; OP^{ESR} = electron spin resonance; OP^{DTT} = dithiothreitol; WC = waist circumference; NI = not investigated.

++ ($p < 0.05$) and + ($p < 0.10$) indicate positive associations of the environmental exposures with the health outcomes; - - ($p < 0.05$) and - ($p < 0.10$) indicate negative associations; 0 indicates that the exposure was not associated with the health outcome.

The odds of being overweight from age three to 17 years decreased with increasing exposure to residential green space in a buffer of 3000m. These associations, however, attenuated after adjustment for ambient air pollution and traffic noise (chapter 3). Green space was not associated with waist circumference, blood pressure, cholesterol, glycated hemoglobin (HbA1c) and a combined cardiometabolic risk score in adolescents aged 12 and 16 years (chapter 4). Multiple pathways have been proposed to explain the potential health benefits of green space, as described in Figure 1 of the General introduction of this thesis. The main pathways are: increasing physical activity levels, reducing stress, enhancing social cohesion and reducing exposure to air pollution, noise and heat.[1-3] For green space to increase physical activity levels and enhance social cohesion, individuals need to use green spaces. This thesis shows that adolescents aged 17 years who live in neighborhoods with higher levels of green space are not more often physically active in green spaces compared to adolescents who live in neighborhoods that are less green (chapter 2). This may explain why we did not observe associations of green space with overweight and cardiometabolic health in children and adolescents. However, we do not know if and how often our study population used green spaces (for physical activities) when they were three to 16 years old.

Residential green space in a buffer of 3000m was related to a larger diurnal decrease in saliva cortisol concentrations, indicating lower chronic stress levels, in children aged 12 years (chapter 5) and a lower odds of poor mental wellbeing from age 11 to 20 years (chapter 6). To our knowledge, no previous epidemiological studies have assessed associations of green space with saliva cortisol or mental health in children or adolescents in the Netherlands. However, several studies have shown that higher exposure to green space is related to better mental health in adults in the Netherlands.[4-6] For example, de Vries et al. found that a higher percentage of residential green space in a buffer of 1000m was associated with a better self-reported mental wellbeing in 6621 adults recruited from the general Dutch population.[6] That study assessed mental wellbeing with the five-item Mental Health Inventory (MHI-5), a short questionnaire that has also been used to assess mental wellbeing in this thesis.

Since people living in urban areas may have a worse mental wellbeing and experience more stress than people who live in less urbanized areas,[7,8] we additionally adjusted our analyses for degree of urbanization. The associations of green space with saliva cortisol and mental wellbeing remained after adjustment for degree of urbanization. Urban-rural differences in lifestyle, stress and mental health may be smaller in the Netherlands than in other countries, since cities and rural areas in the Netherlands are generally smaller than cities and rural areas in other countries. Nevertheless, we observed that adolescents living in more urbanized areas (≥1500 addresses/km^2) had a higher odds of poor mental wellbeing from age 11 to 20 years than adolescents living in a non-urban area (unadjusted odds ratio (OR) 1.38 [95% confidence interval (CI) 1.16 - 1.64]).

The studies presented in this thesis included detailed and specific indicators of residential exposure to green space. In contrast to most previous epidemiological studies, we examined relationships between different types of green space and health outcomes in children and adolescents. The relationships between green space in a buffer of 3000m and a lower odds of poor mental wellbeing throughout adolescence were driven by the percentages of agricultural and natural green space (chapter 6). The percentage of urban green space in a buffer of 3000m was not related to mental wellbeing. Forests and heather located outside population clusters, i.e. localities with at least 25 predominantly residential buildings, were classified as natural green space in this thesis. It is possible that these generally large natural areas may be more conducive to relaxation and psychological restoration than urban green spaces. The associations of green space in a buffer of 3000m with a larger diurnal decrease in saliva cortisol concentrations at age 12 years were driven by associations with the percentage of agricultural green space (chapter 5). It is possible that our observed associations partly reflect urban-rural differences in stress levels and mental wellbeing (for reasons other than air pollution, traffic noise or lack of green space), which is not adequately captured by including degree of urbanization as a dichotomous variable in our analyses. In other words: the associations between (agricultural) green space and the diurnal cortisol slope and mental wellbeing could be partly attributed to residual confounding by degree of urbanization.

We also observed associations of green space in a buffer of 300m with a larger diurnal decrease in saliva cortisol levels at age 12 years (chapter 5) and a lower odds of poor mental wellbeing throughout adolescence (chapter 6). However, these relationships were weaker than the relationships with green space in a buffer of 3000m and not statistically significant. This implies that the availability of green space in a greater area surrounding the adolescents' homes is more closely related to lower stress levels and better mental wellbeing than green space closer to home in our study population. It is likely that the optimal buffer size, in which to assess the quantity of green space, differs per age group. For example, young children have less freedom to move around in their surroundings and may therefore be more dependent on green spaces closer to their homes as compared to adolescents. It is therefore important to include multiple buffer sizes when assessing associations between residential green space and health.

Epidemiological studies conducted in the Netherlands observed associations between residential green space and physical health outcomes in adults (e.g. overweight and diabetes).[9-11] These studies used data from a Dutch national health survey and a large part of this study population was of Dutch origin and had a high level of education, which is comparable with the PIAMA study population.[9-11] In this thesis, no associations of green space with overweight and cardiometabolic health were observed in children and adolescents in the Netherlands. It is possible that adults consider green spaces more valuable and may also use green spaces more often than children. For example, most young children in the Netherlands play outside on sidewalks or playgrounds, which do not necessarily contain green spaces. This could explain the discrepancy between the findings of this thesis and the associations of green space with overweight and cardiometabolic health outcomes observed in adults in the Netherlands. Another possibility is that associations between green space and overweight and diabetes are not readily noticeable in childhood or adolescence and become apparent in adulthood only after longer cumulative exposure. It is therefore important to continue to follow the young adults who participate in the PIAMA study in order to assess associations between residential green space and health outcomes at a later age.

Air pollution

The findings presented in chapter 3 of this thesis show that NO_2 was associated with a higher odds of being overweight throughout childhood. This association remained after adjustment for green space and road traffic noise (adjusted OR 1.54 [95% CI 1.14 - 2.07] per interquartile range (IQR) increase in NO_2 (8.90 $\mu g/m^3$)). This finding is supported by animal studies showing that ambient air pollution is a risk factor for increased weight gain and increased adiposity.[12-14] Differences in study design, health outcomes and ambient air pollution concentrations limit the comparability between our results and findings from previous epidemiological studies. However, two studies performed within the Southern California Children's Health study also observed that traffic-related air pollution may contribute to childhood overweight. A study in 2944 participants of the 1993/1996 cohort found that higher residential exposure to nitrogen oxides (NO_x) was related to a greater increase in body mass index (BMI) from age 10 to 18 years (adjusted difference 1.13 kg/m^2 [95% CI 0.61 - 1.65 kg/m^2] per 16.80 ppb increase in NO_x) and a higher attained BMI at age 18.[15] Another study in 4550 children from the 2002/2003 cohort showed a 13.6% increase in annual BMI growth from age 5 to 11 years when comparing the lowest to the highest decile of residential exposure to NO_x.[16] Additionally, de Bont et al. found that children aged 7-10 years in Barcelona exposed to higher levels of NO_2 at school had a higher odds of being overweight or obese.[17] However, this association was non-linear and only statistically significant when comparing the second (46.1 - 54.4 μg/m^3) to the first tertile of exposure (OR 1.28 [95% CI 1.03 - 1.61]).[17] Given the number of associations that have been examined in this thesis, the association between NO_2 and overweight throughout childhood could have occurred by chance alone. However, the relationship between NO_2 and childhood overweight was consistent across different models with increasing degree of adjustment for potential confounders and remained after additional adjustment for green space and road traffic noise. Additionally, NO_2 was also related to a higher odds of being overweight throughout childhood when we restricted our analytic sample to children who lived in an urban area. We therefore consider it unlikely that this association is a chance finding.

Childhood obesity is a complex disorder resulting from interactions between multiple genetic and non-genetic risk factors.[18] Exposure to certain chemicals, so-called "obesogens", early in life may alter metabolic processes and predispose some individuals to excess weight gain through programming changes, which may enhance dysfunctional eating behaviors later in life.[19,20] Evidence suggests that older children and adolescents are also susceptible to chemical exposures that may alter developmental programming, because childhood and adolescence are marked by continued maturation of key endocrine systems.[20] The observed association between NO_2 and childhood overweight in this thesis supports the plausibility of the obesogen hypothesis.

In this thesis, no associations of ambient air pollution with waist circumference, blood pressure, cholesterol, HbA1c and a combined cardiometabolic risk score at ages 12 and 16 years or with the diurnal saliva cortisol slope at age 12 years were observed (chapters 4 and 5). No previous epidemiological studies have assessed associations of ambient air pollution with HbA1c in children or adolescents. Only one study examined relationships between air pollution and cholesterol levels in adolescents.[21] That study observed that long-term NO_2 exposure, but not exposure to particulate matter with diameters of <10 μm (PM_{10}) or <2.5 μm ($PM_{2.5}$), was associated with higher fasting total cholesterol and low-density lipoprotein (LDL) cholesterol levels in 158 adolescents and young adults aged 17-22 years participating in the Southern California Children's Health study.[21] Table 2 summarizes the findings of other epidemiological studies that have assessed associations of long-term exposure to ambient air pollution with blood pressure in children or adolescents. All studies examined relationships with particulate matter (PM_{10} and/or $PM_{2.5}$) and half of the studies also included gaseous pollutants. Most studies showed that higher exposure to ambient air pollution was related to a higher blood pressure. The results of the studies are, however, inconsistent, i.e. some studies observed associations with systolic blood pressure, whereas other studies only observed associations with diastolic blood pressure. Additionally, most studies have been conducted in areas with (extremely) high concentrations of ambient air pollutants. Future studies are needed that examine associations of long-term air pollution with blood pressure in children and adolescents in countries with lower levels of ambient air pollution.

Table 2. An overview of studies that examined associations of long-term exposure to ambient air pollution with blood pressure in children or adolescents.

Study	Study population	Air pollutants: median (IQR) or mean ± SD	Main findings
Wu et al. 2020 [48]	9354 Chinese children and adolescents aged 5 to 17 years	PM_1: 44.4 (13.2) μg/m³ $PM_{2.5}$: 51.9 (10.0) μg/m³	Higher exposures to residential PM_1 and $PM_{2.5}$ were associated with a higher SBP. No associations with DBP were observed.
Zhang et al. 2019 [49]	43745 children and adolescents aged 7 to 18 years in China	$PM_{2.5}$: 63.1 (14.1) μg/m³ PM_{10}: 96.9 (14.5) μg/m³	Ambient $PM_{2.5}$ and PM_{10} concentrations were associated with a higher SBP (adjusted difference 1.46 [95% CI 0.05, 2.88] mmHg and 1.36 [95% CI 0.34, 2.39] mmHg per 10 μg/m³ increase, respectively). No associations of either $PM_{2.5}$ or PM_{10} with DBP were found.
Dong et al. 2015 [50] Dong et al. 2014 [51]	9354 Chinese children and adolescents aged 5 to 17 years	PM_{10}: 90.4 (30.6) μg/m³ SO_2: 48.4 (23.4) μg/m³ NO_2: 35.0 (13.0) μg/m³ O_3: 43.8 (46.3) μg/m³ CO: 1289.5 (563.4) μg/m³	Higher exposure to ambient air pollution was associated with higher SBP and DBP. The associations, except for NO_2, were strongest in overweight or obese children.
Bilenko et al. 2015 [52]	1432 children aged 12 years participating in the PIAMA birth cohort	NO_2: 21.8 (7.8) μg/m³ $PM_{2.5}$ absorbance: 1.2 (0.3) 10^{-5}/m $PM_{2.5}$: 16.5 (1.1) μg/m³ PM_{10}: 24.5 (1.0) μg/m³	Long-term exposure to NO_2 and $PM_{2.5}$ absorbance was associated with increased DBP in children who lived at the same address since birth (adjusted difference 0.83 [95% CI 0.06, 1.61] mmHg and 0.75 [95% CI -0.08, 1.58] mmHg per IQR increase, respectively), but not with SBP.
Liu et al. 2014 [53]	2368 children aged 10 years from Germany	NO_2: 21.5 (6.4) μg/m³ $PM_{2.5}$: 14.0 (4.1) μg/m³ PM_{10}: 21.8 (4.8) μg/m³ $PM_{2.5}$ absorbance: 1.5 (0.4) 10^{-5}/m	No relationships between the ambient air pollutants and SBP or DBP were observed.
Sughis et al. 2012 [54]	179 children aged 8 to 12 years from two schools in Lahore, Pakistan	Low pollution school: $PM_{2.5}$: 28.5 ± 10.3 μg/m³ PM_{10}: 223.0 ± 93.5 μg/m³ High pollution school: $PM_{2.5}$: 183.0 ± 30.2 μg/m³ PM_{10}: 728.6 ± 53.5 μg/m³	SBP and DBP were significantly higher in children living in the high pollution area than in children living in the low pollution area (SBP: 115.9 vs. 108.3 mmHg; DBP: 70.9 vs. 66.4 mmHg).

Abbreviations: SBP = systolic blood pressure; DBP = diastolic blood pressure; IQR = interquartile range; PM = particulate matter; SO_2 = sulfur dioxide; NO_2 = nitrogen dioxide; O_3 = ozone; CO = carbon monoxide.

Chapter 6 of this thesis shows that higher concentrations of ambient air pollutants were associated with a higher odds of poor mental wellbeing throughout adolescence. However, these associations attenuated after adjustment for green space. This implies that the relationships between air pollution and mental wellbeing were partly explained by lower levels of green space in areas with higher concentrations of air pollution. Only one previous study has assessed associations of both ambient air pollution and green space with self-reported mental wellbeing in adolescents. That study found no associations of neighborhood green space or NO_2 with mental health, measured with the Strengths and Difficulties Questionnaire, in 3683 adolescents aged 10 to 15 years in England and Wales.[22]

Traffic noise

No associations of residential road traffic or railway noise with overweight, cardiometabolic health, saliva cortisol and mental wellbeing in children or adolescents were observed in this thesis. Studies examining relationships between residential traffic noise and children's health are generally scarce. However, several epidemiological studies have assessed associations of traffic noise with blood pressure in children or adolescents. A meta-analysis reported a non-significant increase in systolic and diastolic blood pressure with increasing residential road traffic noise levels in children.[23] A recent study also found no relationships between pre- or postnatal road traffic noise exposure and blood pressure or prehypertension risk in 2597 adolescents aged 16 years from Sweden.[24] In line with these previous studies, this thesis shows that exposure to traffic noise was not associated with blood pressure in adolescents aged 12 and 16 years at the observed exposure levels and range (chapter 4).

The lack of associations with traffic noise could either be due to the true absence of associations between traffic noise and health in our study population or due to methodological limitations of the studies described in this thesis. Two previous epidemiological studies assessed associations of traffic noise, estimated by using the same model as the studies in this thesis, with cardiometabolic health outcomes and mental health in adults in the Netherlands.[5,10] In line with the results of this thesis, those studies found no associations of residential exposure to traffic noise with diabetes and hypertension and only limited evidence for associations with mental health.[5,10] The observed traffic noise levels and the variability in traffic noise levels in this thesis are relatively low (median (IQR) 53.0 (49.9 - 57.0) dB(A) for road traffic noise and 31.2 (29.0 - 38.3) dB(A) for railway noise), which could explain why we did not observe relationships between traffic noise and health outcomes in children or adolescents. The studies in this thesis only included traffic noise levels outside the participants' homes and had no information on indoor insulation, orientation of the bedroom and window type. This implies that indoor (bedroom) noise levels could be substantially lower than the estimated outdoor traffic noise levels. This could also explain the lack of associations between residential traffic noise and health observed in this thesis, since traffic noise may affect health through sleep disturbances.[25] Finally, people who are sensitive to noise may move away from highly noise-exposed areas or decide not to move to these areas in the first place. It is possible that only people who are less sensitive to noise remain in areas with high traffic noise levels, which is called a "healthy resident effect".[26]

Combined exposures

Most previous epidemiological studies have examined the health effects of a single environmental exposure, ignoring potential confounding by other spatially correlated exposures. An important strength of the studies in this thesis is that we assessed the individual and joint associations of green space, air pollution and traffic noise with health outcomes in children and adolescents. The green space indicators, i.e. the average Normalized Difference Vegetation Index (NDVI) and total percentage of green space in buffers of 300m and 3000m, were negatively correlated with air pollution and traffic noise levels. Spearman correlations were highest between green space in a buffer of 3000m and estimated concentrations of ambient air pollution (r = -0.74 to -0.26). Road traffic noise levels were moderately positively correlated with the ambient air pollutants (r = 0.30 to 0.52).

In chapter 3, associations between residential green space in a buffer of 3000m and a lower odds of being overweight throughout childhood were observed. These relationships attenuated after adjustment for ambient concentrations of NO_2 (adjusted OR [95% CI] from 0.86 [0.71 - 1.04] to 0.94 [0.77 - 1.15] per IQR increase in the average NDVI in a buffer of 3000m). This indicates that not green space itself (e.g. by increasing physical activity levels), but lower levels of traffic-related air pollution may be related to a lower risk of childhood overweight. Chapter 6 shows that the relationships between ambient air pollution and a higher odds of poor mental wellbeing from age 11 to 20 years weakened after adjustment for green space and road traffic noise, which was mainly due to adjustment for green space (for example, adjusted OR [95% CI] from 1.22 [1.08 - 1.37] to 1.10 [0.91 - 1.34] per IQR increase in NO_2 after adjustment for the total percentage of green space in 3000m and road traffic noise). This implies that studies likely overestimate associations between air pollution and mental wellbeing in adolescents if green space levels are not taken into account. The results of this thesis demonstrate the importance of examining the health effects of multiple environmental exposures in one study.

7

Methodological considerations

Generalizability

Participants of cohort studies often have a higher socioeconomic status (SES) and may have healthier behaviors than non-participants. Children in the PIAMA study were recruited from the general population, but children of higher educated parents were somewhat overrepresented. Additionally, there was selective loss to follow-up of children with lower parental education.[27] An important question is to what extent the associations that are presented in this thesis are valid for the general population of children and adolescents in the Netherlands. Several epidemiological studies have shown that the beneficial associations between green space and health may be strongest for individuals with a low SES.[3,28,29] For example, a study in 6467 children from England showed that the associations of green space with a lower risk of overweight at age seven years were stronger in children growing up in lower educated families.[30] Another study showed that lower maternal education strengthened the association between low exposure to green space and an increased risk of being overweight/obese in 1489 children aged 4-6 years from Lithuania.[31] This could imply that we may have missed or underestimated positive associations of green space with health outcomes in our study population that has a relatively low proportion of children from lower educated parents.

The findings of this thesis may not be generalizable to children and adolescents living in other countries. Differences in culture and climatic conditions may affect the way people perceive green spaces and their associated benefits. Lafortezza et al. found differences in both the frequency and purposes of green space visits between people living in Italy and the United Kingdom, which are potentially attributable to both climatic and cultural differences between the two countries.[32] It is likely that the health effects of green space are not similar across the world given the large differences in vegetative, cultural and climatic factors.[3]

Residual confounding by SES

One concern in epidemiological studies examining the health effects of green space is residual confounding by individual- and area-level SES. The studies presented in this thesis only included the level of parental education and lacked information on, for example, parental occupation and household income. Since this imperfect indicator of individual-level SES was used for model adjustment, residual confounding could have biased the findings and have led to inflated effect sizes. However, we observed that adjustment for parental level of education hardly changed the associations of green space with health outcomes. Additionally, we have tried to minimize this bias by also adjusting the associations for lifestyle indicators that are correlated with SES: maternal smoking during pregnancy and parental smoking the child's home.

Since area-level SES may be related to both green space levels and health outcomes, observed positive associations with green space could reflect benefits from residing in both a greener and more prosperous neighborhood if SES is not completely accounted for in the analyses. In this thesis, however, no strong correlations between neighborhood SES and the quantity of residential green space were observed. For example, the Spearman correlations between the *statusscores* (a higher *statusscore* indicates a higher neighborhood SES) and the average NDVI in buffers of 300m and 3000m were 0.06 and 0.11, respectively, for all PIAMA home addresses in 2010. Consequently, associations of green space with the health outcomes studied in this thesis hardly changed after adjustment for neighborhood SES. It is therefore unlikely that the observed associations of residential green space in a buffer of 3000m with saliva cortisol and mental wellbeing are explained by residual confounding by neighborhood SES.

Spatial contrasts

In this thesis, land-use regression (LUR) models based on measurement campaigns performed in 2009 were used to estimate ambient air pollution concentrations at the home addresses of the PIAMA participants. The STAMINA model (Standard Model Instrumentation for Noise Assessments) was used to estimate daily average road traffic and railway noise exposure for 2011. Residential exposure to green space was assessed for 2000/2002 and 2010 (the average NDVI) and 1996, 2006 and 2016 (the percentages of green space, based on land-use maps). Associations of green space, air pollution and traffic noise with health outcomes from ages 3 to 20 years were estimated, i.e. approximately between 2000 and 2018. We assumed that the spatial contrasts in green space, air pollution and traffic noise levels remained constant throughout the study period, for children who did not change address over this period.

The assumption of stable spatial contrasts in air pollution and traffic noise levels throughout the study period in this thesis is supported by several epidemiological studies. Studies from Europe have found that the spatial variation in air pollution or road traffic noise levels remain stable over periods of seven to 12 years.[33-36] For example, a study by de Hoogh et al. showed high correlations between ambient NO_2 concentrations measured by the European Environment Agency (EEA) AirBase stations in 2000, 2005 and 2010 in the Netherlands.[36] Additionally, Gulliver et al. used LUR models to develop maps of annual average air pollution concentrations in 1962, 1971, 1981 and 1991 for Great Britain. This study showed that spatial patterns of air pollution concentrations were broadly similar over this period of nearly 30 years.[37]

No other epidemiological studies have assessed whether the spatial distribution of green space levels remain stable over time. In this thesis, high correlations were observed between the average NDVI in buffers of 300m and 3000m in 2000/2002 and 2010 for the home address of participants of the PIAMA study (Table 3). We also observed high correlations between the total percentage of green space in buffers of 300m and 3000m in 1996, 2006 and 2016 (Table 3), suggesting that the spatial contrasts in green space levels in the Netherlands remain constant over a period of 10 years.

Residential self-selection

In studies examining associations between built environment characteristics and health outcomes, there is a possibility of residential self-selection. For example, people with health problems or people who worry about the impact of air pollution on their health may choose to reside in neighborhoods with (perceived) lower concentrations of air pollutants. Additionally, people who have a better health may prefer living in an environment conducive to an active and healthy lifestyle and, therefore, choose to live in a greener neighborhood. In other words: positive relationships between green space and health may be attributable to 1) the effect of green space on health, 2) the effect of health on residential choice, or 3) both. Future epidemiological studies are needed that assess the impact of residential self-selection on the associations of green space, air pollution or traffic noise with health outcomes in children and adolescents.

Chapter 2 of this thesis shows that the quantity of residential green space was not associated with the frequency of green space visits in adolescents. This may imply that self-selection bias, i.e. the decision to reside in neighborhoods that align with preferences for green space visits, does not impact studies examining the health effects of green space in adolescents in the Netherlands.

Table 3. Spearman correlations between the average NDVI in buffers of 300m and 3000m in 2000/2002 and 2010 and the total percentage of green space in buffers of 300m and 3000m in 1996, 2006 and 2016 for 7932 PIAMA home addresses.

		NDVI in 2000/2002		NDVI in 2010		Total green space in 1996		Total green space in 2006		Total green space in 2016	
		300m	**3000m**	**300m**	**3000m**	**300m**	**3000m**	**300m**	**3000m**	**300m**	**3000m**
NDVI in 2000/2002	**300m**	1.00	0.50	0.87	0.55	0.51	0.48	0.59	0.50	0.67	0.50
	3000m		1.00	0.49	0.91	0.20	0.67	0.18	0.70	0.23	0.69
NDVI in 2010	**300m**			1.00	0.60	0.54	0.52	0.63	0.55	0.74	0.56
	3000m				1.00	0.30	0.81	0.30	0.84	0.34	0.85
Total green space in 1996	**300m**					1.00	0.48	0.86	0.46	0.76	0.45
	3000m						1.00	0.43	0.98	0.43	0.96
Total green space in 2006	**300m**							1.00	0.44	0.80	0.44
	3000m								1.00	0.44	0.98
Total green space in 2016	**300m**									1.00	0.45
	3000m										1.00

Future research

Green space

Since the percentage of people living in urban environments continues to increase, there is a need to better understand the various potential impacts of urban green space on a large range of health outcomes. The number of epidemiological studies assessing associations of green space with health outcomes in children or adolescents is small compared to studies that have been conducted in adult populations. More research is needed to assess the health effects of green space in children.

In chapter 2 of this thesis, the frequency and predictors of green space visits in adolescents aged 17 years were examined. The quantity of residential green space was not associated with the frequency of green space visits. In other words: more neighborhood green space did not translate into an increase in the use of these spaces in our study population of Dutch adolescents. This finding has implications for future epidemiological studies examining associations between green space and health in adolescents, especially for those health outcomes for which physical activity or social cohesion are potential mediators (i.e. for which green space visits are likely to be important). Future research on the health effects of green space would benefit from information on the use of green spaces by the study participants. Studies that examine the use of green spaces in different age categories in several countries with different cultures and climates are needed. Researchers could collect objective data on the time that children spend in green spaces by, for example, Global Positioning Systems (GPS) devices or smartphones. Additionally, very few studies have examined the magnitude of the contribution of the various pathways through which green space may affect children's health.[2,3] This thesis shows that adolescents mainly visited green spaces for physical and social activities. Future epidemiological studies should also examine the drivers of green space visits, which would give indications for the relevance of the different pathways.

Finally, information on the quality of green spaces was not available in the studies included in this thesis. Quality characteristics of green spaces, such as walkability, safety, aesthetics and sport/play facilities, have been suggested to be associated with the use of green spaces and health outcomes in children.[2,38,39] Future studies should not only include the quantity of green space, but also assess participants' satisfaction with green space and/or include audits to assess the quality of green spaces. Parental perceptions of green space quality should also be considered, since these are likely to play a role in determining whether young children have contact with green spaces.

The exposome

In daily life, people are simultaneously exposed to a wide range of environmental factors that could affect health. However, the majority of the existing evidence on exposure-health relationships comes from epidemiological studies focused on a single exposure. This thesis examined the individual and joint associations of green space, air pollution and traffic noise with health outcomes in children and adolescents. The results demonstrate the importance of examining the health effects of multiple spatially correlated environmental exposures in one study. Even though the studies in this thesis have improved upon previous epidemiological studies, the associations of only three environmental exposures with health outcomes were investigated. There is a need for more complete environmental exposure assessment in epidemiological studies in order to provide a greater understanding of the relationships between environmental exposures and health outcomes, which could contribute to the prevention of chronic diseases.

The exposome is defined as the totality of human environmental exposures (including lifestyle factors) from conception onwards, complementing the genome.[40,41] Unlike the genome, the exposome is dynamic and evolves throughout the lifetime of an individual.[40] Characterizing the exposome therefore requires longitudinal sampling, particularly during critical life stages, such as fetal development, early childhood and puberty. The assessment of many exposures simultaneously is expected to provide a more accurate assessment of the impact of the environment on health. Moreover, the exposome concept can overcome the limitations of focusing on a single exposure or single family of exposures in epidemiological studies.[41] However, characterizing the exposome is complex. Challenges include the accurate assessment of several hundreds of time-varying exposures and statistical challenges such as the efficiency of variable selection techniques in the presence of numerous correlated covariates.[42] Even though the exposome approach is in its infancy, several exposome research initiatives have been launched and a few recent studies have assessed associations between the early-life exposome and health outcomes in children.[43-46]

Characterizing the exposome may have a critical role in understanding chronic disease formation and progression. Future epidemiological studies should therefore take important steps forward in both measuring the exposome and in estimating associations between the exposome and health outcomes in children and adolescents.

Implications for public health policy

Chapter 3 of this thesis shows that higher exposure to ambient NO_2 may contribute to the development of childhood overweight. The median (IQR) NO_2 concentration observed in this thesis was 23.6 (18.8 - 28.0) µg/m^3, which is substantially lower than the annual mean World Health Organization (WHO) Air Quality Guideline value of 40 µg/m^3.[47] This implies that exposure to ambient NO_2 concentrations lower than the WHO guidelines may have negative health effects in children (beyond the well-studied respiratory health effects). Even if the increased risk of overweight attributable to traffic-related air pollution for an individual may be modest, the overall attributable risk may be considerably higher, given that a large proportion of the population is exposed to ambient air pollutants. The findings of this thesis and previous epidemiological studies, showing that exposure to oxides of nitrogen may be associated with a higher BMI or increased risk of overweight in children,[15-17] indicate that efforts to reduce ambient concentrations of NO_2 could potentially contribute to a lower prevalence of childhood overweight. A potential successful policy measure to improve air quality are low emission zones, which are defined areas – usually within cities and larger towns – with various restrictions on the operation of more polluting vehicles. Exposure to ambient NO_2 concentrations could be reduced by limiting high-pollution traffic from residential areas or places where children play outdoors, such as schools and parks.

Other policy measures could aim for behavioral change regarding urban mobility by, for example, promoting public transport, car-sharing programs or low-emission vehicles.

We found that higher exposure to residential green space may be associated with lower chronic stress levels and a better mental wellbeing in children and adolescents. Future epidemiological studies need to assess the specific features of green space that may be related to lower stress levels and better mental wellbeing in order to design suitable preventive policy measures. However, the results of this thesis suggest that protecting or increasing green spaces may be effective public health interventions to improve mental wellbeing and reduce stress levels in children and adolescents in the Netherlands. Policy measures that aim to increase the amount of green space provide several co-benefits, including improved air quality and the provision of cooling and shade in cities. In other words: interventions that are designed to increase the amount of residential green space would not only potentially contribute to improved mental wellbeing, but would also address the environmental and health impacts of climate change.

Chapter 2 of this thesis shows that the amount of residential green space was not associated with the frequency of green space visits in adolescents. This indicates that interventions that increase the amount of green space would not necessarily increase the use of green spaces. Policy measures that promote the use of green spaces should therefore be implemented. This thesis shows that adolescents with highly educated fathers used green spaces more often than adolescents with lower educated fathers (chapter 2), indicating that policy measures to promote the use of green spaces should mainly be targeted to families with a lower SES. Adolescents who reported that a green environment was (very) important to them, visited green spaces most frequently. This implies that attitudes towards green space might be relevant targets for public health strategies. Future epidemiological studies are needed to explore the predictors of pro-environmental attitudes in children and adolescents so that public health strategies to promote green space visits can be implemented.

Conclusions

The findings of this thesis provide insights into the health effects of residential exposure to green space, ambient air pollution and traffic noise in children and adolescents living in the Netherlands. Given the increase in global urbanization, it is of importance to understand the health impacts of these environmental exposures. The studies presented in this thesis show that green space was not related to overweight throughout childhood and cardiometabolic health at ages 12 and 16 years. Higher exposure to residential green space in a buffer of 3000m was associated with a larger diurnal decrease in saliva cortisol concentrations, indicating lower chronic stress levels, in children aged 12 years and a better mental wellbeing throughout adolescence. These findings add to the growing body of research that suggests beneficial effects of green space on mental health. This thesis further shows that exposure to NO_2 may contribute to childhood overweight. Higher exposure to ambient air pollution was related to a worse mental wellbeing in adolescents. These associations, however, weakened after adjustment for green space in a buffer of 3000m. These results demonstrate the importance of investigating the health effects of multiple spatially correlated environmental exposures in one study. No relationships between road traffic or railway noise and overweight, cardiometabolic health, saliva cortisol or mental wellbeing in children and adolescents were observed in this thesis.

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Summary

Samenvatting

Curriculum vitae

List of publications

Dankwoord

Summary

Chapter 1 provides the background of this thesis. Globally, more people live in urban areas than in rural areas. Urbanization has brought unwanted side effects, such as less availability of natural environments and increasing exposure to air pollution and noise. In daily life, people are exposed to multiple environmental risks (such as air pollution and noise) and environmental amenities with potentially positive health effects (such as green space). Since policy measures affect multiple environmental exposures, knowledge on the combined health effects of green space, air pollution and noise is necessary to evaluate their integrated effects in policy scenarios. The aim of this thesis was to assess the individual and combined associations of residential exposure to green space, air pollution and traffic noise with overweight, cardiometabolic health, saliva cortisol and mental wellbeing in children and adolescents living in the Netherlands. The studies presented in this thesis were embedded in the ongoing Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study that has followed children from birth until young adulthood.

Chapter 2 describes the frequency and predictors of green space visits in adolescents. The study population consisted of 1911 adolescents aged 17 years who reported how often they visited green spaces and for what purposes. Fifty-three percent of the adolescents reported to use a green space at least once a week in summer, mostly for physical and social activities and less often for relaxation or to experience nature and quietness. The strongest predictor of the frequency of green space visits was the perceived importance of a green environment. Adolescents who reported that a green environment was (very) important to them visited green spaces most frequently. Moreover, adolescents who owned a dog used green spaces more often to experience nature and quietness than adolescents who did not own a dog. Boys and adolescents with highly educated fathers visited green spaces more frequently for physical and social activities as compared to girls and adolescents with lower educated fathers. The quantity of green space in buffers of 300m and 3000m surrounding the adolescents' homes, assessed by satellite images and land-use maps, was not related to the frequency of green space visits. In other words: adolescents living in neighborhoods with more green space did not use green spaces more often.

Chapter 3 describes associations of green space, air pollution and traffic noise with overweight throughout childhood. This study included 3680 children for whom height and weight were measured by the parents and reported in at least one out of nine questionnaires from age three to 17 years. Exposure to green space, ambient air pollution and traffic noise was estimated at the children's current home addresses at the times of the parental reported height and weight measurements. The odds of being overweight from age three to 17 years increased with increasing exposure to nitrogen dioxide (NO_2). Higher exposure to green space in a buffer of 3000m surrounding the children's homes was associated with a lower odds of being overweight. After adjustment for NO_2, however, the relationships with green space in a buffer of 3000m weakened. This indicates that future studies investigating associations of green space with childhood overweight should account for air pollution exposure. No relationships were observed between road traffic or railway noise exposure and overweight throughout childhood.

Chapter 4 presents the associations of residential green space, air pollution and traffic noise with cardiometabolic health in adolescents aged 12 and 16 years. Waist circumference, blood pressure, cholesterol and glycated hemoglobin (HbA1c) were measured during medical examinations at ages 12 (n = 1505) and 16 years (n = 797). Based on these parameters, a combined cardiometabolic risk score was calculated for each participant, with a higher score indicating a higher cardiometabolic risk. We observed inverse associations between ambient air pollution and waist circumference at both ages 12 and 16 years. These associations attenuated after adjustment for region of residence (i.e. the northern, western or central region of the Netherlands), except for particulate matter with a diameter of <2.5µm ($PM_{2.5}$) at age 12 years. No relationships between green space, air pollution or traffic noise and the cardiometabolic risk score, blood pressure, cholesterol and HbA1c were found.

Chapter 5 presents associations of exposure to green space, air pollution and traffic noise with the diurnal saliva cortisol change in children aged 12 years. The secretion of the stress hormone cortisol follows a circadian rhythm and the diurnal slope is the change in cortisol concentration from the post-awakening peak to its nighttime low point. A slower rate of decline in cortisol concentrations throughout the day is an indicator of chronic stress. This study included 1027 children who collected three saliva samples during one day: immediately after awakening, thirty minutes after awakening and at 8.00 pm. We calculated the change between the evening cortisol concentrations and the cortisol concentrations thirty minutes after awakening (in nmol/L per hour). Higher exposure to green space in a buffer of 3000m surrounding the children's homes was associated with a stronger diurnal decrease in cortisol concentrations. These associations remained after adjustment for ambient air pollution and road traffic noise. No statistically significant associations were observed between air pollution or traffic noise and the diurnal cortisol change.

Chapter 6 describes relationships of residential green space, air pollution and traffic noise with mental wellbeing throughout adolescence. The study population consisted of 3059 adolescents who completed the five-item Mental Health Inventory (MHI-5) at least once at ages 11, 14, 17 or 20 years. MHI-5 scores ranged from 0 to 100, with higher scores indicating a better mental wellbeing. Adolescents with a MHI-5 score ≤60 were classified as adolescents with a poor mental wellbeing. The odds of poor mental wellbeing from age 11 to 20 years was lower with higher exposure to green space in a buffer of 3000m surrounding the adolescents' homes. Ambient air pollution was associated with a higher odds of poor mental wellbeing. These associations weakened after adjustment for green space and traffic noise, implying that future studies investigating associations between air pollution and mental wellbeing in adolescents should account for exposure to green space. We observed no relationships between traffic noise and poor mental wellbeing throughout adolescence.

Chapter 7 discusses the main findings of the studies presented in this thesis, the methodological considerations and implications for future research and public health policy. We observed that adolescents who live in neighborhoods with more green space do not use green spaces more frequently than their peers living in neighborhoods with less green space. This indicates that future studies examining the health effects of green space in adolescents would benefit from information on the use of green spaces by the study participants. The results of this thesis also suggest that maintaining or increasing green spaces may be effective public health interventions to improve mental wellbeing and reduce stress levels in children and adolescents in the Netherlands. Finally, this thesis demonstrates the importance of examining associations of multiple, spatially correlated environmental exposures with health outcomes in children and adolescents. Studies examining only one of the three environmental exposures (i.e. green space, air pollution or traffic noise) may overestimate the health effects of the studied exposure.

In conclusion, this thesis shows that residential green space may be associated with lower stress levels at age 12 years and a better mental wellbeing throughout adolescence. Higher exposure to ambient NO_2 may contribute to the development of childhood overweight. No associations of exposure to road traffic or railway noise with overweight, cardiometabolic health, saliva cortisol and mental wellbeing were observed in this thesis.

Samenvatting

Hoofdstuk 1 beschrijft de achtergrond van dit proefschrift. Wereldwijd wonen er meer mensen in steden dan in landelijke gebieden. Verstedelijking heeft ongewenste neveneffecten met zich meegebracht, zoals minder beschikbaarheid van natuurlijke omgevingen en een toenemende blootstelling aan luchtverontreiniging en geluid. In het dagelijks leven worden mensen blootgesteld aan meerdere milieurisico's (zoals luchtverontreiniging en geluid) en omgevingsfactoren met mogelijk positieve gezondheidseffecten (zoals groene omgevingen). Omdat beleidsmaatregelen van invloed zijn op meerdere omgevingsfactoren, is kennis over de gecombineerde gezondheidseffecten van groen, luchtverontreiniging en geluid in de leefomgeving nodig om hun geïntegreerde effecten in beleidsscenario's te evalueren. Het doel van dit proefschrift was om de individuele en gecombineerde associaties tussen blootstelling aan groen, luchtverontreiniging en verkeersgeluid in de leefomgeving en overgewicht, cardiometabole gezondheid, speekselcortisol en mentaal welzijn in Nederlandse kinderen en adolescenten te onderzoeken. De studies in dit proefschrift zijn uitgevoerd binnen de lopende Nederlandse Preventie en Incidentie van Astma en Mijt Allergie (PIAMA) geboortecohort studie waarin kinderen vanaf de geboorte tot in de vroege volwassenheid gevolgd zijn.

Hoofdstuk 2 beschrijft de frequentie en de voorspellers van het gebruik van een groene omgeving door adolescenten. De studiepopulatie bestond uit 1911 adolescenten van 17 jaar die rapporteerden hoe vaak ze een groene omgeving bezochten en voor welke doeleinden. Drieënvijftig procent van de adolescenten gaf aan in de zomer minstens één keer per week een groene omgeving te bezoeken, met name voor fysieke en sociale activiteiten, en minder vaak voor ontspanning of voor natuurbeleving, stilte en rust. Hoe belangrijk een groene omgeving was voor de jongeren voorspelde het sterkst hoe vaak zij gebruik maakten van een groene omgeving. Adolescenten die rapporteerden dat een groene omgeving voor hen (zeer) belangrijk was, bezochten het vaakst een groene omgeving. Bovendien gebruikten jongeren die een hond hadden vaker een groene omgeving voor natuurbeleving, stilte en rust dan jongeren die geen hond hadden. Jongens en jongeren met hoogopgeleide vaders maakten vaker gebruik van een groene omgeving voor fysieke en sociale activiteiten dan meisjes en jongeren met laagopgeleide vaders. De hoeveelheid groen in buffers van 300m en 3000m rondom de woningen van de adolescenten, bepaald met satellietbeelden en landkaarten, was niet gerelateerd aan de frequentie van het gebruik van een groene omgeving. Met andere woorden: jongeren die in wijken met meer groen woonden, bezochten niet vaker een groene omgeving.

Hoofdstuk 3 beschrijft de relaties tussen groen, luchtverontreiniging en verkeersgeluid in de leefomgeving en overgewicht gedurende de kindertijd. Deze studie omvatte 3680 kinderen wiens lengte en gewicht werden gemeten en gerapporteerd door hun ouders in ten minste één van de negen vragenlijsten die zijn afgenomen van leeftijd drie tot 17 jaar. Blootstelling aan groen, luchtverontreiniging en verkeersgeluid werden geschat op de huidige woonadressen van de kinderen ten tijde van de lengte- en gewichtsmetingen. De kans op overgewicht van leeftijd drie tot 17 jaar nam toe met toenemende blootstelling aan stikstofdioxide (NO_2). Een hogere blootstelling aan groen in een buffer van 3000m rondom de huizen van de kinderen was geassocieerd met een lagere kans op overgewicht. Na correctie voor NO_2 was het verband tussen groen in een buffer van 3000m en overgewicht echter zwakker. Dit impliceert dat toekomstige studies, die de relaties tussen groen in de leefomgeving en overgewicht in kinderen onderzoeken, rekening zouden moeten houden met blootstelling aan luchtverontreiniging. We vonden geen associaties tussen blootstelling aan wegverkeersgeluid of spoorweggeluid en overgewicht gedurende de kindertijd.

Hoofdstuk 4 presenteert de associaties tussen groen, luchtverontreiniging en verkeersgeluid in de leefomgeving en cardiometabole gezondheid in adolescenten van 12 en 16 jaar. Middelomtrek, bloeddruk, cholesterol en hemoglobine A1c (HbA1c) werden gemeten tijdens medische onderzoeken op leeftijd 12 (n = 1505) en 16 jaar (n = 797). Op basis van deze parameters werd voor elke deelnemer een gecombineerde cardiometabole risicoscore berekend, waarbij een hogere score een hoger cardiometabool risico aangeeft. Luchtverontreiniging was gerelateerd aan een lagere middelomtrek op zowel leeftijd 12 als 16 jaar. Deze associaties verzwakten na correctie voor de regio waarin de adolescenten woonden (d.w.z. het noorden, westen of midden van Nederland), behalve voor fijnstof kleiner dan 2.5µm ($PM_{2.5}$) op leeftijd 12 jaar. We vonden geen relaties tussen de hoeveelheid groen in de leefomgeving, luchtverontreiniging of verkeersgeluid en de cardiometabole risicoscore, bloeddruk, cholesterol en HbA1c.

Hoofdstuk 5 presenteert associaties tussen blootstelling aan groen, luchtverontreiniging en verkeersgeluid in de leefomgeving en de dagelijkse verandering in speeksel cortisolconcentraties in kinderen van 12 jaar. De productie van het stresshormoon cortisol volgt een dag-nacht ritme, met een hoge piek in de ochtend en een afname in de loop van de dag. Een verminderde afname van de cortisolconcentraties gedurende de dag is een indicator voor chronische stress. Aan deze studie namen 1027 kinderen deel die drie speekselmonsters op één dag verzamelden: direct na het wakker worden, dertig minuten na het wakker worden en om 20.00 uur. We berekenden het verschil tussen de cortisolconcentraties in de avond en de cortisolconcentraties dertig minuten na het wakker worden (in nmol/L per uur). Meer groen in een buffer van 3000m rondom de huizen van de kinderen was gerelateerd aan een sterkere dagelijkse afname van cortisolconcentraties. Deze relaties bleven statistisch significant na correctie voor luchtverontreiniging en wegverkeersgeluid. Er werden geen statistisch significante associaties gevonden tussen luchtverontreiniging of verkeersgeluid en de dagelijkse verandering in speeksel cortisol.

Hoofdstuk 6 beschrijft de relaties tussen groen, luchtverontreiniging en verkeersgeluid in de leefomgeving en mentaal welzijn gedurende de adolescentie. De studiepopulatie bestond uit 3059 adolescenten die een gevalideerde vragenlijst bestaande uit 5 vragen (de Mental Health Inventory; MHI-5) ten minste één keer hebben ingevuld op de leeftijd van 11, 14, 17 of 20 jaar. MHI-5 scores varieerden van 0 tot 100, waarbij hogere scores duidden op een beter mentaal welzijn. Adolescenten met een MHI-5 score ≤60 werden geclassificeerd als adolescenten met een slecht mentaal welzijn. Meer groen in een buffer van 3000m rondom de huizen van de adolescenten was gerelateerd aan een lagere kans op slecht mentaal welzijn van leeftijd 11 tot 20 jaar. Luchtverontreiniging was geassocieerd met een grotere kans op een slecht mentaal welzijn. Deze associaties verzwakten na correctie voor groen en wegverkeersgeluid in de leefomgeving. Dit impliceert dat toekomstige studies, die relaties tussen luchtverontreiniging en mentaal welzijn in adolescenten onderzoeken, rekening zouden moeten houden met blootstelling aan groen in de leefomgeving. We hebben geen relaties gevonden tussen verkeersgeluid en een slecht mentaal welzijn in adolescenten.

Hoofdstuk 7 bespreekt de belangrijkste bevindingen van de studies in dit proefschrift, methodologische overwegingen en implicaties voor toekomstig onderzoek en volksgezondheidsbeleid. We vonden dat jongeren die in wijken met meer groen wonen niet vaker een groene omgeving bezoeken dan leeftijdsgenoten die in wijken met minder groen wonen. Dit geeft aan dat toekomstige studies, die de relaties tussen de hoeveelheid groen in de leefomgeving en de gezondheid van adolescenten onderzoeken, baat kunnen hebben bij informatie over het gebruik van groene omgevingen door de deelnemers. De resultaten van dit proefschrift suggereren ook dat het behouden of vergroten van het groen in de leefomgeving effectieve interventies kunnen zijn om het mentale welzijn te verbeteren en stressniveaus te verlagen in kinderen en adolescenten in Nederland. Ten slotte laat dit proefschrift zien dat het belangrijk is om de associaties tussen meerdere, tegelijk voorkomende omgevingsfactoren en gezondheidsuitkomsten in kinderen en adolescenten te onderzoeken. Studies die slechts één van deze drie omgevingsfactoren (groen, luchtverontreiniging of verkeersgeluid) onderzoeken, kunnen de gezondheidseffecten van de onderzochte blootstelling overschatten.

Concluderend laat dit proefschrift zien dat groen in de leefomgeving mogelijk is geassocieerd met lagere stressniveaus in kinderen van 12 jaar en een beter mentaal welzijn tijdens de adolescentie. Een hogere blootstelling aan NO_2 in de leefomgeving kan bijdragen aan de ontwikkeling van overgewicht in kinderen. In dit proefschrift werden geen associaties gevonden tussen blootstelling aan wegverkeersgeluid of spoorweggeluid en overgewicht, cardiometabole gezondheid, speekselcortisol en mentaal welzijn.

Curriculum vitae

Lizan Denise Bloemsma was born on the 4th of July 1992 in Almere, the Netherlands. After completing secondary school in 2010, she studied Health Sciences at VU University Amsterdam. She obtained her Bachelor of Science degree in 2013 and started the master program Epidemiology at Utrecht University. During this two-year program, she developed an interest in environmental epidemiology and conducted a short research project at the Institute for Risk Assessment Sciences (IRAS) at Utrecht University under supervision of dr. ir. Lidwien Smit. This project focused on acute health effects of air pollution in patients with chronic obstructive pulmonary disease (COPD). In September 2015, Lizan started her PhD project entitled ‘Health impact of Environmental Risks and Amenities using Cross-sectional and Longitudinal Epidemiological Studies’ (HERACLES) at the Dutch National Institute for Public Health and the Environment (RIVM). She was supervised by prof. dr. ir. Bert Brunekreef, prof. dr. ir. Erik Lebret, dr. Alet Wijga and dr. Ulrike Gehring. The results of this project are presented in this thesis. Lizan is currently a Postdoctoral Fellow at the Lifecourse Epidemiology of Adiposity and Diabetes (LEAD) Center at the University of Colorado.

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Dankwoord

Almere, 22 maart 2020

Toen ik in april 2015 een sollicitatiebrief stuurde voor de functie als promovendus op het HERACLES project, was ik in eerste instantie niet uitgenodigd voor een sollicitatiegesprek. Ik schrok toen ik in juni in de studentenkamer op het IRAS zat en ineens hoorde: “Ik zoek Lizan Bloemsma?” Gerard Hoek stond in de deuropening en ik dacht dat ik iets verkeerd of illegaals had gedaan. Hij wilde echter vragen of ik toch nog geïnteresseerd was om op gesprek te komen. Een paar dagen later had ik een prettig gesprek met een positieve afloop: ik kon in september 2015 met mijn promotietraject beginnen. Ik ben heel dankbaar dat ik toch de kans heb gekregen om op het HERACLES project te promoveren, met fijne begeleiders en gezellige collega’s. De afgelopen vier jaar zijn voorbij gevlogen en ik kan bijna niet geloven dat ik nu dit dankwoord aan het schrijven ben. Ik heb veel plezier gehad op het RIVM en het IRAS en heb veel geleerd in de afgelopen jaren. Dit proefschrift is mede tot stand gekomen door het werk en de steun van veel personen. Iedereen die - op zijn/haar eigen manier - heeft bijgedragen aan dit proefschrift wil ik hierbij graag bedanken.

Allereerst wil ik mijn copromotoren dr. Alet Wijga en dr. Ulrike Gehring bedanken. Ik heb de afgelopen jaren met veel plezier met jullie samengewerkt en ik waardeer jullie betrokkenheid bij dit proefschrift heel erg. Hoe druk jullie het ook hadden, jullie namen altijd de tijd voor mij en mijn onderzoek. Ik had me geen fijnere copromotoren kunnen wensen.

Lieve Alet, ik heb het meest met jou op het RIVM samengewerkt. Ik bewonder met name je praktische aanpak, iets wat nogal van pas kan komen als je (zoals ik) een perfectionistisch persoon bent. Je bent ontzettend betrokken bij de PIAMA studie. Jouw gedrevenheid is een grote reden waarom ruim 2200 jongvolwassenen een vragenlijst op leeftijd 20 jaar hebben ingevuld. Ik kon altijd bij je terecht, ook voor persoonlijke dingen of een gezellig praatje. Ik herinner me nog goed dat je geopereerd moest worden vlak nadat ik was begonnen aan mijn promotietraject. Je maakte je bijna meer zorgen “of ik het wel zou redden” dan om je operatie en herstel. Dit is slechts één van de vele voorbeelden waaruit blijkt wat voor warm en betrokken persoon je bent. Dank je wel voor alles, ik had me niet kunnen voorstellen om bij iemand anders te promoveren.

Lieve Ulrike, ik heb de afgelopen vier jaar ontzettend veel van je geleerd. Jouw statistische kennis, kritische blik en oog voor details waren van groot belang tijdens mijn promotietraject. Dankzij jou ben ik begonnen met het schrijven van macro’s in SAS en heb ik geleerd om te werken met het programma SigmaPlot. Hier zal ik de rest van mijn carrière profijt van hebben. Ik was minder vaak op het IRAS dan op het RIVM, maar jouw deur stond ook altijd voor me open. Ulrike, ook jij bedankt voor alles en ik hoop dat we elkaar nog vaak zullen tegenkomen (bij bijvoorbeeld de ISEE congressen)!

Ik wil ook mijn promotoren prof. dr. ir. Bert Brunekreef en prof. dr. ir. Erik Lebret bedanken. Bedankt voor jullie begeleiding tijdens mijn promotietraject, vooral in de laatste maanden waarin in de General Introduction en General Discussion aan het schrijven was. Jullie kritische kanttekeningen waren erg waardevol en hebben de kwaliteit van dit proefschrift zeker verbeterd.

Ik wil de leden van de boordelingscommissie, prof. dr. ir. Dick Heederik, prof. dr. Karien Stronks, prof. dr. Ana Maria de Roda Husman, prof. dr. Chantal Kemner en prof. dr. Mark Nieuwenhuijsen, bedanken voor het lezen en beoordelen van dit proefschrift.

Mijn andere collega's binnen het HERACLES project: Jochem, Gerard en Nicole. Jochem, bedankt voor de gezellige praatjes, lunchwandelingen en natuurlijk de vele overleggen en discussies over onze analyses en resultaten. Gerard en Nicole, bedankt voor jullie waardevolle bijdragen aan de artikelen in dit proefschrift. Jullie namen altijd uitgebreid de tijd om kritisch naar mijn papers en abstracts te kijken. Gerard, bedankt voor de leuke en interessante gesprekken op het IRAS.

Ik wil ook mijn PIAMA collega's bedanken. Ik heb me vanaf het begin heel erg welkom gevoeld en mede dankzij jullie heb ik een erg fijn promotietraject gehad. Beste Jet, bedankt voor je warmte en gezelligheid de afgelopen jaren. Bedankt voor je input op mijn analyseplannen en resultaten tijdens de PIAMA PhD meetings en voor je lieve e-mails sinds ik in Denver woon. Marjan Tewis, mede dankzij jou is de PIAMA database en bijbehorende documentatie ontzettend gestructureerd. Je was altijd erg behulpzaam en gaf snel antwoord op mijn vragen. Marieke Oldenwening, bedankt voor de gezellige dagen tijdens het veldwerk voor de Schipholstudie en voor je hulp bij het analyseren van de speekselmonsters van de 12-jarige PIAMA deelnemers. Ik ben blij dat we deze speekselmonsters hebben kunnen gebruiken in mijn proefschrift. Edith, Joseph, Tom, Nina, Linda, Annemarijn, Marieke and Floor: thank you for your feedback and suggestions (and homemade sweets) during the PIAMA PhD meetings and for the nice dinners that we had in Utrecht.

Mijn paranimfen, Anniek en Mariana, wil ik bedanken voor alle hulp rondom mijn promotie. Ik vind het heel leuk dat jullie tijdens mijn promotie naast mij willen staan. Anniek, ik herinner me onze introductieweek op de VU nog als de dag van gisteren. Bedankt voor de gezellige etentjes, shopsessies en vakanties (in Praag en Rhodos) in de afgelopen jaren. Ik kan altijd overal met jou over praten. Mariana, ik vind het heel leuk dat we samen de Master Epidemiology hebben gevolgd en allebei zullen promoveren bij het IRAS. Bedankt voor de gezellige praatjes, lunches en BBQ's!

De afgelopen vier jaar heb ik verschillende kamergenoten op het IRAS gehad, waaronder Luuk, Astrid, Gijs, Lily, Pedro en Mara. Bedankt voor de gezelligheid! Het was fijn om met jullie te kletsen en ideeën uit te wisselen. A special thank you for Jie and Dongsheng: thank you for being such wonderful roommates! We had nice conversations and (pancake) lunches and you made my time at IRAS gezellig. It was not easy to say goodbye to you at the end of my PhD project.

Ik wil ook mijn collega's van de afdeling L&G bedanken. Ik heb weinig met jullie samengewerkt, maar ik kon altijd bij jullie terecht voor een praatje of jullie advies. Bedankt voor de gezellige afdelingsuitjes en afdelingsoverleggen. Ik wil hier specifiek Bette en Floor noemen: bedankt voor de gezellige lunchwandelingen en fijne gesprekken!

In dit dankwoord mag mijn familie natuurlijk niet ontbreken. Lieve mama en papa, ontzettend veel dank voor het bieden van een fijne thuisbasis en voor een rotsvast vertrouwen in mijn kunnen. Jullie steunen me in mijn carrière keuzes, ook als dit betekent dat ik twee jaar lang aan de andere kant van de wereld woon. Lieve mama, bedankt voor ontwerpen en tekenen van de omslag van mijn proefschrift. Lieve Ivon, onze band is een stuk sterker geworden sinds we een stuk minder op elkaars lip zitten. Bedankt voor alle gezellige etentjes en filmavonden (met mama)! Als ik weer in Nederland woon, gaan we dat zeker weer gezellig doen.

Lieve Keith, bedankt voor je steun in de afgelopen jaren en de vrijheid die je me geeft om mijn carrière te vervolgen. Bedankt voor alle ritjes naar het RIVM en voor je begrip als ik weer eens een deel van het weekend aan mijn proefschrift wilde werken. Bedankt dat ik mezelf kan zijn bij jou en dat je er altijd voor me bent!

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