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Early View

Original research article

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Green and blue spaces and lung function in the Generation XXI cohort: a life course approach

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Take home message:

More people are living in urban areas lacking natural spaces, which can have deleterious health effects. Children who increased their life course exposure to greenness had better lung function. So, city greening may lead to improvements in respiratory health.

Abstract

Exposure to natural environments may affect respiratory health. This study examined the association of the exposure to green and blue spaces with lung function in children, and assessed the mediation effect of air pollution and physical activity.

The study used data from the Generation XXI, a population-based birth cohort from the Porto Metropolitan Area (Portugal). Residential Normalized Difference Vegetation Index (NDVI) at different buffers (100, 250 and 500 meters), the accessibility to urban green spaces (UGS) within 400 and 800 meters, and the minimum distance to the nearest UGS, and to the nearest blue spaces were assessed at birth, 4, 7 and 10 years of age. Three life course measures were calculated: averaged exposure, early life exposure (birth) and exposure trend over time (change in exposure). Forced vital capacity (FVC), forced expiratory volume at the first second (FEV1) and forced expiratory flow between 25% and 75% of forced vital capacity (FEF25%-75%) at 10 years were used as outcomes. To assess associations, linear regression models and path analysis were used.

This study included 3278 children. The adjusted models showed that increasing the NDVI exposure over time within 100 meters of the child's residence was associated with higher values of FEV1 (L) and FEF25%-75% (L/s) [β (95% CI) = 0.01 (0.0002; 0.03); and β (95% CI) = 0.02 (0.001; 0.05)]. No significant associations were observed for the remaining measures of exposure, and no mediation effect was found for pollution or physical activity.

Increasing exposure to greenness at close proximity from residences was associated with improved lung function. While the mechanism remains unknown, this study brings evidence that city greening may improve children’s respiratory health.

Introduction

Exposure to natural environments is associated with better health outcomes [1] but green (i.e., vegetated land [2]) and blue space (visible surface water [3]) studies tend to focus on adults. However, childhood may be sensitive for such exposures [4]. Longitudinal studies have shown that decrements of lung function established in the first few years after birth track to adulthood, which indicates that early childhood is a sensitive period in lung function development [5, 6]. Additionally, lung function deficits that have been tracked from childhood into adulthood have been associated with a higher prevalence of respiratory diseases and premature death [7]. Although lung function catch-up might happen, this phenomenon is still not certain [8]. Lung function is an important indicator of child growth, with children with accelerated body mass index (BMI) gain showing a higher predicted Forced vital capacity (FVC) and lower Forced expiratory volume in 1 second (FEV1) to FVC ratio (FEV1/FVC) [9]. These indicators are used to assess lung function, with decreased values of FEV1 and FVC being associated with airway obstruction and lung restriction, respectively [10]. Two of the main airway obstruction diagnosis are asthma and Chronic Obstructive Pulmonary Disease (COPD), with childhood asthma being associated with COPD development later in life [11]. Since the lung function development is a continuum, is crucial to identify the environmental factors that affect lung function in childhood, so that it is possible to intervene early and decrease the risk of respiratory diseases in later life [7].

Exposure to nature might influence lung function through different mediators, namely physical activity and air pollution [12, 13]. Green [12] and blue spaces [1], may promote increased levels of physical activity, which can improve both FEV1 and FVC [14], possibly by the stretch of the airway smooth muscle, leading to a reduced bronchoconstriction [15]. The presence of green [13] and blue spaces [1] may also improve air quality, by filtering air pollutants and/or mitigating the pollution levels. Air pollution is commonly higher in areas with lower amounts of natural spaces, which may lead to chronic inflammation and, consequently, increases in reactivity, smooth muscle contraction and secretions [16].

The association between green spaces and different measures of respiratory health in children [17-27] and adults [28] has been evaluated but several evidence gaps remain. Most studies measured the development of disease, such as asthma (either by questionnaires [18, 19, 22-24], or medication [17]) and only four studies measured lung function [25-29]. Regarding these four studies, one suggested that children living in more vegetated places or in close proximity of green spaces across their life-course have better lung function [29], two reported no association between greenness and the respiratory system resistance and respiratory system reactance [25] and spirometry measures [27], while the other found no effect modification of greenness in the association between pollens and the fractional exhaled nitric oxide [26]. Furthermore, the previous studies assessed the effect of greenness at different moments and using different approaches. Three of the studies used a cross-sectional analysis, evaluating the effect among children [25-27] and recently one longitudinal study assessed the effect of exposure to residential green spaces across life-course and lung function up to 24 years of age [29].

Most studies only used greenness measures [20, 22, 24] but it has been described that accessibility to urban green spaces (UGS) can be better proxies of green space exposure [30]. In addition, to our knowledge, accessibility to blue spaces has seldomly been explored as a potential determinant of lung function [27], although there is a beneficial effect of aerosolized water in asthma in children [31], Finally, there is a lack of work incorporating a life course perspective [32]. Exposures can build up over time and influence health later and people can change residences, and thereby the surrounding natural environment. Also, there are certain time windows (sensitive periods) in which environmental exposures can have a bigger impact, namely the perinatal period [33].

So, under this background, we hypothesize that greenness and geographical accessibility to green and blue spaces have a positive impact on children's lung function. Therefore, we aimed at estimating the association between the longitudinal exposure to greenness and geographical accessibility to green and blue spaces from birth to 10 years of age and the lung function of children at the age of 10, using data from the Generation XXI (G21) birth cohort. Furthermore, we aimed to assess the mediation effect of air pollution and physical activity in the studied associations.

Methods

Study participants

The study used data from the G21, which includes 8495 mothers and 8647 new-borns delivered in 2005 and 2006 in the Porto Metropolitan Area in Northern Portugal (https://www.geracao21.com/en/). The initial recruitment took place between April 2005 and September 2006 at all public maternity units, where 95% of the region's births occur. All participants were invited to be re-evaluated at four (2009/11), seven (2012/14) and ten (2015/17) years of age [34]. At ages 4, 7 and 10 years, 7459, 6889 and 6392 children participated (86%, 80% and 74% of the initial cohort), respectively (Supplemental Material, Figure S1) [35]. Ethical approval for the study was obtained from the Ethics Committee of the University Hospital Center of São João (CES-01/2017) and signed informed consent was obtained from all participant's legal representatives.

Child's residential address was collected during routine telephone calls with the caregiver. If the child changed residence from birth to 10 years of age, the new address was used to estimate the exposure at the time of evaluation. For the present study, the subsample of children living in Porto Metropolitan Area since birth to data collection and with data on lung function parameters at 10 years of age was included, totalling 3278 children.

Health outcomes

Lung function was measured by spirometry at 10 years of age using a portable spirometer (MIR Minispir) by trained technicians, according to American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines [36]. All curves were checked post-hoc by a specialist to ensure that satisfactory reproducibility criteria had been met. The parameters included in this analysis were FVC as a measure of lung volume and size, FEV1 and forced expiratory flow between 25% and 75% of forced vital capacity (FEF25%-75%) as measures of airway obstruction and small airways narrowing, respectively. Higher values in these parameters represent better lung function and respiratory health [10]. All the parameters' values correspond to the predicted volume values for FVC and FEV1 in L, and FEF25%–75% in L/s and were calculated based on the Global Lung Function Initiative (GLI) 2012 reference data [37] using GLI-2012 Excel Sheet Calculator.

Exposure assessment

Greenness

The assessment of greenness was based on the mean Normalized Difference Vegetation Index (NDVI) within 100, 250 and 500 meters of the child's residence at birth, four, seven and ten years of age. These buffer sizes were selected to cover immediate and more distant areas of exposure [38]. The NDVI was calculated based on land surface reflectance of visible red and near-infrared wavelengths. The values range between -1 (water) and 1, with higher positive values indicating denser green vegetation. Only images with 5% or less cloud coverage from Landsat 5 and 8 (spatial resolution: 30 m) during the spring/summer period (peak of vegetation) of the assessment years (2005/6, 2009/11, 2012/14 and 2015/17) were used, as previously described in G21 cohort studies [38]. Negative NDVI values were omitted from the calculation. ArcMap 10.5 was used to process satellite images, and QGIS 3.8 was used to extract the average NDVI.

Proximity, accessibility, and number of urban green spaces

To determine residential proximity and number of UGS, all public and free to access UGS in the Porto Metropolitan Area (N=662) were included, without restrictions regarding size, location, or any particular characteristic. The UGS included public green spaces, such as urban parks, gardens and proximity green spaces, which are administered by the city councils of Porto Metropolitan Area or privately owned but freely accessible to the public. The cartography was obtained from digital maps provided by the different city halls of Porto Metropolitan Area. Similar to previous studies [38], using the location of each child's residence at birth, four, seven and 10 years of age, the following network-based measures were calculated: a) accessibility of UGS within 400 and 800 meters from the residence (yes/no); b) number of green spaces available within 400 and 800 meters from the residence (count); c) proximity to the nearest green space (km). When UGS were delimited (i.e., with fencing), it was considered the distance to the entrance; otherwise, the distance to the nearest boundary was used. For calculations, ArcGIS version 10.5 software and the Network Analyst extension was used, applying an updated street network dataset provided by the Environmental Systems Research Institute.

Proximity to blue spaces

The Portuguese Water Atlas (from the Portuguese "Atlas da Água") was used to assess the Euclidean distance of children's residence to the nearest blue space, including only the sea and rivers, as previously described [38]. Other water bodies, such as urban water sources as fountains, ponds and lakes were not included due to their small size.

Covariates

A comprehensive set of covariates was selected based on previous studies on associations between lung function and personal and environmental factors [39-41]. The following variables were considered: sex, age in months, total physical activity, outdoor levels of nitrogen dioxide (NO_2), maternal educational level, household monthly income, population density, and neighbourhood socioeconomic deprivation.

The practice of physical activity was defined as engagement (yes or no) in physical exercise, and active leisure activities, performed on a repeated and regular basis ("*Does [child's name] engage in any type of repeated and regular physical exercise outside of school?*").

Maternal educational level was measured in years of schooling and categorized into three classes: primary (≤9 years of education); secondary; and tertiary (≥13 years). Household monthly income was collected as a categorical variable and grouped into three classes: ≤1000, 1001–1500 and >1500 euros. Population density at the neighbourhood level (corresponding to the census tract, which in Portugal holds approximately 300 residences) [42] was obtained from the Portuguese National Institute of Statistics (INE) 2011 [43]. Neighbourhood socioeconomic deprivation was measured at the census tract level using the European Deprivation Index, with lower values corresponding to least deprived areas [44]

Outdoor levels of NO_2 (μg/m^3) were obtained from AirBase — The European air quality database from the European Environment Agency (EEA) [45]. The EEA provides 1 km grids for NO_2, which were created based on monitoring station data (more details can be found in Supplementary material). Each participant was assigned the value of the grid of the residential point location.

Statistical analysis

Three models were used to assess the effect of green (NDVI, proximity and number of UGS) and blue spaces on lung function at 10 years of age: 1) averaged exposure; 2) early life exposure (i.e., exposure at time=0); and 3) exposure trend over time (from birth to 10 years of age).

In the first model, the exposure variables were averaged from birth to 10 years of age. The accessibility of UGS within 400 and 800 meters from the residence was operationalized as a categorical variable that distinguishes children who had access to UGS in the majority of the cohort evaluations (≥ 3 times from birth to 10 years of age) from those who had access in half of the cohort evaluations or less (≤ 2 times).

In the second and third models, a two-step analysis based on the results derived from a child's individual exposure curve was performed [46]. For these models, we firstly calculated the intercept and slope parameters (1st step), and then we used the intercept for model 2 and the slope for model 3 (2nd step). In the first step, a regression analysis was performed with age (in days) to lung function assessment as the independent variable and the exposure as the dependent variable (linear regression for continuous variables and logistic regression for dichotomous variables). This regression analysis was performed with the exposure data from birth to 10 years of age for each child separately in a long-structured dataset to obtain child specific exposure curves. Secondly, the calculated intercept parameter (i.e., exposure at time=0) from the first step was included in the new model as an estimate of the early life exposure, capturing how much between-child variability exists in terms of where they start [47]. The slope coefficient – representing the trend of the child's change in exposure over time – was included in this new model to predict lung function parameters at 10 years. The intercept and slope parameters jointly define the underlying exposure trajectory. We also added the standard error of the intercept and slope parameters from the first step to the new model as an indication of fluctuation of the actual exposure measurements. In these models, the longitudinally time-varying exposure was first modelled as a function of time by calculating intercepts and slopes, and then the estimates of these coefficients were used as predictors in the linear regression model. The step-by-step sequence of the statistical analyses is summarized in Supplemental Material, Figure S2.

Linear regressions models were fitted to estimate the crude and adjusted associations and we expressed the estimates for a standard deviation (SD) change in exposures. Adjusted models included the covariates listed in the previous section and identified based on direct acyclic graph (DAG) (developed using the R package "dagitty") (Supplemental Material, Figure S3). Results were expressed as beta coefficients (β) and 95% confidence intervals (95% CI).

The mediation effects of physical activity and outdoor levels of NO_2 were calculated based on the structural equation modelling (SEM). SEM methods are based on path analysis and simultaneously test both direct and indirect effects of predictive variables on the outcome [48]. A SEM was fitted using logistic regression analysis to estimate the indirect effects of physical activity and outdoor levels of NO_2 (R Package lavaan). Effect modification by indicators of socioeconomic position was explored by assessing the statistical significance of multiplicative interactions, using likelihood ratio tests by comparing models with and without interaction terms [49, 50]. The analyses revealed no statistically significant interaction effects and, thus, results were presented without stratification for indicators of socioeconomic position. Additionally, to assess the robustness of the associations found in the main analyses, sensitivity analyses were performed using other buffer sizes (250 and 500 meters), adjusting for residential mobility and for birthweight (Supplemental Material, Table S1, S2 and S3, respectively). Statistical analysis was performed using R software version 3.6.2.

Results

The study participants' characteristics are presented in Table 1. The median (25^{th}; 75^{th} percentile) NDVI within 100 meters increased slightly over time [from 0.148 at birth to 0.203 (0.163; 0.251) at 10 years of age; Table 2]. The median distance to the nearest green space also increased over time [from 0.90 (0.49; 1.50) km at birth to 0.94 (0.51; 1.53) km at 10 years of age; Table 2]. Almost 18% of the children lived within 400 meters from a UGS and 40% lived within 800 meters from a UGS over time. The median distance to the nearest blue space ranged from 4.80 (3.34; 6.69) km at birth to 4.94 (3.44; 6.76) km at 10 years of age (Table 2).

TABLE *1* - Characteristics of participants (Generation XXI, n=3278)

TABLE 2 - Measures of exposure to green and blue spaces in the residential neighbourhood (Generation XXI, n=3278)

Table 3 presents the crude and adjusted associations between NDVI and lung function at 10 years of age. Early life exposure to greenness was associated with higher values of FVC, FEV1 and FEF25%-75%. However, after adjustment, the positive association between early life exposure to NDVI and lung function parameters was no longer statistically significant (Table 3). Differently, increasing NDVI values within 100 meters from the residence were, even after adjustment, associated with higher values of FEV1 (L) and FEF25%-75% (L/s) [β (95% CI) = 0.01 (0.0002; 0.03); and β (95% CI) = 0.02 (0.001; 0.05), respectively] (Table 3). Although not significant, a similar trend was observed between NDVI within 250 m and 500 m and lung function parameters (Supplemental Material, Table S1). No significant associations were observed for the remaining life course measures of green and blue space exposure (Table 4 to Table 7). The associations between proximity, accessibility, and number of urban green spaces and proximity to blue spaces and lung function parameters remained the same when adjusted for residential mobility (Supplemental Material Table S2) and also for birthweight (Supplemental Material Table S3). The mediation analysis (Table 8) revealed that associations between green and blue spaces and lung function do not seem to be mediated by physical activity and outdoor levels of NO_2.

TABLE 3 - Associations (β, 95%CI) between NDVI within 100 m and lung function parameters at 10 years of age (Generation XXI, n=3278)

TABLE 4 - Associations (β, 95%CI) between the accessibility to green spaces and lung function parameters at 10 years of age (Generation XXI, n=3278)

TABLE 5 - Associations (β, 95%CI) between the number of green spaces and lung function parameters at 10 years of age (Generation XXI, n=3278)

TABLE 6 - Associations (β, 95%CI) between the distance to the nearest green space (km) and lung function parameters at 10 years of age (Generation XXI, n=3278)

TABLE 7 - Associations (β, 95%CI) between the distance to the nearest blue space (km) and lung function parameters at 10 years of age (Generation XXI, n=3278)

TABLE 8 - Path coefficients estimated in a Structural Equation Model predicting the indirect effects of physical activity and outdoor levels of NO_2 on lung function at 10 years of age

Discussion

Increasing exposure to greenness over time within a radius of 100 meters of the residence between birth and 10 years of age had a positive association with lung function at 10 years of age, more precisely in FEV1 and FEF25%-75%, markers of airway obstruction and small airways narrowing, respectively. Measures of accessibility to urban green spaces and blue spaces did not seem to influence lung function.

These results suggest that an increasing exposure trend over time to greenness is associated with better lung function. The results are in line with our initial hypothesis, and match those of previous studies [28, 29]. Hence, moving to greener areas and increasing the amount of vegetation may be a possible strategy to improve the lung function of children. However, this effect was only visible when considering a 100 meters buffer around the residence, which suggests that the observed effect is sensible to the residential area considered. Nevertheless, previous studies have shown that vegetation measured within larger buffers may also predict health outcomes including those related with respiratory health [20, 24].

Early life exposure to greenness was not as relevant as the exposure trend over time, which may indicate that this period is not particularly sensitive to the exposure to green spaces. This may happen because new-borns are seldom exposed to outdoor environments. The daily amount of time spent at home by new-borns is nearly 90% [51]. Contrastingly, exposure to indoor (rather than outdoor) biological, physical and chemical agents –which we do not have information about - may be more relevant in early life stages. These results may suggest that the time-varying exposure to greenness may have protective effect on lung. While the underlying pathways for such association was not addressed in the present study, these results may be related to psychosocial mechanisms, Moving to, and interventions to make neighbourhoods greener, have both been associated with better mental health in adults [52], and consequently to better physical health, including respiratory health [53]. This mechanism might explain the observed association between NDVI exposure trend over time and lung function. However, the mediation effect of mental health was not assessed since no information on children mental health is available in G21 cohort. Averaged exposure to greenness was also unrelated to lung function, contrasting with the results from a recent study, that also included adult population, where lifetime average greenness within a 100 m buffer was associated with better lung function at 24 years [29].

The lack of association with the measures of accessibility to UGS was not in line with our initial hypothesis (this result is consistent even when the variable accessibility of UGS is categorized differently [Supplemental Material, Table S4]), although it corroborates previous findings [18, 27]. Evidence suggests that the beneficial effect of UGS can be offset by possible negative aspects: 1) specific characteristics of the flora can have a deleterious effect in respiratory health by inducing chronic airway inflammation [54]; 2) lack of biodiversity [55]; 3) areas where UGS are present could have higher pollution levels [20].

No associations were found between accessibility to blue spaces and lung function. A previous study highlighted the positive effect of blue space on respiratory health by reducing air pollution and aerosolized waterfall had also a beneficial effect on asthma [31]. The lack of association may be partially due to the effect being limited to very close distances and, in our sample, the number of children living within walking distances (e.g. 400, 800 meters) from those spaces is limited (no children lived less than 400 meters from a blue space and only 29, that is, less than 1%, lived at a distance of 800 meters or less).

Several mechanisms may be related in the association between greenness and lung function. The mediation analysis revealed that associations between greenness and lung function do not seem to be mediated by physical activity or outdoor levels of NO_2. However, vegetation may reduce the levels of other air pollutants (as particulate matter, ozone), which are known to have a deleterious effect in lung function [56]. Moreover, the contact with the natural environment may promote an adequate stimulation of immunoregulatory processes [55], improving lung function and thus, reducing the risk of chronic inflammatory diseases, such as asthma.

Although the observed effect estimates were relatively small, they may have important public health impacts, suggesting that the provision of green spaces in the residential neighbourhoods of metropolitan areas may be an effective strategy to improve lung function among children, which in turn may prevent the development of chronic respiratory disease. The provision of green spaces may also contribute to environmental benefits by reducing the emission of air pollutants, noise, and temperature, and by preserving regional ecosystems and biodiversity [57]. Additionally, the results support the growing evidence regarding to the benefits of green spaces on children' respiratory health, namely on lung function.

This study presents various limitations that merit further discussion. Accessibility was used as a proxy of utilization of UGS, but there are other factors influencing utilization (flora, availability of equipment, safety) [58]. The fact that biodiversity was not included in the analysis impairs an in-depth analysis of the effects of UGS (to understand if the null associations were due to a low variety of flora or a specific type of flora, or another characteristic not considered) [17]. The slight variations in NDVI over time may reduce the power of analysis and, consequently the likelihood to find a significant association between exposure to NDVI over time and children' lung function. Moreover, exposure assessment to blue spaces only included the distance to rivers and sea, excluding small water bodies such as fountains, ponds, and lakes. A recent meta-analysis suggested that even smaller water bodies may have a beneficial impact on air pollution levels and cooling [59]. Some of the included studies also observed negative effects of blue spaces, including increased disease transmission and air pollution due to river dust [59]. Like in other cohort studies, losses to follow-up can introduce bias and limit external validity, and our sample may not fully represent the socioeconomic conditions and practice of physical activity of the initial cohort participants. In fact, the included participants differed in the following characteristics: the included children reported practicing more physical activity (63.5% among included participants vs. 59.0% among those excluded, $p=0.019$), lived in less deprived neighbourhoods (14.0% among included participants vs. 12.1% among those excluded, $p<0.05$), and belonged to families with higher household monthly income (household monthly income >1500€ was 36.0% among included participants vs. 28.3% in those excluded, $p<0.05$) and with higher educational levels (maternal educational level >12 years was 28.8% among included participants vs. 21.1% in those excluded, $p<0.05$) (Supplemental Material, Table S5). The assessment of the different mediators also lacks resolution and detail. Although green spaces can promote physical activity, we lacked information to differentiate between indoor and outdoor activities. This can be important because it has been hypothesised that physical activity in green spaces can be more beneficial than in other environments [60]. The mediation effect of air pollution was assessed only resorting to NO_2. However, other pollutants, such as particulate matter and ozone, have also been associated with children's lung function level and growth [56], but were not assessed in our study. Additionally, NO_2 was measured in raster cells of 1 km^2, which may decrease the resolution of the assessment of the mediation effect. In addition, the assessment of mediators and lung function parameters at the same time point may be associated to a risk of bias due to the lack of temporal order of the mediator(s) and the lung function [61]. However, several studies reported the assessment at the same time [61], and according to Goldsmith, Chalder [62] models with contemporaneous paths may also be fitted. Moreover, other covariates may also mediate the association between green spaces and lung function, such as biodiversity [55]. Several potential confounders have also been considered, including socioeconomic factors (maternal educational level, household monthly income, and neighbourhood socioeconomic deprivation). Previous studies have reported that green spaces may be differently distributed according to neighbourhood socioeconomic characteristics and that the effect of urban green spaces on health may also differ among different socioeconomic groups [57, 63]. In our study, we found no statistically significant interactions between nature exposures and socioeconomic indicators and associations persisted after adjustment for socioeconomic factors. However, our adjustment for socioeconomic factors may have been insufficient to capture true differences in socioeconomic characteristics over time and further studies are needed to better understand the complex interaction between socioeconomic and environmental factors on lung function among children. Moreover, in our study we did not use any methods, such as multiple imputation and inverse-probability weighting, to deal with missing data. The missing data on exposures and covariates (Supplemental Material, Table S6) may reduce the power to detect change over time and may also be associated with under- or over-estimation of exposure effects. The missing data may also increase the possibility of selection bias, which may distort the observed associations. However, the missing values is low (6.8% for household monthly income)

(Supplemental Material, Table S6) and some authors suggested that missing rates between 5%-10% are generally less serious [64, 65].

This study brings various novelties to the study of nature and respiratory health relationship. To the best of our knowledge, this is the first study estimating the association between longitudinal accessibility to UGS and lung function among children. It is also the first to use a comprehensive life course approach in exposure assessment, assessing not only averaged exposures, but also early life exposure (birth) and exposure trends over time. To increase the evidence base on this emerging topic, future works should focus on having lung function measured in various moments in time to clarify lung function trajectories and inform about the importance of environmental factors at each phase. Additionally, more refined objective and subjective measures of green and blue space exposure about space quality, biodiversity and frequency and type of utilization are recommended to use in future research.

Conclusions

In conclusion, increases in the exposure to vegetation across childhood were associated with higher lung function. However, no significant associations were found between proximity to urban green spaces, like parks or gardens, or blue spaces, and lung function. While the underlying mechanism remains unknown, it brings about additional evidence that city greening may contribute to better respiratory health.

Authorship contribution statement

Diogo Almeida: Methodology, Investigation, Writing – original draft, Writing – review & editing. Inês Paciência: Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. Carla Moreira: Methodology, Formal analysis, Writing – review & editing. João Cavaleiro Rufo: Formal analysis, Writing – review & editing. André Moreira: Validation of lung function data, Writing – review & editing, Supervision. Ana Cristina Santos: Writing – review & editing, Supervision. Henrique Barros: Supervision, Writing – review & editing. Ana Isabel Ribeiro: Methodology, Formal analysis, Investigation, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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TABLE 1 - Characteristics of participants (Generation XXI, n=3278)

Characteristic	n (%)
At birth	
Sex [female, n (%)]	1654 (50.5)
Maternal education	
Primary (≤9 years)	1372 (41.9)
Secondary (10–12 years)	962 (29.3)
Tertiary (>12 years)	944 (28.8)
Household monthly income (€)	
≤ 1000	1060 (34.7)
1001-1500	895 (29.3)
> 1500	1101 (36.0)
Neighbourhood socioeconomic deprivation**	-0.02 (2.65)
At 10 years	
BMI (kg/m^2)*	18.3 (16.4; 21.0)
Physically active [yes]	2079 (63.5)
FVC before bronchodilation (L)**	2.24 (0.36)
FEV_1 before bronchodilation (L)**	2.01 (0.31)
$FEF_{25\%-75\%}$ before bronchodilation (L/s)**	2.36 (0.52)
Outdoor levels of NO_2 ($\mu g/m^3$)*	23.7 (20.2; 26.8)

* Median (25^{th}; 75^{th} percentile); ** Mean (standard deviation)

FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC; NO_2: nitrogen dioxide

TABLE 2 - Measures of exposure to green and blue spaces in the residential neighbourhood (Generation XXI, n=3278)

Exposure variables	**Median (25th; 75th percentile) or count (%)**			
	At birth	**At 4 years**	**At 7 years**	**At 10 years**
NDVI				
100 m	0.148 (0.105; 0.205)	0.171 (0.124; 0.226)	0.199 (0.160; 0.245)	0.203 (0.163; 0.251)
250 m	0.190 (0.143; 0.251)	0.206 (0.160; 0.266)	0.227 (0.187; 0.273)	0.231 (0.191; 0.279)
500 m	0.212 (0.166; 0.273)	0.228 (0.180; 0.284)	0.242 (0.200; 0.285)	0.247 (0.204; 0.290)
Accessibility to green spaces within 400 m (yes)	606 (18.5%)	604 (18.4%)	605 (18.5%)	597 (18.2%)
No. of green spaces within 400 m*	1.26 (1-4)	1.25 (1-4)	1.24 (1-5)	1.26 (1-5)
Accessibility to green spaces within 800 m (yes)	1473 (44.9%)	1425 (43.5%)	1422 (43.4%)	1430 (43.6%)
No. of green spaces within 800 m*	2.11 (1-9)	2.07 (1-9)	2.09 (1-9)	2.12 (1-9)
Distance to the nearest green space (km)	0.90 (0.49; 1.50)	0.94 (0.50; 1.51)	0.95 (0.50; 1.52)	0.94 (0.51; 1.53)
Distance to the nearest blue spaces (km)	4.80 (3.34; 6.69)	4.94 (3.43; 6.77)	4.93 (3.43; 6.76)	4.94 (3.44; 6.76)

NDVI: Normalized difference vegetation index; * Mean (minimum and maximum)

TABLE 3 - Associations (β, 95%CI) between NDVI within 100 m and lung function parameters at 10 years of age (Generation XXI, n=3278)

NDVI within 100 m	[β (95%CI)]	
	Crude model	Adjusted model*
Averaged exposure		
FVC (L)	0.0101 (-0.0023; 0.0225)	0.0030 (-0.0110; 0.0169)
FEV_1 (L)	0.0025 (-0.0051; 0.0101)	-0.0019 (-0.0097; 0.0060)
$FEF_{25\%-75\%}$ (L/s)	0.0051 (-0.0021; 0.0123)	-0.0016 (-0.0084; 0.0052)
Early life exposure		
FVC (L)	**0.0246 (0.0032; 0.0291)** ǂ	0.0137 (-0.0063; 0.0303)
FEV_1 (L)	**0.0150 (0.0071; 0.0342)** ǂ	0.0147 (-0.0023; 0.0030)
$FEF_{25\%-75\%}$ (L/s)	**0.0218 (0.0043; 0.0480)** ǂ	0.0247 (-0.0093; 0.0403)
Exposure trend over time		
FVC (L)	**0.0237 (0.0020; 0.0345)**ǂ	0.0094 (-0.0032; 0.0330)
FEV_1 (L)	**0.0238 (0.0041; 0.0264)** ǂǂ	**0.0146 (0.0002; 0.0319)**ǂǂ
$FEF_{25\%-75\%}$ (L/s)	**0.0320 (0.0044; 0.0509)**ǂ	**0.0201 (0.0014; 0.0505)**ǂ

NDVI: Normalized difference vegetation index; FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

*adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation; **bold** denotes statistically significant associations ; ǂp <0.05; ǂǂp < 0.01.

TABLE 4 - Associations (β, 95%CI) between the accessibility to green spaces and lung function parameters at 10 years of age (Generation XXI, n=3278)

	[β (95%CI)]	
Accessibility to green spaces within 400 m	Crude model	Adjusted model*
Averaged exposure		
FVC (L)	-0.0016 (-0.0277; 0.0244)	-0.0056 (-0.0294; 0.0182)
FEV_1 (L)	-0.0039 (-0.024; 0.016)	-0.0052 (-0.024; 0.014)
$FEF_{25\%-75\%}$ (L/s)	-0.0191 (-0.0385; 0.0004)	-0.0042 (-0.0208; 0.0125)
Early life exposure		
FVC (L)	-0.0043 (-0.014; 0.0056)	-0.0067 (-0.016; 0.0024)
FEV_1 (L)	-0.0045 (-0.0123; 0.0032)	-0.0054 (-0.0126; 0.0019)
$FEF_{25\%-75\%}$ (L/s)	**-0.010 (-0.0177; -0.0029)**[ǂ]	-0.0047 (-0.011; 0.0016)
Exposure trend over time		
FVC (L)	0.0026 (-0.0073; 0.0126)	0.0037 (-0.0054; 0.0128)
FEV_1 (L)	0.0016 (-0.0062; 0.0093)	0.0029 (-0.0044; 0.0102)
$FEF_{25\%-75\%}$ (L/s)	-0.0010 (-0.0088; 0.0059)	0.0024 (-0.0040; 0.0087)
Accessibility to green spaces within 800 m		
Averaged exposure		
FVC (L)	0.0066 (-0.0130; 0.0262)	0.0077 (-0.0104; 0.0258)
FEV_1 (L)	0.0040 (-0.0114; 0.0194)	0.0062 (-0.0085; 0.0205)
$FEF_{25\%-75\%}$ (L/s)	-0.0035 (-0.0181; 0.0111)	0.0055 (-0.0072; 0.0181)
Early life exposure		
FVC (L)	-0.0004 (-0.0102; 0.096)	0.0005 (-0.0086; 0.0097)
FEV_1 (L)	-0.0011 (-0.0088; 0.0066)	0.0003 (-0.0070; 0.0077)
$FEF_{25\%-75\%}$ (L/s)	-0.0055 (-0.0128; 0.0019)	0.0005 (-0.0059; 0.0068)
Exposure trend over time		
FVC (L)	-0.0048 (-0.0146; 0.0051)	-0.0003 (-0.0093; 0.0086)

FEV_1 (L)	-0.0036 (-0.0114; 0.041)	-0.0003 (-0.0075; 0.0069)
$FEF_{25\%-75\%}$ (L/s)	-0.0026 (-0.0099; 0.0048)	-0.0079 (-0.0059; 0.0055)

FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

*adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation; **bold** denotes statistically significant associations; ǂ*p* <0.05.

TABLE 5 - Associations (β, 95%CI) between the number of green spaces and lung function parameters at 10 years of age (Generation XXI, n=3278)

	[β (95%CI)]	
No. of green spaces within 400 m	Crude model	Adjusted model*
Averaged exposure		
FVC (L)	-0.0023 (-0.0207; 0.0162)	-0.0009 (-0.0177; 0.01594)
FEV_1 (L)	-0.0014 (-0.016; 0.0131)	-0.0006 (-0.0141; 0.0129)
$FEF_{25\%-75\%}$ (L/s)	0.0020 (-0.0121; 0.0161)	-0.0001 (-0.0119; 0.0117)
Early life exposure		
FVC (L)	-0.0035 (-0.0222; 0.0152)	-0.0019 (-0.02; 0.0148)
FEV_1 (L)	-0.0023 (-0.0170; 0.0123)	-0.0017 (-0.0154; 0.0119)
$FEF_{25\%-75\%}$ (L/s)	0.0016 (-0.0127; 0.0159)	-0.0010 (-0.0129; 0.0110)
Exposure trend over time		
FVC (L)	-0.0039 (-0.0226; 0.0148)	-0.0045 (-0.0218; 0.0128)
FEV_1 (L)	-0.0031 (-0.0178; 0.0116)	-0.0037 (-0.0176; 0.0102)
$FEF_{25\%-75\%}$ (L/s)	-0.0033 (-0.0175; 0.0110)	-0.0047 (-0.0169; 0.0074)
No. of green spaces within 800 m		
Averaged exposure		
FVC (L)	-0.0066 (-0.0220; 0.0088)	-0.0015 (-0.0156; 0.0127)
FEV_1 (L)	-0.0053 (-0.0174; 0.0067)	-0.0012 (-0.0125; 0.0102)
$FEF_{25\%-75\%}$ (L/s)	-0.0055 (-0.0169; 0.0059)	-0.0018 (-0.0117; 0.0082)
Early life exposure		
FVC (L)	-0.0059 (-0.0193; 0.0075)	-0.0016 (-0.0139; 0.0108)
FEV_1 (L)	-0.0047 (-0.0152; 0.0058)	-0.0013 (-0.0112; 0.0087)
$FEF_{25\%-75\%}$ (L/s)	-0.0048 (-0.0147; 0.0052)	-0.0018 (-0.0104; 0.0068)
Exposure trend over time		
FVC (L)	0.0015 (-0.0119; 0.0149)	0.0025 (-0.0021; 0.0071)

FEV_1 (L)	0.0008 (-0.0097; 0.0113)	0.0053 (-0.0047; 0.0153)
$FEF_{25\%-75\%}$ (L/s)	-0.0013 (-0.0113; 0.0086)	0.0039 (-0.0047; 0.0126)

FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

*adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation.

TABLE 6 - Associations (β, 95%CI) between the distance to the nearest green space (km) and lung function parameters at 10 years of age (Generation XXI, n=3278)

	[β (95%CI)]	
Distance to the nearest green space (km)	Crude model	Adjusted model*
Averaged exposure		
FVC (L)	-0.003 (-0.013; 0.006)	-0.006 (-0.015; 0.004)
FEV_1 (L)	-0.002 (-0.009; 0.006)	-0.004 (-0.012; 0.003)
$FEF_{25\%-75\%}$ (L/s)	0.004 (-0.003; 0.011)	-0.004 (-0.010; 0.003)
Early life exposure		
FVC (L)	-0.003 (-0.013; 0.007)	-0.005 (-0.014; 0.004)
FEV_1 (L)	-0.001 (-0.009; 0.006)	-0.004 (-0.011; 0.003)
$FEF_{25\%-75\%}$ (L/s)	0.005 (-0.003; 0.012)	-0.003 (-0.099; 0.003)
Exposure trend over time		
FVC (L)	-0.005 (-0.014; 0.005)	-0.004 (-0.013; 0.005)
FEV_1 (L)	-0.004 (-0.011; 0.004)	-0.003 (-0.010; 0.004)
$FEF_{25\%-75\%}$ (L/s)	-0.003 (-0.010; 0.005)	-0.002 (-0.008; 0.004)

FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

*adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation.

TABLE 7 - Associations (β, 95%CI) between the distance to the nearest blue space (km) and lung function parameters at 10 years of age (Generation XXI, n=3278)

	[β (95%CI)]	
Distance to the nearest blue spaces (km)	Crude model	Adjusted model*
Averaged exposure		
FVC (L)	-0.0028 (-0.0124; 0.0069)	0.0002 (-0.0088; 0.0091)
FEV_1 (L)	-0.0015 (-0.0091; 0.0061)	0.0004 (-0.0068; 0.0075)
$FEF_{25\%-75\%}$ (L/s)	0.0013 (-0.0059; 0.0085)	0.0004 (-0.0061; 0.0063)
Early life exposure		
FVC (L)	-0.0025 (-0.0121; 0.0072)	0.0007 (-0.0082; 0.0097)
FEV_1 (L)	-0.0012 (-0.0089; 0.0063)	0.0008 (-0.0064; 0.0080)
$FEF_{25\%-75\%}$ (L/s)	0.0016 (-0.0056; 0.0088)	0.0009 (-0.0054; 0.0071)
Exposure trend over time		
FVC (L)	-0.0030 (-0.0127; 0.0067)	-0.0033 (-0.0122; 0.0056)
FEV_1 (L)	-0.0022 (-0.0096; 0.0054)	-0.0025 (-0.096; 0.0046)
$FEF_{25\%-75\%}$ (L/s)	-0.0015 (-0.0087; 0.0058)	-0.0024 (-0.0086; 0.0038)

FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

*adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation.

TABLE 8 - Path coefficients estimated in a Structural Equation Model predicting the indirect effects of physical activity and outdoor levels of NO_2 on lung function at 10 years of age

	[β (95%CI)]	
NDVI within 100 m	**Indirect effect of physical activity**	**Indirect effect of outdoor levels of NO_2**
Averaged exposure		
FVC (L)	0.001 (-0.001; 0.001)	0.001 (-0.001; 0.001)
FEV_1 (L)	0.001 (-0.001; 0.001)	0.001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	0.001 (-0.001; 0.001)	0.001 (-0.001; 0.001)
Early life exposure		
FVC (L)	-0.001 (-0.005; 0.006)	0.02 (-0.05; 0.09)
FEV_1 (L)	-0.001 (-0.004; 0.005)	0.02 (-0.04; 0.07)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.003; 0.004)	0.02 (-0.03; 0.07)
Exposure trend over time		
FVC (L)	0.75 (-11.3; 12.8)	-34.6 (-146.5; 77.3)
FEV_1 (L)	0.60 (-9.05; 10.3)	-35.6 (-125.5; 54.3)
$FEF_{25\%-75\%}$ (L/s)	0.47 (-7.18; 8.12)	-42.7 (-121.2; 35.9)
Accessibility to green spaces within 400 m		
Averaged exposure		
FVC (L)	-0.0001 (-0.001; 0.001)	-0.0001 (-0.005; 0.004)
FEV_1 (L)	-0.0001 (-0.001; 0.0001)	-0.0001 (-0.004; 0.003)
$FEF_{25\%-75\%}$ (L/s)	-0.0001 (-0.001; 0.0001)	-0.001 (-0.004; 0.002)
Early life exposure		
FVC (L)	-0.0001 (-0.001; 0.001)	-0.0001 (-0.004; 0.003)
FEV_1 (L)	-0.0001 (-0.001; 0.0001)	-0.0001 (-0.003; 0.003)
$FEF_{25\%-75\%}$ (L/s)	-0.0001 (-0.001; 0.0001)	-0.001 (-0.003; 0.002)
Exposure trend over time		

FVC (L)	0.07 (-0.11; 0.25)	-0.11 (-0.54; 0.32)
FEV_1 (L)	-0.06 (-0.08; 0.20)	-0.10 (-0.45; 0.25)
$FEF_{25\%-75\%}$ (L/s)	0.05 (-0.07; 0.16)	-0.12 (-0.43; 0.19)
No. of green spaces within 400 m		
Averaged exposure		
FVC (L)	0.0001 (-0.001; 0.002)	0.0001 (-0.001; 0.001)
FEV_1 (L)	0.0001 (-0.001; 0.002)	0.0001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
Early life exposure		
FVC (L)	-0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
FEV_1 (L)	0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	-0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
Exposure trend over time		
FVC (L)	0.26 (-0.41; 0.93)	0.003 (-0.08; 0.09)
FEV_1 (L)	0.21 (-0.33; 0.74)	0.002 (-0.07; 0.07)
$FEF_{25\%-75\%}$ (L/s)	0.15 (-0.31; 0.62)	-0.005 (-0.08; 0.07)
Accessibility to green spaces within 800 m		
Averaged exposure		
FVC (L)	-0.0001 (-0.001; 0.001)	-0.002 (-0.006; 0.003)
FEV_1 (L)	-0.0001 (-0.001; 0.0001)	-0.001 (-0.005; 0.003)
$FEF_{25\%-75\%}$ (L/s)	-0.0001 (-0.001; 0.0001)	-0.002 (-0.005; 0.002)
Early life exposure		
FVC (L)	-0.0001 (-0.001; 0.001)	-0.001 (-0.006; 0.004)
FEV_1 (L)	-0.001 (-0.005; 0.003)	-0.0001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	-0.0001 (-0.001; 0.001)	-0.001 (-0.005; 0.002)
Exposure trend over time		
FVC (L)	0.09 (-0.08; 0.25)	-0.10 (-0.64; 0.43)
FEV_1 (L)	0.07 (-0.06; 0.20)	-0.09 (-0.52; 0.34)

$FEF_{25\%-75\%}$ (L/s)	0.06 (-0.05; 0.16)	-0.12 (-0.50; 0.26)
No. of green spaces within 800 m		
Averaged exposure		
FVC (L)	0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
FEV_1 (L)	0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
Early life exposure		
FVC (L)	-0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
FEV_1 (L)	-0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	-0.0001 (-0.001; 0.001)	-0.0001 (-0.001; 0.001)
Exposure trend over time		
FVC (L)	0.09 (-0.07; 0.25)	-0.01 (-0.07; 0.04)
FEV_1 (L)	0.07 (-0.05; 0.20)	-0.01 (-0.05; 0.03)
$FEF_{25\%-75\%}$ (L/s)	0.05 (-0.05; 0.16)	-0.01 (-0.05; 0.03)
Proximity to the nearest green space (km)		
Averaged exposure		
FVC (L)	-0.0001 (-0.004; 0.004)	0.03 (-0.03; 0.08)
FEV_1 (L)	-0.0001 (-0.003; 0.003)	0.02 (-0.02; 0.07)
$FEF_{25\%-75\%}$ (L/s)	-0.0001 (-0.003; 0.002)	0.02 (-0.01; 0.06)
Early life exposure		
FVC (L)	0.0001 (-0.004; 0.005)	0.02 (-0.03; 0.06)
FEV_1 (L)	0.0001 (-0.003; 0.004)	0.02 (-0.02; 0.05)
$FEF_{25\%-75\%}$ (L/s)	0.0001 (-0.002; 0.003)	0.02 (-0.02; 0.05)
Exposure trend over time		
FVC (L)	-0.55 (-1.62; 0.51)	1.41 (-3.88; 6.71)
FEV_1 (L)	-0.44 (-1.30; 0.41)	1.23 (-3.03; 5.49)
$FEF_{25\%-75\%}$ (L/s)	-0.35 (-1.05; 0.35)	1.50 (-2.22; 5.23)
Distance to blue spaces (km)		

Averaged exposure		
FVC (L)	0.0001 (-0.001; 0.001)	0.0001 (-0.001; 0.001)
FEV_1 (L)	0.0001 (-0.001; 0.001)	0.0001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	0.0001 (-0.001; 0.001)	0.0001 (-0.001; 0.001)
Early life exposure		
FVC (L)	0.0001 (-0.001; 0.001)	0.0001 (-0.001; 0.001)
FEV_1 (L)	0.0001 (-0.001; 0.001)	0.0001 (-0.001; 0.001)
$FEF_{25\%-75\%}$ (L/s)	0.0001 (-0.001; 0.001)	0.0001 (-0.001; 0.001)
Exposure trend over time		
FVC (L)	0.11 (-0.13; 0.34)	-0.39 (-1.59; 0.81)
FEV_1 (L)	0.09 (-0.10; 0.27)	-0.33 (-1.29; 0.63)
$FEF_{25\%-75\%}$ (L/s)	0.07 (-0.08; 0.22)	-0.39 (-1.23; 0.46)

NDVI: Normalized difference vegetation index; FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

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Supplementary material

Green and blue spaces and lung function in the Generation XXI cohort: a life course approach

Methods

Outdoor levels of NO_2

The methodology for creating the concentration maps of NO_2 follows the two-step methodology developed in Horálek J, et al. [1]: a linear regression model on the basis of European wide station measurement data, followed by kriging of the residuals produced from that regression model (residual kriging). Supplementary data for linear regression include, among others, traffic, land uses, road typologies, and population density. Separate map layers are created for the rural and the urban background areas on a grid at 10x10 km resolution. The rural background map layer is based on the rural background stations and the urban background map layer on the urban and the suburban background stations. Subsequently, the rural background map layer and the urban background map layer are merged into one combined final map using a weighting procedure based on the population density grid at 1x1 km resolution.

Figure S1 Participants evaluated in the Generation XXI cohort

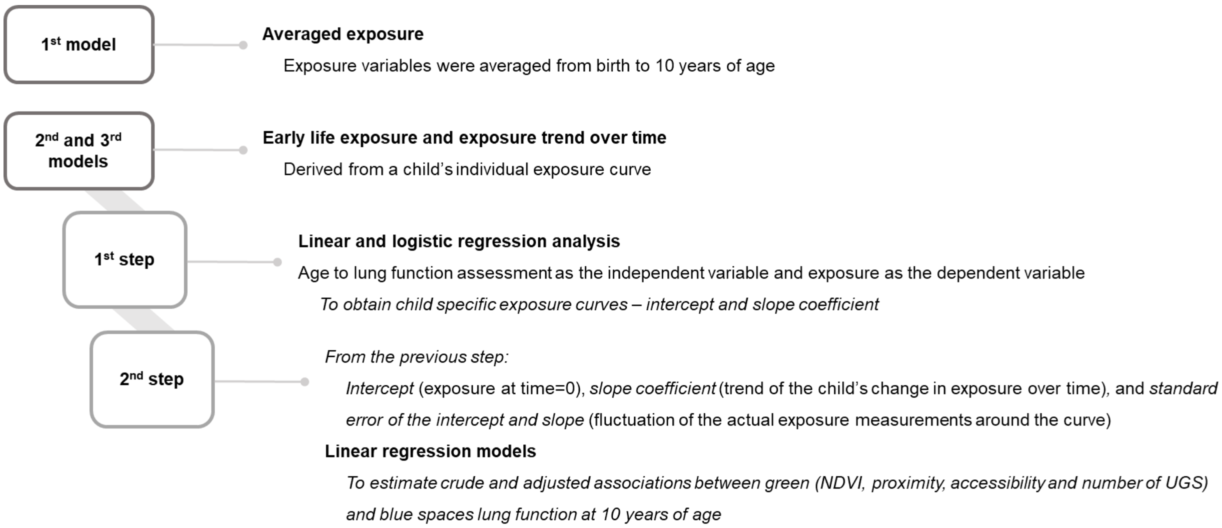

Figure S2 Schematic representation of the statistical analysis workflow

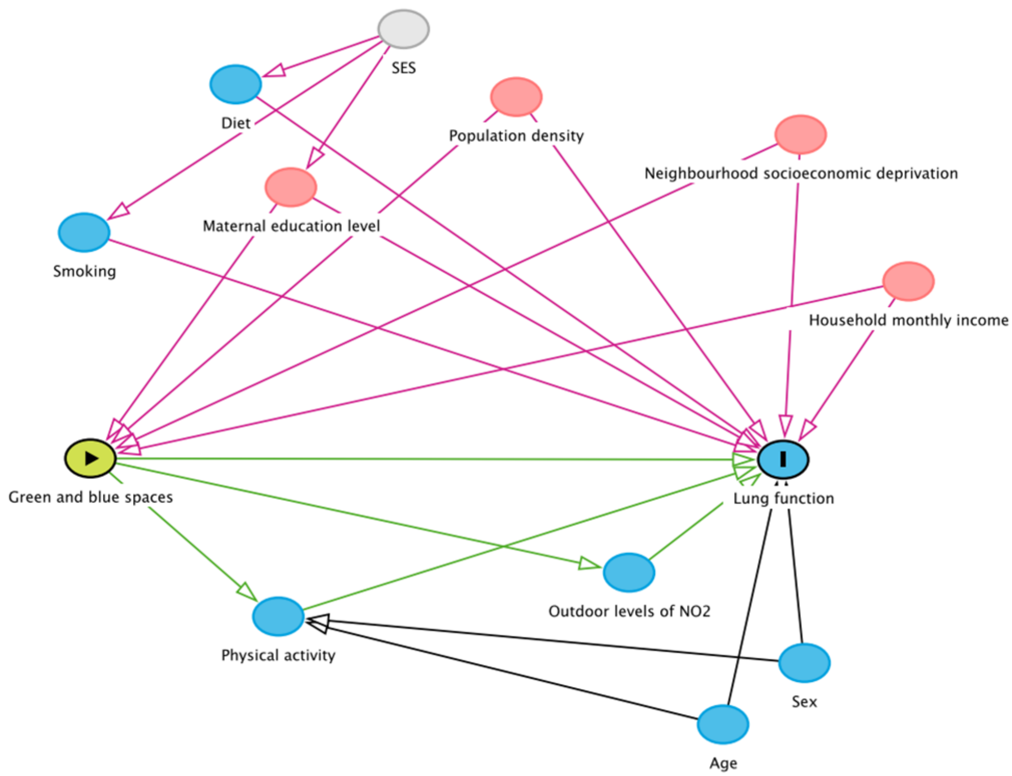

Figure S3 The direct acyclic graph (DAG) for the association between green and blue spaces and lung function

SES: socio-economic status; NO_2: nitrogen dioxide
green circle with play symbol: exposure; blue circle with an I: outcome; blue circle: ancestor of outcome; pink circle: ancestor of exposure and outcome; dark grey circle: other variable; light grey circle: latent variable; green line: causal path; red line: biasing path

TABLE S1 Associations (β, 95%CI) between NDVI within 250 and 500 m and lung function parameters at 10 years of age (Generation XXI, n=3278)

	[β (95%CI)]	
NDVI within 250 m	**Crude model**	**Adjusted model***
Averaged exposure		
FVC (L)	0.01 (-0.0002; 0.02)	0.008 (-0.006; 0.02)
FEV_1 (L)	0.002 (-0.005; 0.01)	-0.001 (-0.009; 0.007)
$FEF_{25\%-75\%}$ (L/s)	0.005 (-0.002; 0.01)	-0.0007 (-0.007; 0.006)
Early life exposure		
FVC (L)	0.02 (-0.0007; 0.03)	0.009 (-0.009; 0.03)
FEV_1 (L)	0.02 (0.004; 0.03)	0.01 (-0.004; 0.03)
$FEF_{25\%-75\%}$ (L/s)	0.03 (0.005; 0.05)	0.02 (-0.007; 0.04)
Trend over time		
FVC (L)	0.005 (-0.01; 0.02)	0.001 (-0.02; 0.02)
FEV_1 (L)	0.007 (-0.007; 0.02)	0.004 (-0.01; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.02 (-0.006; 0.04)	0.02 (-0.007; 0.04)
NDVI within 500 m		
Averaged exposure		
FVC (L)	0.009 (-0.003; 0.02)	0.004 (-0.01; 0.02)
FEV_1 (L)	0.01 (4.18e-6; 0.02)	0.004 (-0.008; 0.02)
$FEF_{25\%-75\%}$ (L/s)	0.01 (-0.004; 0.03)	0.003 (-0.02; 0.02)
Early life exposure		
FVC (L)	0.01 (-0.004; 0.03)	0.002 (-0.01; 0.02)
FEV_1 (L)	0.01 (0.0002; 0.02)	0.006 (-0.008; 0.02)
$FEF_{25\%-75\%}$ (L/s)	0.02 (-0.003; 0.04)	0.007 (-0.02; 0.03)
Trend over time		
FVC (L)	0.004 (-0.01; 0.02)	0.002 (-0.01; 0.02)

FEV_1 (L)	0.005 (-0.008; 0.02)	0.004 (-0.009; 0.02)
$FEF_{25\%-75\%}$ (L/s)	0.009 (-0.01; 0.03)	0.008 (-0.01; 0.03)

NDVI: Normalized difference vegetation index; FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC;

*adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation

TABLE S2 Associations (β, 95%CI) between the NDVI, proximity, accessibility, and number of urban green spaces and proximity to blue spaces and lung function parameters at 10 years of age adjusted for residential mobility (Generation XXI, n=3278)

	[β (95%CI)]		
NDVI within 100 m	Crude model	Adjusted model (1)*	Adjusted model (2)*
Averaged exposure			
FVC (L)	0.01 (-0.002; 0.02)	0.003 (-0.01; 0.02)	0.003 (-0.01; 0.02)
FEV_1 (L)	0.003 (-0.005; 0.01)	-0.002 (-0.01; 0.006)	-0.002 (-0.01; 0.006)
$FEF_{25\%-75\%}$ (L/s)	0.005 (-0.002; 0.01)	-0.002 (-0.008; 0.005)	-0.002 (-0.009; 0.005)
Early life exposure			
FVC (L)	**0.02 (0.003; 0.03)**	0.01 (-0.006; 0.03)	0.01 (-0.005; 0.02)
FEV_1 (L)	**0.02 (0.007; 0.03)**	0.01 (-0.002; 0.003)	0.02 (-0.002; 0.003)
$FEF_{25\%-75\%}$ (L/s)	**0.02 (0.004; 0.05)**	0.02 (-0.009; 0.04)	0.02 (-0.009; 0.03)
Exposure trend over time			
FVC (L)	**0.02 (0.002; 0.03)**	0.01 (-0.003; 0.03)	0.02 (-0.003; 0.03)
FEV_1 (L)	**0.02 (0.004; 0.03)**	**0.01 (0.0002; 0.03)**	**0.02 (0.0003; 0.03)**
$FEF_{25\%-75\%}$ (L/s)	**0.03 (0.004; 0.05)**	**0.02 (0.001; 0.05)**	**0.02 (0.002; 0.05)**
Accessibility to green spaces within 400 m			
Averaged exposure			
FVC (L)	-0.002 (-0.03; 0.02)	-0.006 (-0.03; 0.02)	-0.006 (-0.03; 0.02)
FEV_1 (L)	-0.004 (-0.02; 0.02)	-0.005 (-0.02; 0.01)	-0.005 (-0.03; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.02 (-0.04; 0.0004)	-0.004 (-0.02; 0.01)	-0.005 (-0.02; 0.01)
Early life exposure			
FVC (L)	-0.004 (-0.01; 0.006)	-0.007 (-0.02; 0.002)	-0.00004 (-0.00009; 0.00001)
FEV_1 (L)	-0.005 (-0.01; 0.003)	-0.005 (-0.01; 0.002)	-0.00003 (-0.00007; 0.00001)
$FEF_{25\%-75\%}$ (L/s)	**-0.01 (-0.02; -0.003)**	-0.005 (-0.01; 0.002)	-0.00003 (-0.00006; 0.00001)
Exposure trend over time			
FVC (L)	0.003 (-0.007; 0.01)	0.004 (-0.005; 0.01)	0.004 (-0.005; 0.01)
FEV_1 (L)	0.002 (-0.006; 0.009)	0.003 (-0.004; 0.01)	0.003 (-0.004; 0.01)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.009; 0.006)	0.002 (-0.004; 0.009)	0.002 (-0.004; 0.009)
No. of green spaces within 400 m			
Averaged exposure			
FVC (L)	-0.002 (-0.02; 0.02)	-0.0009 (-0.02; 0.02)	-0.001 (-0.02; 0.02)
FEV_1 (L)	-0.002 (-0.02; 0.01)	-0.0006 (-0.01; 0.01)	-0.0007 (-0.01; 0.01)
$FEF_{25\%-75\%}$ (L/s)	0.002 (-0.01; 0.02)	-0.0001 (-0.01; 0.01)	-0.0002 (-0.01; 0.01)
Early life exposure			
FVC (L)	-0.004 (-0.02; 0.02)	-0.002 (-0.02; 0.01)	-0.002 (-0.02; 0.01)
FEV_1 (L)	-0.002 (-0.02; 0.01)	-0.002 (-0.02; 0.01)	-0.002 (-0.02; 0.01)
$FEF_{25\%-75\%}$ (L/s)	0.002 (-0.01; 0.02)	-0.001 (-0.01; 0.01)	-0.001 (-0.01; 0.01)
Exposure trend over time			
FVC (L)	-0.004 (-0.02; 0.01)	-0.005 (-0.02; 0.01)	-0.004 (-0.02; 0.01)
FEV_1 (L)	-0.003 (-0.02; 0.01)	-0.004 (-0.02; 0.02)	-0.004 (-0.02; 0.01)

$FEF_{25\%-75\%}$ (L/s)	-0.003 (-0.02; 0.01)	-0.005 (-0.02; 0.007)	-0.005 (-0.02; 0.007)
Accessibility to green spaces within 800 m			
Averaged exposure			
FVC (L)	0.007 (-0.01; 0.03)	0.008 (-0.01; 0.03)	0.007 (-0.01; 0.03)
FEV_1 (L)	0.004 (-0.01; 0.02)	0.006 (-0.009; 0.02)	0.005 (-0.009; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.003 (-0.02; 0.01)	0.005 (-0.007; 0.02)	0.005 (-0.008; 0.02)
Early life exposure			
FVC (L)	-0.0004 (-0.01; 0.01)	0.0005 (-0.009; 0.01)	0.000004 (-0.00003; 0.00004)
FEV_1 (L)	-0.002 (-0.02; 0.01)	0.0003 (-0.007; 0.008)	0.0006 (-0.007; 0.008)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.01; 0.002)	0.0005 (-0.006; 0.007)	0.000003 (-0.00002; 0.00003)
Exposure trend over time			
FVC (L)	-0.004 (-0.01; 0.004)	-0.0003 (-0.008; 0.007)	-0.0005 (-0.008; 0.007)
FEV_1 (L)	-0.003 (-0.01; 0.03)	-0.0003 (-0.006; 0.006)	-0.0006 (-0.008; 0.007)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.008; 0.004)	-0.007 (-0.006; 0.005)	-0.0008 (-0.006; 0.004)
No. of green spaces within 800 m			
Averaged exposure			
FVC (L)	-0.007 (-0.02; 0.009)	-0.001 (-0.02; 0.01)	-0.001 (-0.02; 0.01)
FEV_1 (L)	-0.005 (-0.02; 0.007)	-0.001 (-0.01; 0.01)	-0.0009 (-0.01; 0.01)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.02; 0.006)	-0.002 (-0.01; 0.008)	-0.002 (-0.01; 0.008)
Early life exposure			
FVC (L)	-0.006 (-0.02; 0.008)	-0.002 (-0.01; 0.01)	-0.001 (-0.01; 0.01)
FEV_1 (L)	-0.005 (-0.02; 0.006)	-0.001 (-0.01; 0.009)	-0.001 (-0.01; 0.009)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.01; 0.005)	-0.002 (-0.01; 0.007)	-0.002 (-0.01; 0.007)
Exposure trend over time			
FVC (L)	0.002 (-0.01; 0.01)	0.007 (-0.006; 0.02)	0.007 (-0.006; 0.02)
FEV_1 (L)	0.0008 (-0.01; 0.01)	0.005 (-0.005; 0.02)	0.005 (-0.005; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.01; 0.009)	0.004 (-0.005; 0.01)	0.004 (-0.005; 0.01)
Proximity to the nearest green space (km)			
Averaged exposure			
FVC (L)	-0.003 (-0.01; 0.006)	-0.006 (-0.01; 0.004)	-0.006 (-0.02; 0.003)
FEV_1 (L)	-0.002 (-0.009; 0.006)	-0.004 (-0.01; 0.003)	-0.005 (-0.01; 0.003)
$FEF_{25\%-75\%}$ (L/s)	0.004 (-0.003; 0.01)	-0.004 (-0.01; 0.003)	-0.004 (-0.01; 0.002)
Early life exposure			
FVC (L)	-0.003 (-0.01; 0.007)	-0.005 (-0.01; 0.004)	-0.006 (-0.01;0.004)
FEV_1 (L)	-0.001 (-0.009; 0.006)	-0.004 (-0.01; 0.003)	-0.004 (-0.01; 0.003)
$FEF_{25\%-75\%}$ (L/s)	0.005 (-0.003; 0.01)	-0.003 (-0.01; 0.003)	-0.004 (-0.01; 0.003)
Exposure trend over time			
FVC (L)	-0.005 (-0.01; 0.005)	-0.004 (-0.01; 0.005)	-0.003 (-0.01; 0.006)
FEV_1 (L)	-0.004 (-0.01; 0.004)	-0.003 (-0.01; 0.004)	-0.002 (-0.01; 0.005)
$FEF_{25\%-75\%}$ (L/s)	-0.003 (-0.01; 0.005)	-0.002 (-0.008; 0.004)	-0.002 (-0.008; 0.004)
Proximity to the nearest blue spaces (km)			
Averaged exposure			
FVC (L)	-0.003 (-0.01; 0.007)	0.0002 (-0.009; 0.009)	-0.0002 (-0.009; 0.009)
FEV_1 (L)	-0.002 (-0.009; 0.006)	0.0004 (-0.007; 0.008)	-0.00007 (-0.007; 0.007)

$FEF_{25\%-75\%}$ (L/s)	0.001 (-0.006; 0.009)	0.0004 (-0.006; 0.007)	0.0002 (-0.006; 0.006)
Early life exposure			
FVC (L)	-0.002 (-0.01; 0.007)	0.0007 (-0.008; 0.01)	0.0003 (-0.009; 0.009)
FEV_1 (L)	-0.001 (-0.009; 0.006)	0.0008 (-0.006; 0.008)	0.0004 (-0.007; 0.008)
$FEF_{25\%-75\%}$ (L/s)	0.002 (-0.006; 0.009)	0.0009 (-0.005; 0.007)	0.0006 (-0.006; 0.007)
Exposure trend over time			
FVC (L)	-0.003 (-0.01; 0.007)	-0.003 (-0.01; 0.006)	-0.003 (-0.01; 0.006)
FEV_1 (L)	-0.002 (-0.01; 0.005)	-0.003 (-0.01; 0.005)	-0.002 (-0.01; 0.005)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.009; 0.006)	-0.002 (-0.009; 0.004)	-0.002 (-0.008; 0.004)

NDVI: Normalized difference vegetation index; FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

*model 1: adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation; model 2: adjusted for sex, age in months, change of residence's address, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation; bold denotes statistically significant associations (p <0.05).

TABLE S3 Associations (β, 95%CI) between the NDVI, proximity, accessibility, and number of urban green spaces and proximity to blue spaces and lung function parameters at 10 years of age adjusted for birthweight (Generation XXI, n=3278)

	[β (95%CI)]		
NDVI within 100 m	Crude model	Adjusted model (1)*	Adjusted model (2)*
Averaged exposure			
FVC (L)	0.01 (-0.002; 0.02)	0.003 (-0.01; 0.02)	0.003 (-0.01; 0.02)
FEV_1 (L)	0.003 (-0.005; 0.01)	-0.002 (-0.01; 0.006)	-0.002 (-0.01; 0.006)
$FEF_{25\%-75\%}$ (L/s)	0.005 (-0.002; 0.01)	-0.002 (-0.008; 0.005)	-0.002 (-0.009; 0.005)
Early life exposure			
FVC (L)	**0.02 (0.003; 0.03)**	0.01 (-0.006; 0.03)	0.01 (-0.006; 0.03)
FEV_1 (L)	**0.02 (0.007; 0.03)**	0.01 (-0.002; 0.003)	0.01 (-0.002; 0.002)
$FEF_{25\%-75\%}$ (L/s)	**0.02 (0.004; 0.05)**	0.02 (-0.009; 0.04)	0.02 (-0.009; 0.04)
Exposure trend over time			
FVC (L)	**0.02 (0.002; 0.03)**	0.01 (-0.003; 0.03)	0.01 (-0.002; 0.03)
FEV_1 (L)	**0.02 (0.004; 0.03)**	**0.01 (0.0002; 0.03)**	**0.01 (0.0003; 0.03)**
$FEF_{25\%-75\%}$ (L/s)	**0.03 (0.004; 0.05)**	**0.02 (0.001; 0.05)**	**0.02 (0.001; 0.05)**
Accessibility to green spaces within 400 m			
Averaged exposure			
FVC (L)	-0.002 (-0.03; 0.02)	-0.006 (-0.03; 0.02)	-0.006 (-0.03; 0.02)
FEV_1 (L)	-0.004 (-0.02; 0.02)	-0.005 (-0.02; 0.01)	-0.005 (-0.02; 0.01)
$FEF_{25\%-75\%}$ (L/s)	-0.02 (-0.04; 0.0004)	-0.004 (-0.02; 0.01)	-0.004 (-0.02; 0.01)
Early life exposure			
FVC (L)	-0.004 (-0.01; 0.006)	-0.007 (-0.02; 0.002)	-0.007 (-0.02; 0.002)
FEV_1 (L)	-0.005 (-0.01; 0.003)	-0.005 (-0.01; 0.002)	-0.005 (-0.01; 0.002)
$FEF_{25\%-75\%}$ (L/s)	**-0.01 (-0.02; -0.003)**	-0.005 (-0.01; 0.002)	-0.005 (-0.01; 0.002)

Exposure trend over time			
FVC (L)	0.003 (-0.007; 0.01)	0.004 (-0.005; 0.01)	0.003 (-0.006; 0.01)
FEV_1 (L)	0.002 (-0.006; 0.009)	0.003 (-0.004; 0.01)	0.003 (-0.005; 0.01)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.009; 0.006)	0.002 (-0.004; 0.009)	0.002 (-0.004; 0.008)
No. of green spaces within 400 m			
Averaged exposure			
FVC (L)	-0.002 (-0.02; 0.02)	-0.0009 (-0.02; 0.02)	-0.002 (-0.02; 0.02)
FEV_1 (L)	-0.002 (-0.02; 0.01)	-0.0006 (-0.01; 0.01)	-0.001 (-0.01; 0.01)
$FEF_{25\%-75\%}$ (L/s)	0.002 (-0.01; 0.02)	-0.0001 (-0.01; 0.01)	-0.0006 (-0.01; 0.01)
Early life exposure			
FVC (L)	-0.004 (-0.02; 0.02)	-0.002 (-0.02; 0.01)	-0.003 (-0.02; 0.01)
FEV_1 (L)	-0.002 (-0.02; 0.01)	-0.002 (-0.02; 0.01)	-0.002 (-0.02; 0.01)
$FEF_{25\%-75\%}$ (L/s)	0.002 (-0.01; 0.02)	-0.001 (-0.01; 0.01)	-0.001 (-0.01; 0.01)
Exposure trend over time			
FVC (L)	-0.004 (-0.02; 0.01)	-0.005 (-0.02; 0.01)	-0.004 (-0.02; 0.01)
FEV_1 (L)	-0.003 (-0.02; 0.01)	-0.004 (-0.02; 0.02)	-0.003 (-0.02; 0.01)
$FEF_{25\%-75\%}$ (L/s)	-0.003 (-0.02; 0.01)	-0.005 (-0.02; 0.007)	-0.004 (-0.02; 0.008)
Accessibility to green spaces within 800 m			
Averaged exposure			
FVC (L)	0.007 (-0.01; 0.03)	0.008 (-0.01; 0.03)	0.007 (-0.01; 0.03)
FEV_1 (L)	0.004 (-0.01; 0.02)	0.006 (-0.009; 0.02)	0.006 (-0.009; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.003 (-0.02; 0.01)	0.005 (-0.007; 0.02)	0.005 (-0.007; 0.02)
Early life exposure			
FVC (L)	-0.0004 (-0.01; 0.01)	0.0005 (-0.009; 0.01)	0.0003 (-0.009; 0.009)

FEV_1 (L)	-0.002 (-0.02; 0.01)	0.0003 (-0.007; 0.008)	0.0002 (-0.007; 0.007)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.01; 0.002)	0.0005 (-0.006; 0.007)	0.0003 (-0.006; 0.007)
Exposure trend over time			
FVC (L)	-0.004 (-0.01; 0.004)	-0.0003 (-0.008; 0.007)	-0.0005 (-0.009; 0.008)
FEV_1 (L)	-0.003 (-0.01; 0.03)	-0.0003 (-0.006; 0.006)	-0.0005 (-0.008; 0.007)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.008; 0.004)	-0.007 (-0.006; 0.005)	-0.0009 (-0.007; 0.005)
No. of green spaces within 800 m			
Averaged exposure			
FVC (L)	-0.007 (-0.02; 0.009)	-0.001 (-0.02; 0.01)	-0.002 (-0.02; 0.01)
FEV_1 (L)	-0.005 (-0.02; 0.007)	-0.001 (-0.01; 0.01)	-0.002 (-0.01; 0.01)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.02; 0.006)	-0.002 (-0.01; 0.008)	-0.002 (-0.01; 0.008)
Early life exposure			
FVC (L)	-0.006 (-0.02; 0.008)	-0.002 (-0.01; 0.01)	-0.002 (-0.01; 0.01)
FEV_1 (L)	-0.005 (-0.02; 0.006)	-0.001 (-0.01; 0.009)	-0.002 (-0.01; 0.008)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.01; 0.005)	-0.002 (-0.01; 0.007)	-0.002 (-0.01; 0.006)
Exposure trend over time			
FVC (L)	0.002 (-0.01; 0.01)	0.007 (-0.006; 0.02)	0.007 (-0.006; 0.02)
FEV_1 (L)	0.0008 (-0.01; 0.01)	0.005 (-0.005; 0.02)	0.005 (-0.004; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.01; 0.009)	0.004 (-0.005; 0.01)	0.004 (-0.005; 0.01)
Distance to the nearest green space (km)			
Averaged exposure			
FVC (L)	-0.003 (-0.01; 0.006)	-0.006 (-0.01; 0.004)	-0.005 (-0.01; 0.004)
FEV_1 (L)	-0.002 (-0.009; 0.006)	-0.004 (-0.01; 0.003)	-0.004 (-0.01; 0.003)
$FEF_{25\%-75\%}$ (L/s)	0.004 (-0.003; 0.01)	-0.004 (-0.01; 0.003)	-0.003 (-0.01; 0.003)

Early life exposure			
FVC (L)	-0.003 (-0.01; 0.007)	-0.005 (-0.01; 0.004)	-0.005 (-0.01;0.004)
FEV_1 (L)	-0.001 (-0.009; 0.006)	-0.004 (-0.01; 0.003)	-0.004 (-0.01; 0.004)
$FEF_{25\%-75\%}$ (L/s)	0.005 (-0.003; 0.01)	-0.003 (-0.01; 0.003)	-0.003 (-0.01; 0.003)
Exposure trend over time			
FVC (L)	-0.005 (-0.01; 0.005)	-0.004 (-0.01; 0.005)	-0.003 (-0.01; 0.006)
FEV_1 (L)	-0.004 (-0.01; 0.004)	-0.003 (-0.01; 0.004)	-0.003 (-0.01; 0.005)
$FEF_{25\%-75\%}$ (L/s)	-0.003 (-0.01; 0.005)	-0.002 (-0.008; 0.004)	-0.002 (-0.008; 0.004)
Distance to the nearest blue spaces (km)			
Averaged exposure			
FVC (L)	-0.003 (-0.01; 0.007)	0.0002 (-0.009; 0.009)	-0.0003 (-0.009; 0.009)
FEV_1 (L)	-0.002 (-0.009; 0.006)	0.0004 (-0.007; 0.008)	-0.00004 (-0.007; 0.007)
$FEF_{25\%-75\%}$ (L/s)	0.001 (-0.006; 0.009)	0.0004 (-0.006; 0.007)	0.00008 (-0.006; 0.006)
Early life exposure			
FVC (L)	-0.002 (-0.01; 0.007)	0.0007 (-0.008; 0.01)	0.0002 (-0.009; 0.01)
FEV_1 (L)	-0.001 (-0.009; 0.006)	0.0008 (-0.006; 0.008)	0.0004 (-0.007; 0.008)
$FEF_{25\%-75\%}$ (L/s)	0.002 (-0.006; 0.009)	0.0009 (-0.005; 0.007)	0.0005 (-0.006; 0.007)
Exposure trend over time			
FVC (L)	-0.003 (-0.01; 0.007)	-0.003 (-0.01; 0.006)	-0.003 (-0.01; 0.006)
FEV_1 (L)	-0.002 (-0.01; 0.005)	-0.003 (-0.01; 0.005)	-0.002 (-0.01; 0.005)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.009; 0.006)	-0.002 (-0.009; 0.004)	-0.002 (-0.009; 0.004)

NDVI: Normalized difference vegetation index; FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

*model 1: adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation; model 2: adjusted for sex, age in months, low birth weight, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation; bold denotes statistically significant associations (p <0.05).

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	[β (95%CI)]	
	Crude model	Adjusted model*
Green spaces within 400 m		
Averaged exposure		
FVC (L)	-0.008 (-0.04; 0.02)	-0.009 (-0.04; 0.02)
FEV_1 (L)	-0.01 (-0.03; 0.01)	-0.007 (-0.03; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.03 (-0.05; -0.008)	-0.007 (-0.03; 0.01)
Early life exposure		
FVC (L)	-0.004 (-0.01; 0.006)	-0.007 (-0.02; 0.002)
FEV_1 (L)	-0.005 (-0.01; 0.003)	-0.005 (-0.01; 0.002)
$FEF_{25\%-75\%}$ (L/s)	**-0.01 (-0.02; -0.003)**	-0.005 (-0.01; 0.002)
Exposure trend over time		
FVC (L)	0.003 (-0.007; 0.01)	0.004 (-0.005; 0.01)
FEV_1 (L)	0.002 (-0.006; 0.009)	0.003 (-0.004; 0.01)
$FEF_{25\%-75\%}$ (L/s)	-0.001 (-0.009; 0.006)	0.002 (-0.004; 0.009)
Green spaces within 800 m		
Averaged exposure		
FVC (L)	-0.002 (-0.02; 0.02)	0.002 (-0.02; 0.02)
FEV_1 (L)	-0.003 (-0.02; 0.01)	0.002 (-0.01; 0.02)
$FEF_{25\%-75\%}$ (L/s)	-0.01 (-0.03; 0.002)	0.002 (-0.01; 0.02)
Early life exposure		
FVC (L)	-0.0004 (-0.01; 0.01)	0.0005 (-0.009; 0.01)
FEV_1 (L)	-0.002 (-0.02; 0.01)	0.0003 (-0.007; 0.008)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.01; 0.002)	0.0005 (-0.006; 0.007)
Exposure trend over time		

FVC (L)	-0.004 (-0.01; 0.004)	-0.0003 (-0.008; 0.007)
FEV_1 (L)	-0.003 (-0.01; 0.03)	-0.0003 (-0.006; 0.006)
$FEF_{25\%-75\%}$ (L/s)	-0.005 (-0.008; 0.004)	-0.007 (-0.006; 0.005)

NDVI: Normalized difference vegetation index; FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC.

$^{\perp}$children who had access to UGS in all the cohort evaluations (4 times from birth to 10 years of age) from those who had access to one of the cohort evaluations (1 time).

*adjusted for sex, age in months, maternal education, household monthly income, population density, and neighbourhood socioeconomic deprivation.

TABLE S5 Characteristics of participants included and excluded (Generation XXI, n=3278)

Characteristics	**Participants included** **n (%)**	**Participants excluded** **n (%)**	**p value**
At birth			
Sex [female, n (%)]	1654 (50.5)	2756 (51.3)	0.312
Maternal education			<0.05
Primary (≤9 years)	1372 (41.9)	2877 (53.7)	
Secondary (10–12 years)	962 (29.3)	1352 (25.2)	
Tertiary (>12 years)	944 (28.8)	1129 (21.1)	
Household monthly income (€)			<0.05
≤ 1000	1060 (34.7)	2080 (44.4)	
1001-1500	895 (29.3)	1275 (27.2)	
> 1500	1101 (36.0)	1327 (28.3)	
Neighbourhood socioeconomic deprivation			<0.05
Q1 (least deprived)	460 (14.0)	645 (12.1)	
Q2	712 (21.7)	969 (18.2)	
Q3	809 (24.7)	1329 (24.9)	
Q4	744 (22.7)	1180 (22.1)	
Q5 (most deprived)	553 (16.9)	1213 (22.7)	
At 10 years			
Physically active [yes]	2079 (63.5)	1839 (59.0)	0.019

TABLE S6 Missing data (Generation XXI, n=3278)

Characteristic	**n (%)**
At birth	
NDVI	0 (0)
Accessibility to green spaces within 400 m (yes)	0 (0)
No. of green spaces within 400 m*	0 (0)
Accessibility to green spaces within 800 m (yes)	0 (0)
No. of green spaces within 800 m*	0 (0)
Distance to the nearest green space (km)	0 (0)
Distance to the nearest blue spaces (km)	0 (0)
Sex [female, n (%)]	0 (0)
Maternal education	0 (0)
Household monthly income (€)	222 (6.8)
Neighbourhood socioeconomic deprivation**	0 (0)
At 4 years	
NDVI	
100 m	27 (0.8)
250 m	3 (0.1)
500 m	0 (0)
Accessibility to green spaces within 400 m (yes)	0 (0)
No. of green spaces within 400 m*	0 (0)
Accessibility to green spaces within 800 m (yes)	0 (0)
No. of green spaces within 800 m*	0 (0)
Distance to the nearest green space (km)	0 (0)
Distance to the nearest blue spaces (km)	0 (0)
At 7 years	
NDVI	0 (0)
Accessibility to green spaces within 400 m (yes)	0 (0)

No. of green spaces within 400 m*	0 (0)
Accessibility to green spaces within 800 m (yes)	0 (0)
No. of green spaces within 800 m*	0 (0)
Distance to the nearest green space (km)	0 (0)
Distance to the nearest blue spaces (km)	0 (0)
At 10 years	
BMI (kg/m^2)*	4 (0.1)
Physically active [yes]	5 (0.2)
FVC before bronchodilation (L)**	0 (0)
FEV_1 before bronchodilation (L)**	0 (0)
$FEF_{25\%-75\%}$ before bronchodilation (L/s)**	0 (0)
Outdoor levels of NO_2 ($\mu g/m^3$)*	0 (0)
NDVI	0 (0)
Accessibility to green spaces within 400 m (yes)	0 (0)
No. of green spaces within 400 m*	0 (0)
Accessibility to green spaces within 800 m (yes)	0 (0)
No. of green spaces within 800 m*	0 (0)
Distance to the nearest green space (km)	0 (0)
Distance to the nearest blue spaces (km)	0 (0)

NDVI: Normalized difference vegetation index; FVC: forced vital capacity; FEV_1: forced expiratory volume at the first second; $FEF_{25\%-75\%}$: forced expiratory flow between 25% and 75% of the FVC; NO_2: nitrogen dioxide

References

1. Horálek J, de Smet P, Schneider P, Kurfürst P, F L. Inclusion of land cover and traffic data in NO2 mapping methodology ETC/ACM Technical Paper 2016/12. European Environment Agency;2017.