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Residential greenspace and lung function up to 24 years of age: The ALSPAC birth cohort

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ABSTRACT

Background: Residing in greener areas is increasingly linked to beneficial health outcomes, but little is known about its effect on respiratory health.

Objective: We examined associations between residential greenness and nearby green spaces with lung function up to 24 years in the UK Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort.

Methods: Lung function was measured by spirometry at eight, 15 and 24 years of age. Greenness levels within circular buffers (100–1000 m) around the birth, eight-, 15- and 24-year home addresses were calculated using the satellite-derived Normalized Difference Vegetation Index and averaged (lifetime greenness). The presence and proportion of green spaces (urban green spaces, forests and agricultural land) within a 300 m buffer was determined. First, associations between repeated greenness and green space variables and repeated lung function parameters were assessed using generalized estimation equations (N = 7094, 47.9% male). Second, associations between lifetime average greenness and lifetime average proportion of green spaces with lung function at 24-years were assessed using linear regression models (N = 1763, 39.6% male). All models were adjusted for individual and environmental covariates.

Results: Using repeated greenspace and lung function data at eight, 15 and 24 years, greenness in a 100 m buffer was associated with higher FEV$_1$ and FVC (11.4 ml [2.6, 20.3] and 12.2 ml [1.8, 22.7], respectively, per interquartile range increase), as was the presence of urban green spaces in a 300 m buffer (20.3 ml [−0.1, 40.7] and 23.1 ml [-0.3, 46.5] for FEV$_1$ and FVC, respectively). These associations were independent of air pollution, urbanicity and socio-economic status. Lifetime average greenness within a 100 m buffer and proportion of agricultural land within a 300 m buffer were associated with better lung function at 24 years but adjusting for asthma attenuated these associations.

Discussion: This study provides suggestive evidence that children whose homes are in more vegetated places or are in close proximity of green spaces have better lung function up to 24 years of age.

Abbreviations: ALSPAC, Avon Longitudinal Study of Parents and Children; FVC, forced vital capacity; FEV$_1$, forced expiratory volume in one second; FEF$_{25}$, forced expiratory flow at 25% of forced vital capacity; FEF$_{25\text{-}75}$, forced expiratory flow between 25% and 75% of forced vital capacity; FEF$_{50}$, forced expiratory flow at 50% of forced vital capacity; FEF$_{75}$, forced expiratory flow at 75% of forced vital capacity; NDVI, Normalized Difference Vegetation index; PM$_{10}$, particulate matter with diameters less than 10 µm

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1. Introduction

Studies are increasingly demonstrating that the presence and amount of vegetation around one's home is likely to have beneficial effects on physical and mental health and well-being (Twohig-Bennett and Jones, 2018). Potential mechanisms include reducing harm (e.g. reducing exposure to adverse environmental exposures such as air pollution), restoring capacities (e.g. attention restoration and physiological stress recovery) and building capacities (e.g. increasing physical activity and facilitating social cohesion; (Markevych et al., 2017)). In contrast, the evidence supporting a role for vegetation on respiratory health is substantially weaker and heterogeneous.

To date, four studies have examined whether spatial variation in vegetation metrics may be associated with lung function development. A cross-sectional study of 360 school children (aged 5–12 years) living on the outskirts of an industrial area in Western Australia found no associations between greenness levels in buffers 100–500 m around the home and respiratory health measures derived using the forced oscillation technique, although mean greenness levels were rather low and the range in greenness values was limited (Boeyen et al., 2017). A null finding was also reported for percent predicted forced expiratory volume in one second (FEV_1) in an analysis on 1033 children aged 6–12 years from six European cohorts in which prenatal (during pregnancy) and postnatal (birth to five years) residential greenspace (defined as mean greenness in 100 m buffers as well as the presence of major green or blue spaces within 300 m) exposures were examined (Agier et al. 2019). Only one analysis has so far shown beneficial associations for greenspaces around the home address; increasing mean greenness and urban tree canopy coverage near the home at six months and seven years were associated with improved forced vital capacity (FVC), FEV_1 and forced expiratory flow between 25% and 75% of forced vital capacity ($FEF_{25\text{-}75}$) at seven years in 378 participants of the Cincinnati Childhood Allergy and Air Pollution Study (published in abstract form only; (Wright et al., 2018)). A further study on 701 children from 20 primary schools in Porto, Portugal, also demonstrated that children attending schools with greener areas had (non-significantly) higher values of FVC, FEV_1 and $FEF_{25\text{-}75}$ (Paciência et al., 2019). Given the increasing evidence that lung function in childhood is a good predictor of lung function in adulthood (Bui et al., 2018), and that low lung function in early adulthood appears to occur in conjunction with higher risks of disease in later life (Agusti and Faner, 2019), the identification of factors capable of affecting how lungs develop is critical.

It is currently difficult to draw conclusions regarding the role of vegetation on lung function development given the few existing studies, relatively small sample sizes used and the reliance on a single measure of lung function taken during childhood (a period of lung growth), which is before maximal lung function has been reached (occurs around 20–25 years; (Agusti and Faner, 2019)). The aim of this analysis was to examine whether the level of greenness and presence of green spaces (collectively hereon referred to as "greenspace") around the home are associated with lung function parameters repeatedly measured at eight, 15 and 24 years of age (hence capturing the maximal lung function peak) in a large population-based sample of participants in the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort of children born in 1991–92 in/around Bristol, United Kingdom.

2. Materials and methods

2.1. Study population

The analysis was conducted on data collected as part of the large, UK population-based ALSPAC birth cohort. Initial recruitment of pregnant women took place in 1990–1992 and the health and development of the index children from these pregnancies and their family members have been followed ever since. The study now comprises of three generations: the original parents/carers (Generation 0, G0); the index children (Generation 1, G1); and the index children's offspring (Generation 2, G2).

ALSPAC recruited 14,541 pregnant women (G0) who were resident in and around the City of Bristol (South West UK) with expected dates of delivery 1st April 1991 to 31st December 1992. Of these initial pregnancies, there were a total of 14,676 foetuses, resulting in 14,062 live births and 13,988 children who were alive at one year of age. The eligible sampling frame was constructed retrospectively using linked recruitment and health service records. Additional offspring that were eligible to enrol in the study have been welcomed through major recruitment drives at the ages of seven and 18 years; and through opportunistic contacts since the age of seven. A total of 913 additional G1 participants have been enrolled in the study since the age of seven years with 195 of these joining since the age of 18 (Northstone et al. 2019). This additional enrolment provides a baseline sample of 14,901 G1 participants who were alive at one year of age, of which 14,471 were singletons. Study data (from later clinics) are collected and managed using REDCap electronic data capture tools (Harris et al. 2009, 2019), hosted at the University of Bristol.

The ALSPAC catchment area was centered around the city of Bristol and includes the neighboring counties of Bath & North East Somerset, North Somerset and South Gloucestershire following the breakup of the historic county of Avon in 1996. The area is predominately urban with the city of Bristol (100%) and the three neighbouring counties ranging from 79% to 87% urban populations (Boyd et al., 2019).

Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinic visits were obtained from participants following the recommendations of the ALSPAC Ethics and Law committee at the time. The cohort has been previously described in detail (Boyd et al., 2013; Fraser et al., 2013; Northstone et al., 2019) and the study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool: www.bristol.ac.uk/alspac/researchers/our-data/.

2.2. Lung function

Lung function was measured by spirometry at eight (01/10/1999–31/12/2001), 15 (01/10/2006–30/11/2008) and 24 (01/06/2015–31/10/2017) years of age (Vitalograph pneumotachograph system, Spirotrac, United Kingdom, including Spirotrac software) by trained technicians, according to American Thoracic Society (1994, eight years) and American Thoracic Society/European Respiratory Society (2005, 15 and 24 years) recommendations (American Thoracic Society, 1994; Beydon et al., 2007; Miller et al., 2005). Calibration checks were performed with a standard 1L (eight years) and 3L (15 and 24 years) calibration syringe according to the manufacturer's instructions at the start of each half-day clinic session. Subjects were seated with a nose clip in place and asked to inhale to total lung capacity, then instructed to perform a forced expiration through a mouthpiece to residual volume. After a suitable rest, participants were asked to repeat this procedure, until three acceptable and reproduceable blows (within 0.2L of each other) were obtained from a maximum of eight attempts. If three acceptable blows were not collected the remainder of the session was stopped. At eight years, flow-volume curves were considered acceptable if they reached a clear plateau of flow and the expiration had continued for more than one second and was judged by the tester to be a maximal effort (most children could not sustain forced expiration for the recommended six seconds). All curves were inspected post-hoc by a respiratory paediatrician to ensure that satisfactory reproducibility criteria had been met. At 15 and 24 years, technically "acceptable blows" were determined by the technicians during the taking of the measurements. The technicians were trained in the interpretation of on-screen lung function acceptability criteria (assisted by built-in algorithms in the Spirotrac programme based on American Thoracic Society/European Respiratory Society criteria for reproducibility of respiratory function measurements).

The parameters of interest in this analysis are FVC as a measure of lung volume and size, FEV_1 and the FEV_1/FVC ratio as measures of airway inflammation or obstruction, as well as forced expiratory flow at 25% (FEF_{25}), 50% (FEF_{50}) 75% (FEF_{75}) of FVC as well as $FEF_{25\text{-}75}$, as measures of small airways and airway narrowing. At age eight and 15 years, the lung function measurements for analysis were taken from the best of the three curves, defined as an acceptable curve with the highest FVC measurement. At age 24 years, the highest FEV_1 value was used from the three acceptable blows. Similarly, the highest FVC value was used, with all forced expiratory flow (FEF) variables taken from the blow with the highest FVC. This means that the FEV_1 and FVC/FEF values may have come from different blows at 24 years.

Lung function measures after administration of a bronchodilator (salbutamol) were performed at 15 and 24 years but not at age eight years. Hence, post-bronchodilator lung function measurements are not considered in this manuscript focused on lung function development throughout childhood and adolescence.

2.3. ALSPAC as a geo-spatial resource

Participant residential address histories have been geo-coded to 1 m resolution: from birth to age 18 these were calculated using the property centroid(s); from age 18 to 24 these, at the time of analysis, had only been calculated using the postcode centroid(s) (Boyd et al. 2019). These geo-coordinates enable privacy-preserving linkage of greenness/green space exposures to participants at or between different timepoints.

2.4. Greenness

Greenness was assessed by the Normalized Difference Vegetation Index (NDVI) derived from Landsat 5 Thematic Mapper satellite images (Tucker, 1979). The calculation of the NDVI is based on the difference of surface reflectance in visible (0.4–0.7 µm) and near-infrared (0.7–1.1 µm) wavelengths. Values range from negative one (water) through zero (rock, sand and snow) to positive one (dense green vegetation). For ALSPAC participants living in the south-west of England and Wales, which comprises the ALSPAC recruitment area and a surrounding buffer zone capturing some of the residential movement occurring since recruitment, high-resolution cloud-free images were obtained during vegetation-rich months to maximize spatial contrasts for the years corresponding to the time of birth and each of the clinic visits at eight, 15 and 24 years (details provided in the Supplementary Material, Table S1). From these images, NDVI maps were calculated at a resolution of 30 m by 30 m.

Using these maps, the mean of NDVI values, from this point on referred to as "greenness", was calculated in 100 m, 300 m, 500 m and 1000 m circular buffers around the residential addresses at birth, eight, and 15 years of age and at the residential postcode level at 24 years (the extract function from the raster package (Hijmans et al., 2019) was used to spatially link the greenness values to the address data). Essentially, the same procedure was used for the 24-year addresses as for the other addresses, with the exception that the centre of the postcode in which a participant's home fell was used for assigning the greenness exposures at 24 years rather than the exact home address, as the data required for exact geocoding to the residential address at age 24 years had not been acquired by ALSPAC at the time of analysis. The median and mean size of a postcode in Avon is 7293 m^2 and 43,612 m^2, respectively. Each UK postcode covers on average 15 properties (BPH Postcodes, 2019), with rural areas having fewer properties over larger geographical areas and urban areas having more properties over smaller geographical areas. Exposure values were rounded and outliers suppressed to meet disclosure control requirements.

The 100 m buffer captures the immediate neighbourhood, the 300 m buffer is commonly used as an accessibility threshold and is the World Health Organization standard (Annerstedt van den Bosch et al., 2016) and the 500 and 1000 m buffers refer to walking distances within five to ten minutes (Smith et al., 2017). These buffers were selected to cover nearby and more proximal greenness, as limited information exists on how proximity to vegetation may influence children's lung function. For those with information at each address, lifelong average greenness exposures, based on the average of the birth, eight-, 15- and 24-year estimates, were derived for each buffer (e.g. as in (Dadvand et al., 2017)).

2.5. Green spaces

The presence of green spaces in a circular 300 m buffer (commonly used accessibility threshold and World Health Organization standard (Annerstedt van den Bosch et al., 2016)) around participants' home addresses was assessed using data from the freely available Urban Atlas (images used from years 2005–2010, details in Supplementary Material, Table S1; (Urban Atlas, 2011)). These data are only available for metropolitan areas but could nonetheless be assigned to a high percentage of participants with available greenness information (ranged from 99% for the birth addresses to 89% for the 24-year addresses). We considered three target green space categories: urban green spaces (defined as public green areas used predominantly for recreation, such as gardens, zoos and parks), forests and agricultural land.

ALSPAC staff created 300 m buffer polygons around participant addresses at each of the four timepoints: birth, eight, 15 and 24 years (gBuffer function from rgeos package (Bivand et al., 2018)). The presence of the three target green space categories was searched and populated with a 1(present)/0(not present) if they fell within participant buffer areas for each timepoint (intersect function from raster package (Hijmans et al., 2019)). The proportion of each participant's 300 m buffer that was made up of each of the three target green space categories was also calculated (range 0–1). Finally, a lifetime average proportion (calculated as the average of the birth, eight-, 15- and 24-year values) was calculated.

2.6. Air pollution exposure

Modeling of annual average concentrations of particulate matter with diameters less than 10 µm (PM_{10}) has been established for the ALSPAC cohort up to the 15th year of life (Gulliver et al., 2018). ALSPAC staff extracted annual averages for the first, eighth and 15th year of participants' lives to correspond with the clinic follow-up visits. Furthermore, a cumulative exposure capturing PM_{10} concentrations between ages one and 15 years was calculated. Comparable data at 24 years is not available.

2.7. Statistical analyses

First, associations between repeated measures of the greenspace variables (at eight, 15 and 24 years) and lung function parameters (at eight, 15 and 24 years) were assessed using generalized estimation equations (geeglm function from the geepack package (Halekoh et al., 2006)). Any participant with lung function and greenspace data for at least one time point was included. An exchangeable correlation structure was used to account for repeated observations on the same individual for participants with more than one observation. Second, associations between lifetime average greenness and lifetime average proportion of green spaces with lung function at 24-years of age were assessed using linear regression models. Only participants with greenspace information at birth, 8-, 15- and 24-years were included, as these were necessary inputs for the calculation of lifetime average greenspace exposures. Effect estimates (and their 95% confidence intervals) are presented per interquartile range increase for all continuous exposure variables and per presence versus absence of green space for the categorical exposure variables. All models were run as complete-case analyses.

Model covariates were selected based on previous literature on associations between lung function and environmental factors (greenspaces and air pollution). Adjusted models ultimately contained the following variables: sex, age, age-squared (to capture non-linear lung function growth), measured height and weight, presence of older siblings, breast feeding for at least three months, daycare attendance at 15 months of life, parental education (highest of mother or father, classified as low: none/Certification of Secondary Education/vocational; medium: O-level (Ordinary Level); high: A-level (Advanced Level)/University degree), maternal smoking during pregnancy and reported smoking (≥ 1 once per day or ≥ 6 cigarettes per week) by the participants at age 15 and 24 years (all assumed to be non-smokers at eight years). All confounders were entered based on the value extracted from medical records at the time of birth or assessed using questionnaires administered during the prenatal and postnatal periods, except for age, height, weight and participant smoking, which were entered 1) as time-varying in the models assessing associations between repeated measures and 2) as the value provided at the 24-year follow-up in the models assessing associations with lung function at 24 years.

The following sensitivity analyses were conducted. To assess the robustness of the lung function values, models were replicated using standard deviation scores (z-scores) and percent of predicted values, both calculated using the GLI-2012 equations (available for FEV$_1$, FVC, FEV$_1$/FVC, FEF$_{25\text{-}75}$ and FEF$_{75}$; Quanjer et al., 2012). To address potential residual confounding by environmental factors, models were further separately adjusted for cumulative exposure to PM$_{10}$ between one and 15 years (Gulliver et al., 2018) and degree of urbanisation (defined as living in a city (densely populated areas), towns/suburbs (intermediate density areas) and rural areas (thinly populated areas), according to the EU Degree of Urbanisation classification for the year 2001; (DEGURBA - Eurostat)). Models were also individually adjusted for BMI instead of weight, birth weight and self-reported doctor diagnosed asthma, all of which may lie in the causal pathway. Finally, a

Table 1
Characteristics of study population with available data on at least one lung function measurement and one greenspace metric (N = 7094).

Characteristic			N	n (%) / mean ± SD / median ± IQR
At early-life	Male		7094	3400 (47.9)
	Birthweight (grams)[a]		6615	3436 ± 530
	Has older sibling		6187	3383 (54.7)
	Breastfeeding (> 3 months)		6083	3371 (55.4)
	Daycare attendance at 15 months		6092	5691 (93.4)
	Parental education	Low	6209	846 (13.6)
		Medium	6209	1623 (26.1)
		High	6209	3740 (60.2)
	Parental social class	Low	5253	536 (10.2)
		Medium	5253	1403 (26.7)
		High	5253	3314 (63.1)
	Parental atopy[b]		5628	4760 (84.6)
	Maternal smoking during pregnancy		5945	1313 (22.1)
	Furry pets (dog/cat) in home		6131	2683 (43.8)
	Secondhand smoke in home		5645	1960 (34.7)
	Mould in home		6121	2995 (48.9)
At 8 years	Age (years)[c]		6249	8.6 ± 0.2
	Height (cm)[a]		6108	132.5 ± 5.8
	Weight (kg)[c]		5864	29.2 ± 6.9
	Self-reported ever doctor diagnosed asthma		5439	1132 (20.8)
	Atopy[d]		5260	1125 (21.4)
	Annual average PM$_{10}$ (μg/m^3)[a]		6119	23.9 ± 1.7
	Living in a city		5687	4134 (72.7)
	Moved between birth and 8 years		6204	3520 (56.7)
At 15 years	Age (years)[c]		4697	15.3 ± 0.3
	Height (cm)[a]		4646	169.2 ± 8.3
	Weight (kg)[c]		4634	59.9 ± 13.7
	Self-reported ever doctor diagnosed asthma		4166	1018 (24.4)
	Personal smoking		4352	98 (2.3)
	Annual average PM$_{10}$ (μg/m^3)[a]		5945	21.2 (1.7)
	Living in a city		4075	2867 (70.4)
	Moved between 8 and 15 years		4128	1143 (27.7)
At 24 years	Age (years)[a]		3510	24.5 ± 0.8
	Height (cm)[a]		3479	171.2 ± 9.3
	Weight (kg)[c]		3478	70.3 ± 20.7
	Self-reported ever doctor diagnosed asthma		3077	768 (25.0)
	Personal smoking		3240	468 (14.4)
	Annual average PM$_{10}$ (μg/m^3)		na	na
	Living in a city		2775	1971 (71.0)
	Moved between 15 and 24 years		2626	1155 (44.0)

na = not available.
IQR = interquartile range; SD = standard deviation.
N = 7094 corresponds to the number of children with greenspace and lung function measurements at 8, 15 or/and 24 years who also have information on sex, age and height.

[a] Mean and standard deviation presented as numeric variables are normally distributed.

[b] Yes if either parent reporting hayfever, asthma, eczema or allergies.

[c] Median and interquartile range presented as numeric variables are skewed to the right.

[d] Yes if sensitized to one or more of house dust mite (*Dermatophagoides pteronyssinus*), cat or grass pollen at 7.5 years of age.

model was tested with further simultaneous adjustments for parent-related variables available for a lower number of participants (parental social class (highest of mother or father, classified as high: professional/managerial; medium: skilled non-manual; low: skilled manual/partly skilled/unskilled, (Office of Population Census and Survey, 1991)) and parental atopy (either parent reporting hayfever, asthma, eczema or allergies)), as well as for home environment factors (furry pets (cat/dog), any secondhand smoke exposure and mould/dampness in the home) in the first year of life.

To exclude the influence of potential vulnerable groups, those born preterm (< 37 weeks gestation) and reporting chest infections three weeks before lung function testing (only available at ages eight and 15 years) were excluded in separate analyses. We also controlled for birth during a time of probable high pollen exposure using season (spring: March to May; summer: June to August; autumn: September to November; winter: December to February), which has been associated with reduced lung function (Lambert et al., 2019). Effect modification by the following factors was examined: sex, self-reported doctor diagnosed asthma, atopic status (assessed at seven and a half years, positive if child sensitized to one or more of house dust mite (*Dermatophagoides pteronyssinus*), cat or grass pollen, which identifies > 95% of sensitized subjects in ALSPAC (Roberts et al., 2005)), parental education, parental social class, tertiles of cumulative PM_{10} concentrations, always living in a city versus not (i.e. urbanisation) as well as moving behaviour (never vs ever moved between birth and 24 years).

The hypothesized causal relationships between the greenspace exposures, lung function parameters, confounders and potential mediators are presented in Figure S1.

3. Results

3.1. Study population

Of the 14,471 singleton children alive at one year of age, information on at least one lung function measurement (and sex, height and age) and one greenspace variable at the same age was available for 7094 participants (characteristics presented in Table 1). Compared to those originally recruited in the ALSPAC cohort of singleton births but who did not have the required data for participation in this analysis (N = 7377, characteristics compared between included/excluded groups in the Supplementary Material, Table S2), those included in the analysis using repeated measures (N = 7094) were more likely to be female, to have a higher birthweight, to have been breastfed for at least three months, to have parents of high education and high social class and to have been exposed to mould in early-life. They were however less likely to have siblings, have gone to daycare, have been exposed to tobacco smoke *in utero* and secondhand smoke in early life.

Information on lifetime average greenness or lifetime average proportion of green space and lung function at 24 years was only available for 1,763 participants as only participants with greenspace information at birth, 8-, 15- and 24-years could be included (characteristics of this population, and that without the necessary data, are presented in Supplementary Material, Table S3). An overall flow chart is provided in the Supplementary Material, Figure S2.

3.2. Distribution of lung function variables

The mean and standard deviation of the lung function variables are presented in Table 2 for the raw values and in the Supplementary Material, Table S4, for the z-scores. At 24 years of age, the means of the z-scores for all lung function parameters were slightly negative.

3.3. Distribution of greenspace variables

Mean greenness increased slightly with increasing buffer sizes (e.g., from 0.49 in the 100 m buffer to 0.53 in the 1000 m buffer for lifetime average greenness; Fig. 1). Although values appear lower for the birth addresses, direct comparisons of the absolute values across addresses should be avoided as cloud-free images for the same dates of a given year could not be obtained for all addresses. As examples, the spatial distribution of the greenness values in the 300 m buffer for the 15-year home addresses is presented in Fig. 2 and of the green spaces within a 300 m buffer for the 15-year home addresses in Figure S3.

Correlations between the greenness variables are presented in the Supplementary Material, Table S5. Lifetime average greenness values across the buffer sizes were highly correlated (Pearson r's ranged from 0.76 to 0.96). The lowest correlations were between the greenness estimates at the birth address and those assigned to addresses later in life – unsurprisingly and reassuringly, correlations were higher in those participants who had not moved. For example, the correlation between mean greenness in the 100 m buffer at the birth address and at the 24-year address was 0.28 for the entire study population but increased to 0.66 when restricting to those who had not reported moving.

The percentage of participants with agricultural land and forests within 300 m of their home address increased slightly with age (e.g. from 39.1% to 42.0% from ages eight to 24 years and 11.4% to 12.7% from ages eight to 24 years, for agricultural land and forests, respectively; Table 3). The proportion of urban green space and agricultural land in a 300 m buffer was highly skewed to the right. The proportion of forests within a 300 m buffer was too low to allow any statistical analyses.

Cumulative PM_{10} exposure concentrations were negatively correlated with lifetime average greenness (Pearson r's were −0.37, −0.43, −0.46 and −0.49 for greenness in the 100 m, 300 m, 500 m and 1000 m buffers) and lifetime average proportion of agricultural land in a 300 m buffer (Pearson r: −0.44) but weakly positively correlated

Table 2
Spirometric lung function variables.

	At 8 years		At 15 years		At 24 years	
	N	mean ± SD / median ± IQR	N	mean ± SD / median ± IQR	N	mean ± SD / median ± IQR
FEV_1 (ml)	5638	1693 ± 265	3793	3334 ± 744	2960	3708 ± 806
FVC (ml)	5730	1918 ± 319	3864	3710 ± 854	2960	4504 ± 1037
FEV_1/FVC (%)[a]	5638	89.0 ± 8.2	3793	91.2 ± 10.2	2960	83.4 ± 8.3
FEF_{25-75} (ml/s)	5724	2064 ± 525	3859	3945 ± 1096	2960	3753 ± 1081
FEF_{25} (ml/s)	5724	3398 ± 704	3752	5831 ± 1518	2960	6447 ± 1805
FEF_{50} (ml/s)	5724	2337 ± 586	3752	4280 ± 1178	2960	4338 ± 1257
FEF_{75} (ml/s)	5724	1103 ± 368	3752	2418 ± 812	2960	1942 ± 680

IQR = interquartile range; SD = standard deviation.

N values correspond to the number of children with lung function measurements at each respective age who also have corresponding greenspace data, among the 7,094 children with greenspace and lung function measurements at 8, 15 or/and 24 years who also have information on sex, age and height.

[a] Median and interquartile range presented as numeric variables are skewed to the left.

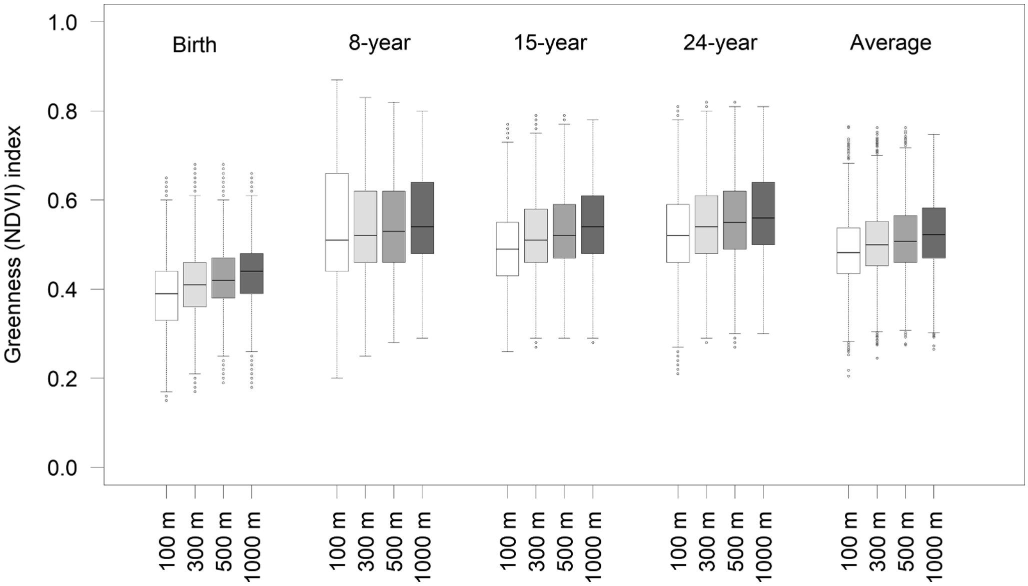

Fig. 1. Distribution of mean greenness values within circular 100 m, 300 m, 500 m and 1000 m buffers around each home address, and the lifetime average. Comparisons across addresses are not appropriate as it was not possible to obtain cloud-free images at the same time (i.e. date of a given year) for all addresses.

with lifetime average proportion of urban green space in a 300 m buffer (Pearson r: 0.17).

3.4. Associations between greenspace and lung function

Associations were apparent between repeated measures of FEV_1 and FVC with repeated measures of greenness in a 100 m buffer and the presence and (to a lesser extent) proportion of any urban green space in a 300 m buffer (Table 4). There was also rather weak evidence of an association between lifetime average greenness in the smaller buffers (100 and 300 m buffer) and the lung function parameters at 24 years as all effect estimates were above one but only one reached statistical significance (Table 5). There were more consistent associations between increasing lifetime average proportion of agricultural green space in a 300 m buffer and better lung function for all parameters except FVC and FEF_{25} (Table 5). All other tested associations were null. Results were similar in models adjusted only for sex, age and height (Supplementary Material, Tables S6 and S7).

3.5. Sensitivity analyses

Results were similar when using lung function standard deviation scores (z-scores; Supplementary Material, Tables S8 and S9) and percent of predicted values (Supplementary Material, Tables S10 and S11). Further adjustment for BMI (instead of weight), birth weight, season of conception, parental social class, parental atopy as well as pets, secondhand smoke and mould in the home during early life did not affect the associations, nor did excluding those born preterm (4%) or those reporting chest infections in the three weeks before lung function testing (18%). Adjustment for self-reported doctor diagnosed asthma did not affect the associations between repeated measures (Supplementary Material, Table S12), but attenuated the previously consistent associations between lifetime average proportion of agricultural land and lung function at 24 years (Supplementary Material, Table S13). There was no consistent evidence to suggest effect modification by sex, self-reported doctor diagnosed asthma, parental education, parental social class, or atopy at 7.5 years (defined as (1) atopic

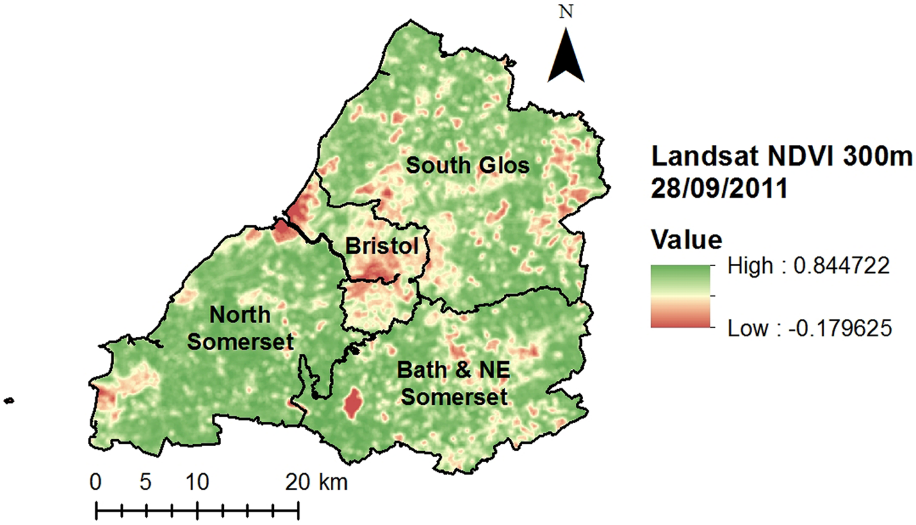

Fig. 2. Spatial distribution of greenness within a 300 m buffer at the time of the 15-year clinic visit.

Table 3
Distribution of green space variables.

		N	Urban green n (%) / min, max (IQR)	Agricultural land n (%) / min, max (IQR)	Forests n (%) / min, max (IQR)
Presence of any green space	8 years	5408	3001 (55.5)	2217 (39.1)	616 (11.4)
	15 years	3577	1939 (54.2)	1469 (41.1)	444 (12.4)
	24 years	2637	1447 (54.9)	1108 (42.0)	334 (12.7)
Average proportion in 300 m buffer[a]	8 years	5408	0.00, 0.62 (0.06)	0.00, 0.93 (0.09)	–
	15 years	3577	0.00, 0.56 (0.06)	0.00, 0.93 (0.11)	–
	24 years	2637	0.00, 0.54 (0.06)	0.00, 0.95 (0.12)	–
	Lifetime average	1573	0.00, 0.46 (0.06)	0.00, 0.89 (0.11)	–

IQR = interquartile range.
N values correspond to the number of children with each greenspace measure at each respective age who also have corresponding lung function data, among the 7094 children with greenspace and lung function measurements at 8, 15 or/and 24 years who also have information on sex, age and height.

[a] As these numeric variables are skewed to the right, the minimum and maximum values, as well as the interquartile range are presented. The proportion of forests with a 300 m buffer was too low to allow any statistical analyses.

to house dust mite, cat or mixed grasses, or (2) atopic to mixed grasses only).

Adjusting the models for lifetime average PM_{10} and degree of urbanisation, separately (Supplementary Material, Tables S14 and S15) and simultaneously, confirmed the observed associations. Stratified models yielded higher effect estimates for the associations between repeated measures of the presence and proportion of urban green space in a 300 m buffer among those living in the highest tertile of PM_{10} concentrations (Fig. 3A). Higher effect estimates were also found for the presence (but not proportion) of urban green space among those who had always lived in a city from birth to 24 years, compared to not (Fig. 3B). These trends were not observed for the other exposure metrics (Figures S4-S5), as well as in the models assessing associations between lifetime average greenness and lifetime average proportion of green spaces with lung function at 24 years, although these latter stratified models are based on smaller sample sizes (~300–600 participants).

Trends suggesting that more greenspace leads to better lung function appeared clearest in children who had not moved since birth for the associations modelled using repeated measures, although confidence intervals were large (Fig. 4). The notable exception was for the presence of any urban green space in a 300 m buffer, for which effect estimates were below one among those who had not moved and above one among those who had. Trends by moving status were less clear for associations between lifetime average greenness and lifetime average proportion of green space with lung function at 24 years (Supplementary Material, Figure S6). There was no consistent trend to suggest that moving behaviour was linked to increasing/decreasing levels of greenspaces throughout life, as those that moved between birth and eight years tended to move to areas with more greenspace whereas those that moved between 15 and 24 years tended to move to areas with less greenspace (moving between eight and 15 years represented a mix of these trends).

4. Discussion

4.1. Main findings

In an analysis using repeated measures of greenspace and lung function in a large English regional birth cohort, we found evidence that suggests that children with higher greenness close to their home and the presence of urban green spaces within 300 m of the home across their lifecourse had higher FEV_1 and FVC up to 24 years of age, when they are likely to have reached their maximal lung function. Although the observed effect sizes were relatively small, they may have important public health impacts when considered at the population-level. The associations were independent of self-reported doctor diagnosed asthma status, PM_{10} concentrations, degree of urbanisation and socio-economic status, and appeared greater among participants living in cities and in areas of high PM_{10} concentrations. This latter result may suggest a greater importance of greenness and urban green spaces (i.e. public green areas used predominantly for recreation) in urban settings, where these factors may be scarcer. A possible importance of having greenspace very close by is also suggested by our results, as associations with greenness were most consistent for the 100 m buffer.

Associations were also observed between lifetime average greenness within a 100 m buffer and several lung function parameters (especially after adjustment for lifetime average PM_{10} exposure) and proportion of agricultural land within a 300 m buffer with maximally attained lung function by 24 years of age in a smaller subset of the study population. These associations were attenuated when adjusting for self-reported ever doctor diagnosis of asthma by age 24 years, which suggests that asthma may be an important confounder, may be closely related to another unknown confounder or may lie in the causal pathway between exposure to greenspace and lung function development up to 24 years. In this study population, a self-reported doctor diagnosis of asthma was not associated with any of the greenspace measures considered (and hence no mediation analyses were pursued), although highly heterogenous evidence for a link between asthma and vegetation has been demonstrated in other settings (Fuertes et al., 2016; Lambert et al., 2017).

4.2. Potential mechanisms

There are several mechanisms by which greenspace may influence lung function development. First, areas with more greenspace are likely to have lower levels of air pollution. The observed associations were not attenuated when we adjusted for cumulative PM_{10} concentrations (from one to 15 years), suggesting that the investigated associations are not confounded by this pollutant. As similar lifetime exposure data are unfortunately not available for other pollutants (such as NO_2, $PM_{2.5}$ mass or ozone), we are unable to assess potential confounding effects of these air pollution markers. The higher effect estimates we observed for the urban green space exposure metrics in areas of high PM_{10} concentrations and among consistent city dwellers may suggest a more important role of greenspace in high air pollution, urban settings. Second, greenspace may be a marker for higher pollen exposure, which has been linked to reduced lung function (Gruzieva et al., 2015). Under this hypothesis, we would expect effect estimates between the greenspace variables and lung function to be negative, of which we found no evidence. Furthermore, we found no differences between atopic and non-atopic individuals. Third, as has been suggested by the “biodiversity hypothesis” for allergies and other chronic inflammatory diseases (Hanski et al., 2012), it is plausible that exposure to greenspace may influence one's microbiome, which in turn, could influence lung function development. However, evidence supporting this hypothesis is currently lacking. Fourth, greenspace exposure may promote increased

Table 4
Associations between repeated measures of greenspace (ages 8 to 24 years) and lung function (ages 8 to 24 years).

		Greenness in various buffers[a]					Presence in 300 m buffer[b]			Proportion in 300 m buffer[c]	
	Number of participants	100 m	300 m	500 m	1000 m	Number of participants	Urban green	Agricultural	Forest	Urban green	Agricultural
FEV_1 (ml)	4730	11.4 (2.6, 20.3)	7.6 (−3.2, 18.4)	6.2 (−5.5, 18.0)	4.3 (−8.9, 17.4)	4413	20.3 (−0.1, 40.7)	8.9 (−11.4, 29.2)	13.6 (−17.2, 44.4)	6.2 (−1.9, 14.4)	5.6 (−0.1, 11.3)
FVC (ml)	4775	12.2 (1.8, 22.7)	9.8 (−2.9, 22.6)	8.9 (−4.8, 22.6)	8.2 (−7.1, 23.6)	4459	23.1 (−0.3, 46.5)	2.8 (−20.6, 26.2)	18.0 (−17.6, 53.6)	7.5 (−2.0, 17.0)	3.8 (−2.9, 10.4)
FEV_1/FVC (%)	4730	−0.1 (−0.3, 0.1)	−0.1 (−0.3, 0.1)	−0.2 (−0.3, 0.0)	−0.2 (−0.4, 0.0)	4413	0.0 (−0.3, 0.3)	0.0 (−0.3, 0.4)	−0.1 (−0.6, 0.4)	0.0 (−0.1, 0.1)	0.0 (−0.1, 0.1)
FEF_{25-75} (ml/s)	4775	7.1 (−9.3, 23.4)	−1.2 (−20.8, 18.4)	−4.7 (−26.3, 16.8)	−13.9 (−38.4, 10.7)	4459	28.5 (−10.5, 67.5)	2.4 (−35.7, 40.5)	−22.2 (−80.3, 36.0)	8.1 (−7.5, 23.8)	5.9 (−4.8, 16.7)
FEF_{25} (ml/s)	4763	18.1 (−5.5, 41.8)	15.8 (−12.9, 44.5)	12.5 (−19.4, 44.4)	−8.4 (−44.8, 28.0)	4447	22.0 (−33.3, 77.3)	20.9 (−34.7, 76.6)	−10.8 (−92.8, 71.3)	12.3 (−10.3, 35.0)	22.8 (7.8, 37.9)
FEF_{50} (ml/s)	4763	14.3 (−4.0, 32.7)	7.1 (−15.0, 29.2)	2.1 (−22.0, 26.2)	−8.7 (−36.2, 18.9)	4447	26.1 (−17.3, 69.4)	5.6 (−37.1, 48.2)	−25.7 (−90.8, 39.3)	10.3 (−7.1, 27.6)	11.0 (−0.6, 22.7)
FEF_{75} (ml/s)	4763	0.8 (−10.9, 12.5)	−5.5 (−19.5, 8.5)	−8.8 (−24.1, 6.4)	−14.1 (−31.3, 3.2)	4447	26.7 (−0.7, 54.1)	7.4 (−20.1, 34.8)	−6.7 (−49.2, 35.7)	6.2 (−5.1, 17.6)	1.7 (−6.0, 9.4)

Models were adjusted for sex, age, age^2, height, weight, personal smoking at 15 and 24 years, older siblings, breast feeding, daycare attendance, parental education and maternal smoking during pregnancy.
N values correspond to the number of children with greenspace and lung function measurements at 8, 15 or/and 24 years who also have complete covariate information.

[a] A positive estimate represents the average increase in lung function per interquartile range increase in greenness.

[b] A positive estimate represents the average increase in lung function comparing presence versus absence of green space.

[c] A positive estimate represents the average increase in lung function per interquartile range increase in proportion of green space.

Table 5
Adjusted associations between the lifetime average greenspace metrics and lung function at 24 years.

	Lifetime average greenness in various buffers					Lifetime average proportion in 300 m buffer		
	Number of participants	100 m	300 m	500 m	1000 m	Number of participants	Urban green	Agricultural
FEV_1 (ml)	1097	37.2 (0.7, 73.6)	21.5 (−14.3, 57.4)	12.4 (−25.2, 50.0)	−1.3 (−41.1, 38.5)	964	14.4 (−16.6, 45.4)	31.4 (8.8, 54.0)
FVC (ml)	1097	21.5 (−21.5, 64.5)	3.5 (−38.7, 45.8)	−4.6 (−49.0, 39.7)	−14.3 (−61.2, 32.7)	964	−1.8 (−38.6, 34.9)	15.2 (−11.7, 42.1)
FEV_1/FVC (%)	1097	0.4 (−0.1, 1.0)	0.4 (−0.1, 0.9)	0.4 (−0.1, 0.9)	0.3 (−0.3, 0.8)	964	0.4 (−0.1, 0.8)	0.4 (0.1, 0.7)
FEF_{25-75} (ml/s)	1097	65.3 (−7.9, 138.6)	42.4 (−29.7, 114.5)	33.4 (−42.2, 109.0)	6.4 (−73.5, 86.3)	964	38.9 (−22.9, 100.7)	59.5 (14.3, 104.6)
FEF_{25} (ml/s)	1097	47.7 (−64.7, 160.1)	26.0 (−84.5, 136.6)	1.0 (−114.9, 116.9)	−41.1 (−163.5, 81.4)	964	62.2 (−32.9, 157.2)	67.7 (−1.8, 137.3)
FEF_{50} (ml/s)	1097	68.4 (−17.4, 154.2)	46.2 (−38.2, 130.6)	38.3 (−50.2, 126.7)	8.8 (−84.8, 102.4)	964	51.0 (−21.9, 124.0)	68.9 (15.7, 122.2)
FEF_{75} (ml/s)	1097	45.0 (−2.9, 92.9)	32.5 (−14.6, 79.6)	26.8 (−22.6, 76.2)	8.9 (−43.3, 61.1)	964	21.8 (−18.1, 61.6)	39.8 (10.7, 68.9)

Models were adjusted for sex, age, height, weight, personal smoking at 24 years, older siblings, breast feeding, daycare attendance, parental education and maternal smoking during pregnancy. A positive estimate represents the increase in lung function at 24 years per interquartile range increase in lifetime average greenness or lifetime average proportion of green space.
N values correspond to the number of children with lifetime average greenspace information, lung function data at 24 years and complete covariate information.

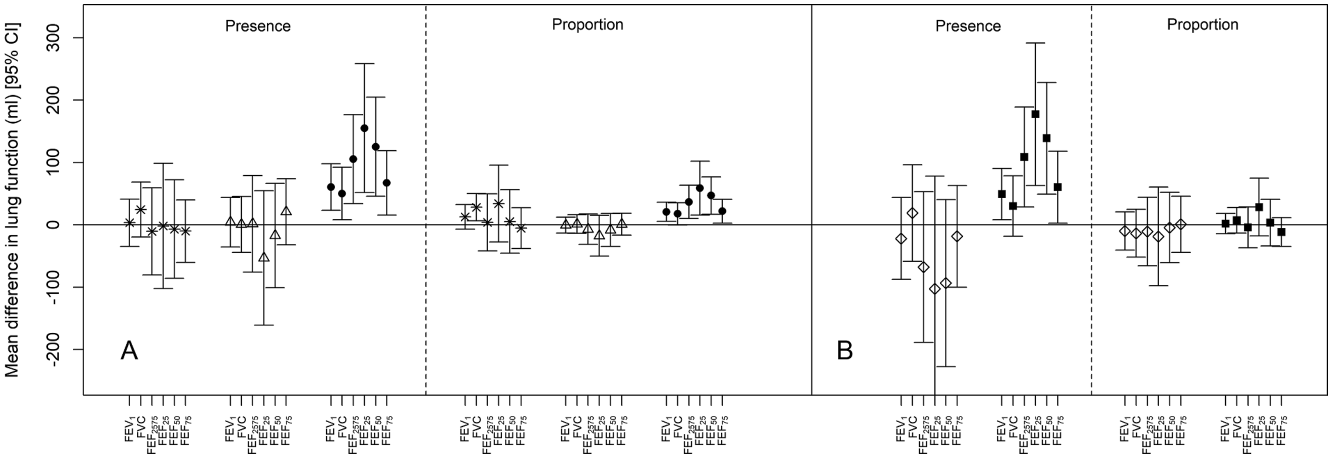

Fig. 3. Estimated mean difference in lung function (ml) for the presence (yes versus no) and proportion (per interquartile range increase) of urban green space in a 300 m buffer. Associations presented by (A) tertiles of PM_{10} concentrations (low: stars; medium: open triangles; high: filled circles) and (B) whether a participant always lived in a city from birth to 24 years (filled squares) compared to not (open diamonds). Results for the FEV_1/FVC ratio are not presented. Interaction terms were significant ($p < 0.05$) between PM_{10} concentrations (high tertile versus low tertile) and the presence of urban green space for all lung function parameters except FEV_1 and FVC, PM_{10} concentrations (medium tertile versus low tertile) and the proportion of urban green spaces for FVC, as well as always living in a city versus not and the presence of urban green space for FEF_{2575}, FEF_{25} and FEF_{50}.

levels of physical activity (Fong et al., 2018; van den Bosch and Ode Sang, 2017), which have been associated with better lung function in the ALSPAC cohort (Roda et al., 2019). We were unable to adequately test this hypothesis as physical activity data measured by accelerometry were only available for less than 25% of the study sample. However, given that associations with greenness were only apparent for the smallest 100 m buffer, physical activity is unlikely to be the dominant mechanism. Finally, as aforementioned, greenspace exposure may influence an individual's risk of asthma (by any of the aforementioned mechanisms), which could affect later lung function. The slight attenuation of some of the associations in the current study after adjustment for self-reported doctor diagnosed asthma provides some support for this mechanistic pathway. Given the highly heterogeneous existing body of literature on the link between greenspace and asthma, further research is warranted.

4.3. Strengths and limitations

This large prospective analysis adds substantially to the literature by being the first to consider repeated greenspace exposures and objective lung function measurements, the latter of which span up to 24 years and thus capture the maximal peak in lung function. We were able to consider effects on a full range of objectively measured lung function variables indicative of airway inflammation or obstruction (FEV_1, FEV_1/FVC), lung volume and size (FVC), as well as more rarely investigated measures of small airways and airway narrowing (FEF_{25}, FEF_{50}, FEF_{75}) and mean flow rate ($FEF_{25\text{-}75}$). Given the rich high-quality data, we were able to adjust for most recognized potential confounders. Our adjustment for parental education level and parental social class may however have been insufficient to capture true differences in socioeconomic status over the lifecourse. Further, we were unable to adjust for air pollution or pollen levels on the day of or leading up to the lung function measurements, although both have been shown to influence lung function (Gruzieva et al., 2015; Ward and Ayres, 2004). We were also only able to consider the potential confounding effect of lifetime PM_{10} mass exposures, but not of other potentially relevant air pollutants. Participation bias is a concern for all cohorts with long follow-ups. Participants included in this study differed from those in the initial birth cohort regarding several characteristics and this non-random retention may have affected the effect estimates.

Limitations related to the exposure assessment include 1) the NDVI is a general marker of green vegetation and does not provide information about the specific types of vegetation present, 2) in contrast to the greenness data which was available near the time of each of the lung function measurement campaigns, the green space data were derived from images from a single timepoint (2005–2010), and hence we made the explicit assumption that the spatial distribution of these green spaces did not change throughout the 24-year follow-up and 3) we have no information on whether, how or for how long participants may interact with and use greenspace (i.e. what the “direct exposure” may be, White et al., 2019), or how they perceive the natural environment (Kruize et al., 2019).

Analyses stratified by moving behaviour generally led to stronger associations among those who had never moved between birth and 24 years of age, compared to those who had, the former of which may represent a group with lower exposure misclassification. However, as we used home addresses as our only proxy for the location of participants, some exposure misclassification likely remains for all subgroups, especially at the older ages when participants are more likely to spend a larger proportion of their time away from home. At this older age, it is also possible that participants continue to use their parents address for correspondence with the ALSPAC study although they themselves have moved. We have no way to verify the extent of this issue. Greenspace exposures that occur away from the home may also influence lung function, such as those that occur at schools (Paciência et al., 2019). Additionally, the addresses at birth, eight and 15 years were assigned to the exact home address, whereas those at 24 years were assigned at the postcode level. We expect this to be a minor limitation as the correlation between greenness levels estimated at the home- and postcode-level at birth, eight and 15 years was very high (Pearson's $r > 0.92$). Finally, it should be acknowledged that only a small subset of the associations tested yielded statistically significant associations, some of which may represent false positives. Further analyses should be conducted to confirm or refute our findings.

In conclusion, our study is the first to use repeated data on greenspace exposures and lung function measurements to identify a potentially beneficial role of higher greenness around the home and close proximity of urban green spaces on modest increases in lung function up to 24 years of age. As changes in adolescent lung function can carry long-term implications for overall respiratory health and given that greenspace levels can vary greatly within populations, these findings could have important public health consequences and may need to be

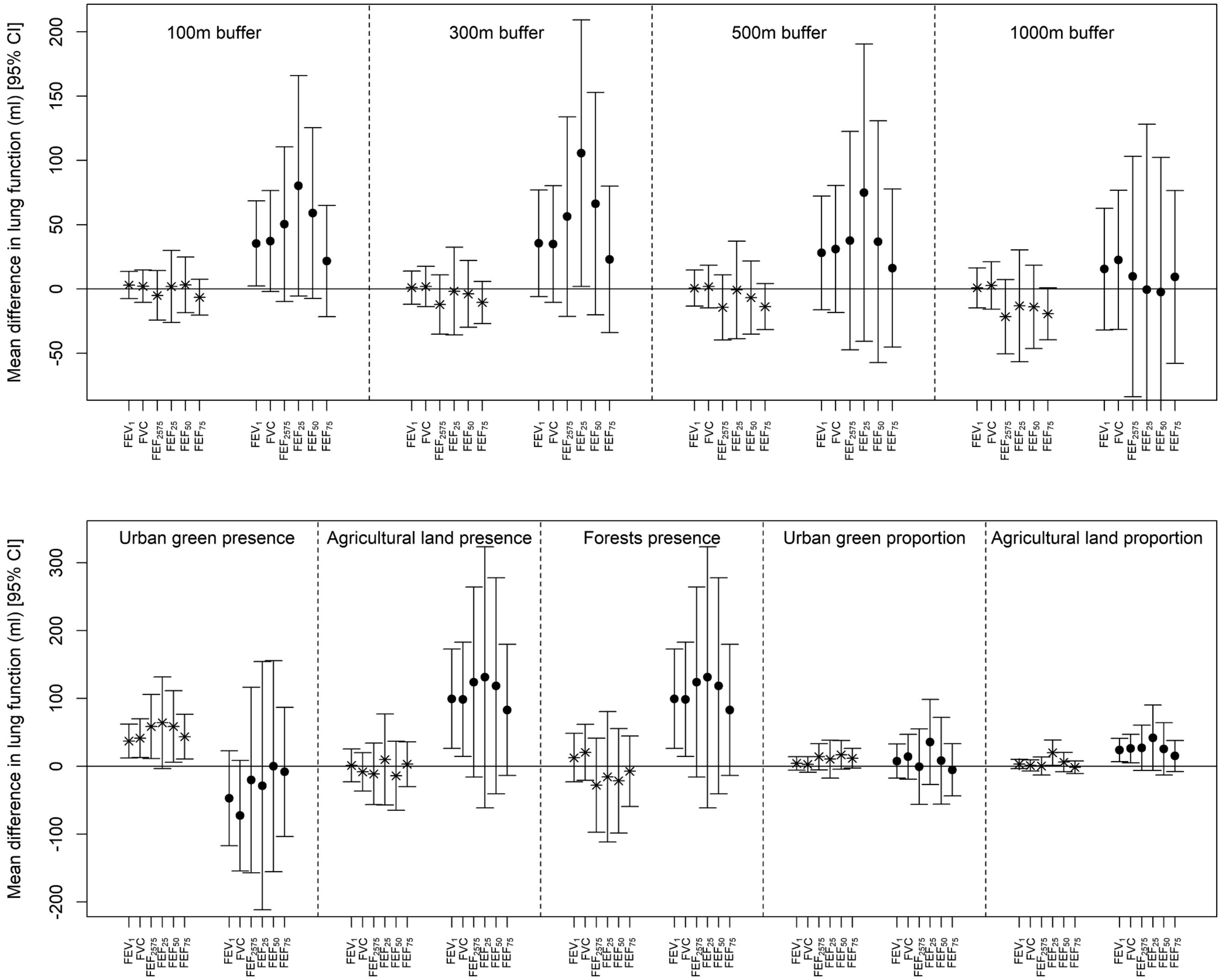

Fig. 4. Estimated mean difference in lung function (ml) per interquartile range increase in greenness (top panel), presence versus absence of green spaces and interquartile range increase in proportion of green spaces (bottom panel). Associations presented for those who moved between birth and 24 years (stars) and those who did not (filled circles). Results for the FEV$_1$/FVC ratio are not presented. Interaction terms were significant ($p < 0.05$) between moving and greenness in a 100 m buffer for FEV$_1$ and FEF$_{25}$, moving and greenness in a 300 m for FEF$_{25}$, moving and the presence of any urban green space for FEV$_1$ and FVC, as well as moving and the proportion of agricultural land for FEV$_1$ and FVC.

considered in urban planning initiatives. Currently, there is no evidence to inform public health guidelines and policy makers as to how to green our cities for respiratory health benefit.

CRediT authorship contribution statement

Elaine Fuertes: Conceptualization, Methodology, Software, Formal analysis, Writing - original draft, Visualization, Project administration. **Iana Markevych:** Software, Investigation, Writing - review & editing. **Richard Thomas:** Software, Investigation, Data curation, Writing - review & editing. **Andy Boyd:** Investigation, Data curation, Writing - review & editing. **Raquel Granell:** Investigation, Data curation, Writing - review & editing. **Osama Mahmoud:** Investigation, Data curation, Writing - review & editing. **Joachim Heinrich:** Conceptualization, Writing - review & editing, Funding acquisition. **Judith Garcia-Aymerich:** Software, Data curation, Writing - review & editing, Funding acquisition. **Célina Roda:** Software, Data curation, Writing - review & editing. **John Henderson:** Conceptualization, Resources, Project administration, Funding acquisition. **Debbie Jarvis:** Conceptualization, Methodology, Supervision, Project administration, Funding acquisition, 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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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.105749.

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