Residential greenness during pregnancy and early life and development of asthma up to 27 years of age: The Espoo Cohort Study

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Abstract

Background: Evidence on the effects of residential green spaces on asthma is contradictory. We investigated potential association between the amount of greenness in the residential area during pregnancy and early life and development of asthma in the first 27 years of life. **Methods:** The study population included all 2568 members of the Espoo Cohort Study, Finland. We calculated individual-level exposure to green space measured as cumulative Normalized Difference Vegetation Index (cumNDVI in unit-months) within 300 m of the participant's residence during pregnancy and the first two years of life in both spring and summer seasons. The onset of asthma was assessed using information from the baseline and follow-up surveys. **Results:** Exposure to residential greenness in the spring season during pregnancy was associated with an increased risk of asthma up to 6 years of age, with an adjusted hazard ratio (aHR) of 3.72 (95% confidence interval (CI) 1.11-12.47) per a unit increase in cumNDVI. Increased greenness in the summer during pregnancy associated with asthma with an aHR of 1.41 (95% CI 0.85-2.32) up to 6 years. The effect was found to be related to increased greenness particularly during the third trimester of pregnancy, with an aHR of 2.37 (95% CI 1.36-4.14) per unit increase of cumNDVI. These associations were weaker at the ages of 12 and 27 years. No association was found between NDVI in the first two years of life and the development of asthma. **Discussion:** Our findings provide evidence that exposure to greenness during pregnancy increases the risk of developing asthma.

Introduction

Increasing evidence has shown that exposure to green vegetation in the vicinity of home is related to health. While several studies have reported beneficial associations between residential greenness and health outcomes, literature on respiratory health has been contradictory: some studies have reported beneficial but other studies harmful effects in relation to greenness.

According to some recent studies, residential greenness is associated with decreased risk of childhood asthma. However, other studies have reported harmful effects or inconclusive results associated with an increase in greenness. These observational studies have highlighted the complexity of such multidimensional relations between green spaces and asthma. Inconsistencies in previous findings could be explained by differences in the study design, geographic region of the study, outcome definitions, and exposure assessment in these studies. For example, exposure assessment has differed in the definitions used for green spaces and in the timing of studied exposures. The most commonly used indicator of greenness is the Normalized Difference Vegetation Index (NDVI), the values of which change throughout the year depending on the season and vegetation growth. However, in many studies the greenness exposure was measured at one point in time, which overlapped with the study period and was most frequently assessed during the summer (i.e. during maximum vegetation).

Although several studies have reported that the prenatal period represents the time window of environmental exposures related to special susceptibility to asthma, it is still unknown what kind of role the timing of exposure to green spaces during pregnancy plays for the risk of asthma. Previous observational studies have reported an association between greenness during pregnancy and the risk of asthma, but only Sbihi et al. and Lin et al. actually investigated the residential greenness during pregnancy and the risk of asthma and allergic diseases, and none of the previous studies evaluated trimester-specific exposure in the relation between exposure to greenness during pregnancy and childhood asthma. Even though greenness can be rather stable around homes, families often move during pregnancy or after the birth of a child due to the increasing need for space. Both changes in the residential address and season of pregnancy may influence cumulative exposure to greenness.

The objective of the present study was to investigate the potential association between residential greenness during pregnancy and early life and the development of asthma up to the age of 27 years, with special focus on trimester-specific and seasonal effects. We addressed this research question using the prospective population-based Espoo Cohort Study with a full residential history of the families during pregnancy and early life. We studied the timing of exposure during pregnancy by assessing trimester-specific exposure to greenness in relation to the development of asthma. Furthermore, we considered exposure to greenness during spring and summer separately to assess potential effect of the season on the studied relation.

Methods

Study population

The source population included all children of the city of Espoo, Finland, who were born between January 1, 1984, and March 31, 1990. Espoo is an urban-suburban municipality with a population of over 300 000, located across the western border of Helsinki, the capital of Finland. We took a random sample of children living in Espoo in 1991 drawn from the roster of Statistics Finland. The baseline study population included a total of 2 568 children (response rate 80.3%) whose parents gave informed consent and filled in the questionnaire. Espoo is an urban-suburban municipality located across the western border of Helsinki, the capital of Finland. In 1997, we conducted the 6-year follow-up survey of the cohort, with a follow-up rate of 77.3%, and in 2010–2011, the 20-year follow-up (follow-up rate 63.2% of the baseline population). The life-time home coordinates of the mothers and children were retrieved from the Population Register Centre of Finland. The study protocol was approved by the Ethics Committee of Oulu University Hospital (Oulu, Finland).

Outcome of interest

Our outcome of interest was the onset of asthma during the follow-up period. In the baseline and 6-year follow-up surveys, this was determined with the following question: "Has the child ever had physician-diagnosed asthma?" If the answer was yes, the age at diagnosis was requested. The following questions were asked in the 20-year follow-up: "Have you ever had physician-diagnosed asthma? If yes, at what age was it diagnosed?"

Exposure assessment

We measured exposure to greenness in the residential environment as our exposure of interest. Greenness was measured using the mean Normalized Difference Vegetation Index (NDVI) within 100 m, 300 m, 500 m, and 1000 m of the participant's residence(s) during pregnancy and the first two years of life in both spring and summer seasons.' We selected the 300 m radius for NDVI for the main analyses, as this has been recommended by the WHO and UNICEF. The calculation of the NDVI was based on land surface reflectance of visible red (VISR) and near-infrared (NIR) wavelengths, applying the following equation (Eq. (1)):

$$NDVI = \frac{NIR-VISR}{NIR+VISR} \quad (1)$$

The NDVI values range from -1 to 1, where negative values represent water, zero values rock, sand or snow (without vegetation), and positive values indicate density of green vegetation (i.e., the highest NDVI values are observed from photosynthetically active and healthy vegetation). We used only cloud-free images during the spring (April–May) and summer (June–August) seasons from Landsat 5 (spatial resolution: 30 m) between conception (1983-90) and the first two years of life (1984-92) to capture maximum spatial contrasts in greenness (Figure 1). The used images represented the highest available quality and processing level (https://earthexplorer.usgs.gov/). We included NDVI values higher than zero to investigate the role of green vegetation on the risk of asthma. In southern Finland, the spring usually begins in April and the summer begins in late May (https://en.ilmatieteenlaitos.fi/seasons-in-finland). ArcMap 10.5 was used to process satellite images, and QGIS 3.8 was used to extract the average NDVI within each buffer size.

We calculated individual-level cumulative exposure to NDVI (cumNDVI) during pregnancy and early life (first two years of life) by taking the average of monthly exposure over the residential history, while weighting by the days spent in each residential address and time of pregnancy in the spring and summer seasons. Estimates were based on the number of pregnancy or early-life days during spring and summer [Eq. (2)].

$$\text{Cumulative exposure to NDVI}_{\,residence,\ i} = \sum \text{mean exposure to NDVI}_j * duration\ of\ exposure_j \tag{2}$$

where $residence_i$ corresponds to i$^{\text{th}}$ participant, *mean exposure to* $NDVI_j$ corresponds to the mean exposure to NDVI in j$^{\text{th}}$ residential addresses during months 4-5 (April-May) for spring and during months 6-8 (June-August) for summer, and the *duration of* $exposure_j$ corresponds to the number of estimated days within specific month during spring/summer periods in j$^{\text{th}}$ residential addresses during pregnancy or early life.

We defined individual cumNDVI during the entire pregnancy, the first trimester (defined as gestational months 1 to 3), the second trimester (gestational months 4 to 6) and the third trimester (gestational months 7 to the end of pregnancy) by taking the average of exposure during each pregnancy month. The child was exposed to the average spring NDVI level during pregnancy months from April to May, to the average summer NDVI level during pregnancy months from June to August, and to NDVI level 0 from September to March. The latter corresponded to a lack of exposure outside of the growing season when NDVI values decrease significantly for all types of land use in vegetation zones like southern Finland in the Baltic Sea region.

We conducted a sensitivity analysis where *mean exposure to* $NDVI_j$ corresponded to the mean exposure to NDVI in j$^{\text{th}}$ residential address during the months 3-5 (March-May) for spring and the months 6-9 (June-September) for summer.

Covariates

The following known or suggested determinants of asthma were included in the analysis as potential confounders: age, sex, family socioeconomic status, environmental tobacco smoke exposure and maternal smoking. Information on these covariates was obtained from the baseline.

Statistical analysis

We assessed the association between exposure to green spaces, measured as the cumulative exposure to NDVI during pregnancy and during early life, and the risk of asthma applying Cox's proportional hazard regression models. The analysis was based on the time to onset of asthma, and crude and adjusted hazard ratios (HR) with 95% confidence intervals (CI) were analyzed as the measure of effect. We applied three overlapping age periods (baseline age to the ages of 6, 12 and 27 years) to investigate the influence of greenness on the risk of asthma over time. We fitted the exposure in the models as a continuous (for a 1 NDVI-month change in exposure) and as a categorical (4 quartiles) variable. Multivariate analyses were adjusted for all potential confounders, and NDVI in the spring and summer as well as in pregnancy and early life were mutually included in the model.

Results

Characteristics of the study population

Characteristics of the study population are shown in Table 1. The cumulative incidence of asthma was 5.4% up to 6 years, 10.7% up to 12 years and 14.7% up to 27 years of age.

Residential greenness during pregnancy and early life in the spring and summer seasons and **the *risk of asthma***

Distribution of the mean values of the neighborhood levels and cumulative levels of NDVI are presented in Table 2.

The risk of asthma by the age of 6 years increased monotonously by an increase in residential greenness during pregnancy with an aHR of 3.72 (95% CI: 1.11, 12.47) per 1 unit-month increase in cumNDVI (Table 3 and Table S1). This association was found to be linear between the quartiles of cumNDVI exposure: children whose mothers were exposed to the highest quartile of cumNDVI during pregnancy in the spring had a significantly increased risk of asthma between 0 to 6 years of age compared to children whose mothers were exposed to the third, second and first quartiles of cumNDVI, the aHR being 2.31 (95% CI: 1.20, 4.45) for the highest NDVI quartile contrasted with the lowest quartile. Similar pattern was present for asthma up to 12 and 27 years of age, although the confidence intervals were broader and included unity (Table 3). The risk of asthma by the age of 6 years was also related to greenness in the summer during pregnancy (aHR=1.41; 95% CI: 0.85, 2.32), although the effect estimate was weaker than the corresponding effect estimate for the spring and the 95% CI was broader including unity.

There was no consistent evidence of an association between NDVI in early childhood and the risk of asthma (Table 3 and Table S1).

In the sensitivity analysis, we calculated season-specific effects estimates for cumNDVI exposure, defining March-May as the spring and June-September as the summer season. The adjusted HR of asthma by the age of 6 years (aHR=2.51; 95% CI: 1.14, 5.54) (Table S2) was somewhat weaker for the spring exposure compared to the main analysis shown in Table 3 (aHR=3.72).

Residential greenness during the entire pregnancy and in different trimesters and the risk of asthma

Distribution of the mean values of cumNDVI within 100 m, 300 m, 500 m, and 1000 m of the participant's residence during different time periods of pregnancy are presented in Table 4.

Figure 2 and Table S3 show the aHR of asthma in relation to the cumulative exposure to NDVI during different time periods of pregnancy. Increased residential greenness during the entire pregnancy was associated with an increased risk of asthma at 6 years of age with an aHR of 1.61 (95% CI: 1.08, 2.41) per 1 unit increase in NDVI, but the effect was somewhat weaker by 12 years and 27 years of age (Figure 2). The risk of asthma was significantly related to the increased greenness during the third trimester, with an aHR of 2.37 (95% CI: 1.36, 4.14) per 1 unit increase in cumNDVI, and the risk was significantly increased in relation to the highest quartile of the mean cumNDVI (aHR=1.57; 95% CI: 1.04, 2.36) (Table S3). The effect estimates during the third trimester were somewhat weaker and non-significant at the age of 12 years with an aHR of 1.47 (95% CI: 0.96, 2.26) and at the age of 27 years with an aHR of 1.24 (95% CI: 0.85, 1.82) per 1 unit increase in cumNDVI (Figure 2).

Residential greenness in different trimesters and the risk of asthma based on birth seasons

In the trimester-specific analysis of four birth seasons, a significant association between increased cumNDVI during pregnancy and the risk of asthma was detected particularly for exposure in the third trimester among children who were born in the spring, with an aHR of 1.57 (95% CI: 1.23, 2.01) for asthma by 6 years of age, an aHR of 1.31 (95% CI: 1.07, 1.60) for asthma by 12 years, and an aHR of 1.22 (95% CI: 1.01, 1.46) for asthma by 27 years of age per 1 increase in NDVI, suggesting a significant effect related to increased greenness in the spring season (Table S4). However, the results should be interpreted with caution, because they are based on a rather small number of individuals in each group.

Discussion

The current analysis of the population-based Espoo Cohort Study aimed to investigate the association between residential green vegetation during pregnancy and early life and the risk of asthma, with a special interest in trimester-specific and seasonal effects. Our study showed that exposure to abundant greenness during pregnancy is associated with an increased risk of asthma in children. Specifically, maternal exposure during pregnancy to residential greenness during the spring season was related to a significantly increased risk of asthma in the offspring. Furthermore, the association was stronger when the mothers had such exposure to greenness in their third trimester in comparison to when exposure was in earlier trimesters.

Validity of results

This study was based on a prospective follow-up of a large population-based cohort from Finland from early childhood to the ages of 20-27 years. The response rates were relatively high (80.3% at baseline and 77.3% and 63.2% at follow-ups) and no substantial differences were detected between the baseline and follow-up study populations, suggesting that any major selection bias was unlikely.

One major advantage of the present study is that we assessed exposure to green spaces at the individual level, including both the prenatal and early-life residential addresses, which is likely to improve the exposure assessment. Furthermore, we estimated the cumulative exposure, which took into account the duration of exposure in different places of residence from the estimated conception to the end of the follow-up period. In addition, we assessed the season-specific cumulative exposure to green spaces separately for the spring and summer seasons, whereas most of the previous studies have used annual averages of greenness exposure based on one time-point in the summer, when the vegetation growth is at its maximum. It has been suggested that seasonal differences in timing of exposure assessment could explain some of the heterogeneity detected in the effects estimates in previous studies. Taking into account the abundance of the season-specific vegetation during pregnancy enabled an accurate assessment of trimesters-specific effects of greenness in different seasons.

NDVI is an objective measure to assess green vegetation density, but its disadvantage is that it does not provide information on plant species, biodiversity, or accessibility to these green spaces. Season affects the type, distribution, and abundance of vegetation, as well as the levels of allergenic material, such as pollen grains, which have been shown to play a role in the development of allergic diseases. We did not measure exposure to pollen, but our season-specific exposure assessment indirectly provides information on the temporal succession and changes in the abundance of allergologically potent vegetation.

The definition of asthma was based on parental- and self-administered questionnaire information on the presence of asthma and the age of onset. We evaluated possible misclassification by contacting those parents who reported physician-diagnosed asthma, and all the parents were found to be well-informed about the presence of asthma in their children. It is also reasonable to assume that young adults at the 20-year follow-up were well aware of the asthma diagnosis. The Finnish healthcare system provides rather good reimbursement for the costs of asthma medications when the diagnosis is made according to the criteria approved by the Finnish Social Insurance Institution, which is a strong economic incentive for people to have their asthma clinically diagnosed. Moreover, a study that used Finnish version of ISAAC questionnaire on parental reports for physician-diagnosed asthma in children showed that questionnaires provide a reliable method for health outcome assessment in epidemiological studies.

Synthesis with previous knowledge

Our findings are consistent with findings from three previous observational studies focusing on similar associations between prenatal exposure to greenness and childhood asthma. A population-based birth cohort study including children from New York City showed a positive association between high residential urban tree canopy cover at the time of recruitment in the third trimester of pregnancy and asthma at 7 years of age. Tischer et al. conducted a study in Spain and found that higher residential NDVI exposure at the time of birth was associated with an increased risk of asthma in the Euro-Siberian region (North Spain), but not in the Mediterranean region (South Spain). The authors suggested that non-native species in the green urban areas in the north might be potential sources of exposure to harmful allergens. Moreover, a study from an urban area of China reported a positive relation between residential NDVI during the entire pregnancy and any allergic disease by 2 years of age.

On the other hand, five previous observational studies reported contradictory findings suggesting negative or no clear association between maternal exposure to greenness during pregnancy and the risk of asthma. The results from a Portugues population-based birth cohort study provided evidence that high residential NDVI exposure at birth was associated with a lower risk of asthma at 7 years of age. In contrast, birth cohort studies from both Germany and USA reported inconsistent associations between NDVI at the birth address and asthma in childhood. Furthermore, a Canadian study found that annual increased average NDVI exposure during pregnancy was protective against asthma before school age, but they did not find any significant association with increased risk of different phenotypes of asthma, including transient and chronic asthma.

There are also two epidemiologic studies reporting an association between residential greenness during childhood and increased risk of asthma or allergy. Parmes et al. investigated 8 063 children from nine European population-based studies and reported that increased greenness in land cover was associated with an increased risk of lifetime and current asthma at the age from 3 to 14 years, but there was substantial heterogeneity between the results of these cohorts. In a recent study from Denmark combined information on land cover, biodiversity measured as the bioscore in the first two years of life, and diagnosis of childhood asthma from the registers and found out that green space was associated with a higher risk of asthma, but with a reduced risk of developing severe asthma.

Biological plausibility

Suggested mechanisms for the beneficial health effects of residential green spaces include protection against inflammatory responses through more diverse microbial exposure, and improvement of air quality due to removal of air pollutants. In the present study, there was little evidence of any protective effect of greenness on the risk of asthma. In contrast, the results indicated adverse effects of maternal exposure to greenness during pregnancy on the risk of developing asthma in childhood. This effect was most prominent with exposure to high density of greenness in the spring. The mechanisms underlying such adverse effects are not yet fully understood, but are likely to be related to allergens, such as pollen, released into the air from high density of vegetation biomass during the spring season.

None of the previous studies had evaluated the role of the timing of exposure during pregnancy (e.g. trimesters) for the effect of exposure to greenness during pregnancy on the risk of asthma. It has been suggested that during the third trimester of gestation and the first year of life the immune system maturates towards a balanced Th1/Th2 response, which is critical for healthy immunity. As environmental exposures acting during these critical time periods of pregnancy are likely to influence the development of the immune-related diseases, such as asthma and allergy, it is important to fill in this gap in the knowledge.

Conclusions

We provide evidence that is consistent with the hypothesis that maternal exposure to greenness during pregnancy increases the risk of developing asthma in childhood. Our results indicate that this is strongest when the exposure occurs in the spring season and in the third trimester of pregnancy. The mechanisms underlying these adverse effects are not fully understood, but they are likely to be related to high allergen concentrations, especially pollen from high vegetation biomass. Moreover, it is important to note that the timing of exposure during pregnancy may play a critical role in the effects of greenness on risk of developing asthma in childhood and later in life.

References

Tables

Table 1 . Characteristics of the baseline study population (n = 2568), The Espoo Cohort Study 1983-2011

Characteristics	**n (%)[a]**
Total	**2568 (100%)**
Sex	
female	1257 (48.9)
male	1311 (51.1)
Age, years	
1	424 (16.5)
2	405 (15.8)
3	411 (16.0)
4	400 (15.6)
5	415 (16.2)
6-7	513 (20.0)
Family socioeconomic status	
Low	667 (26.1)
Medium or high	1889 (73.9)
Maternal smoking during pregnancy	
Yes	364 (14.2)
No	2199 (85.8)
Second-hand smoke exposure during pregnancy	
Yes	101 (5.11)
No	1874 (94.9)

[a]Missing information: family socioeconomic status, n=12; maternal smoking during pregnancy, n=5; secondhand smoke exposure, n=593

Table 2. The mean Normalized Difference Vegetation Index (NDVI) within 100 m, 300 m, 500 m, and 1000 m of the child's residence during pregnancy and early life by season (modified from Paciencia et al.).

	Pregnancy	**Pregnancy**	**Pregnancy**	**Early life**	**Early life**	**Early life**
		Neighbourhood levels (NDVI units)	**Cumulative exposure (NDVI unit-months)**		**Neighbourhood levels (NDVI units)**	**Cumulative exposure (NDVI unit-months)**
NDVI	**n**	**Mean ± SD**	**Mean ± SD**	**n**	**Mean ± SD**	**Mean ± SD**
Spring[a]						
100 m	1962	0.141 ± 0.102	0.246 ± 0.208	2444	0.155 ± 0.099	0.598 ± 0.313
300 m	1939	0.139 ± 0.094	0.240 ± 0.197	2424	0.153 ± 0.091	0.587 ± 0.288
500 m	1908	0.140 ± 0.091	0.241 ± 0.196	2426	0.155 ± 0.090	0.585 ± 0.283
1000 m	1860	0.141 ± 0.090	0.241 ± 0.194	2348	0.154 ± 0.090	0.589 ± 0.277
Summer[b]						
100 m	2309	0.362 ± 0.130	0.830 ± 0.457	2474	0.364 ± 0.126	2.097 ±0.713
300 m	2330	0.357 ± 0.115	0.818 ± 0.436	2483	0.364 ± 0.105	2.091 ± 0.615
500 m	2331	0.363 ± 0.113	0.832 ± 0.439	2484	0.371 ± 0.101	2.128 ± 0.603
1000 m	2293	0.374 ± 0.113	0.859 ± 0.446	2474	0.378 ± 0.100	2.184 ± 0.607

n, number; NDVI, normalized difference vegetation index; SD, standard deviation

[a]Spring: April–May

[b]Summer: June–August

Table 3. Association between cumulative Normalized Difference Vegetation Index (NDVI) within 300 m of the participant's residence during pregnancy and early life and the risk of asthma up to 27 years of age.

	Asthma at 0-6 years	**Asthma at 0-12 years**	**Asthma at 0-27 years**
cumNDVI	**Adjusted HR (95% CI)[a]**	**Adjusted HR (95% CI)[a]**	**Adjusted HR (95% CI)[a]**
Pregnancy			
Spring			
Q1	1	1	1
Q2	1.23 (0.65-2.31)	1.07 (0.68-1.66)	1.05 (0.71-1.57)
Q3	1.34 (0.70-2.57)	1.18 (0.74-1.88)	1.28 (0.84-1.94)
Q4	**2.31 (1.20-4.45)**	1.58 (0.96-2.59)	1.49 (0.94-2.35)
per 1 unit	3.72 (1.11-12.47)	*1.88 (0.73-4.86)*	*1.91 (0.80-4.59)*
Summer			
Q1	1	1	1
Q2	1.18 (0.66-2.11)	0.96 (0.62-1.50)	0.91 (0.61-1.35)
Q3	1.09 (0.60-1.96)	1.06 (0.70-1.61)	0.92 (0.63-1.34)
Q4	1.42 (0.80-2.54)	0.98 (0.63-1.52)	0.85 (0.57-1.26)
per 1 unit	*1.41 (0.85-2.32)*	*1.12 (0.77-1.63)*	*0.95 (0.68-1.33)*
Early life			
Spring			
Q1	1	1	1
Q2	0.56 (0.29-1.08)	0.87 (0.54-1.40)	0.87 (0.56-1.34)
Q3	0.77 (0.40-1.48)	0.79 (0.47-1.33)	0.74 (0.46-1.19)
Q4	0.68 (0.34-1.35)	0.85 (0.49-1.46)	0.81 (0.46-1.33)
per 1 unit	*1.56 (0.68-3.56)*	*1.14 (0.59-2.19)*	*1.15 (0.63-2.10)*
Summer			
Q1	1	1	1
Q2	1.02 (0.54-1.95)	1.23 (0.74-2.03)	1.10 (0.70-1.75)
Q3	1.19 (0.60-2.35)	1.27 (0.74-2.17)	1.47 (0.91-2.36)
Q4	0.86 (0.41-1.81)	1.10 (0.62-1.97)	1.15 (0.68-1.94)
per 1 unit	*0.71 (0.44-1.14)*	*0.91 (0.64-1.30)*	*0.93 (0.68-1.28)*

CI, confidence interval; HR, hazard ratio; NDVI, normalized difference vegetation index; Q, quartile

[a]Adjusted for age, sex, family socioeconomic status, environmental tobacco smoke exposure and maternal smoking at baseline. NDVI during spring and summer and during pregnancy and early life were mutually included in the model. Bold denotes statistically significant ($p<0.05$) associations.

Table 4. Cumulative Normalized Difference Vegetation Index (NDVI) within 100 m, 300 m, 500 m, and 1000 m of the participant's residence applying unit NDVI-month during the different time periods of pregnancy.

CumNDVI unit month	**n**	**Mean ± SD**	**Minimum**	**Maximun**
Entire pregnancy				
100 m	2352	1.009 ± 0.536	0.0018	3.021
300 m	2371	0.989 ± 0.511	0.0011	2.759
500 m	2374	1.000 ± 0.517	0.0002	2.803
1000 m	2339	1.023 ± 0.525	0.0008	2.788
First trimester				

CumNDVI unit month	n	Mean ± SD	Minimum	Maximun
100 m	2352	0.321 ± 0.396	0	1.894
300 m	2370	0.315 ± 0.380	0	1.713
500 m	2373	0.319 ± 0.384	0	1.671
1000 m	2338	0.328 ± 0.396	0	1.669
Second trimester				
100 m	2351	0.324 ± 0.413	0	1.968
300 m	2371	0.321 ± 0.405	0	1.927
500 m	2374	0.326 ± 0.411	0	1.900
1000 m	2339	0.332 ± 0.419	0	1.740
Third trimester				
100 m	2352	0.365 ± 0.448	0	2.097
300 m	2371	0.353 ± 0.431	0	1.923
500 m	2374	0.356 ± 0.437	0	1.707
1000 m	2339	0.363 ± 0.445	0	1.796

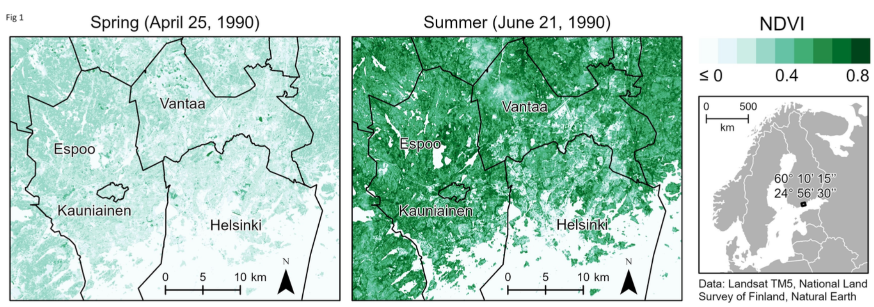
NDVI, normalized difference vegetation index; SD, standard deviation

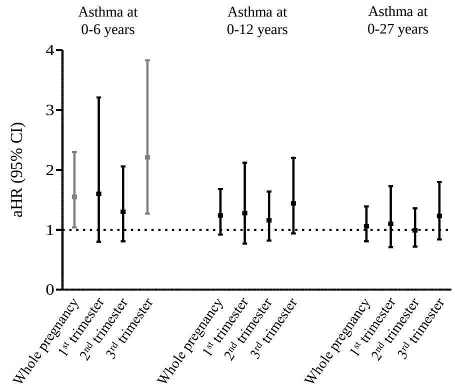
Duration of the first and second trimester was 3 months (13 gestational weeks) and for the third trimester the average of the duration was 3.1 months (13.4 gestational weeks). NDVI exposure 0 corresponds to a lack of exposure outside of the growing season when NDVI values decrease significantly (approach zero).

Figure Captions

Figure 1. Normalized Difference Vegetation Index (NDVI) in the residential area of the Espoo Cohort Study population in the spring and summer of 1990.

Figure 2. Association between residential greenness during different trimesters of pregnancy and the adjusted hazard ratio (aHR) of asthma up to 27 years of age per unit increase in cumulative Normalized Difference Vegetation Index (NDVI), The Espoo Cohort Study 1983-2011. Multivariate model adjusted for age, sex, family socioeconomic status, environmental tobacco smoke exposure, maternal smoking at baseline, and for cumNDVI during early life.





Asthma at
0-6 years
Asthma at
0-12 years
Asthma at
0-27 years
aHR (95% CI)
4
3
2
1
0
Whole pregnancy
1st trimester
2nd trimester
3rd trimester
Whole pregnancy
1st trimester
2nd trimester
3rd trimester
Whole pregnancy
1st trimester
2nd trimester
3rd trimester