

Atopic sensitization in childhood depends on the type of green area around the home in infancy

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To the editor,

The prevalence of allergy has increased worldwide (1) and a green environment is essential in developing immune responses and may protect against allergy (2, 3). However, previous studies have not distinguished the effects of different green area types.

Here we tested how the type and spatial scale of green area around the infancy home are associated with atopic sensitization up to the age of 9 years.

The study group comprised 280 children from the Estonian DIABIMMUNE project birth cohort (4) whose sera were measured for different allergen-specific IgE (sIgE) antibodies at the ages 0.5, 1.5, 3, and 9 years. Subjects were divided into 3 groups by sIgE results. 86 children who had at least one sIgE [?]0.7 kU/L were categorized into the group of definite atopic sensitization (Group I); 44 children had some sIgE between 0.35-0.69 kU/L and were classified as uncertain sensitization (Group II); 150 children had all measured sIgE below 0.35 KU/L, and they formed the control group (Group III). The types of surrounding green areas during the first six months of life were obtained from digital maps of Estonia. The land was divided into agricultural fields, forests, grasslands and wetlands (Figure 1A).

The combination of various green area types at a radius of 1-10 km around homes in infancy was related to signs of atopy by ordinal regressions, and model weights were compared.

This is the first study addressing the correlation between the land-use intensity around child homes and the development of atopic sensitization. A model with the green areas within 8 km had the highest protective weight (Fig. 1B). Among the various types of green areas, the impact of forests was the largest (Fig. 1C), but the best model also included grasslands and wetlands. Agricultural fields had an impact only at 1-2 km scales, and their weight declined strongly at larger scales (Table 1). We used the best model (area of forest, grasslands and wetlands within 8 km) and examined how it predicts atopic sensitization groups (Fig. 1D). The model predicted a decrease in Group I and an increase in control Group III. The uncertain Group II showed a slightly decreasing tendency. The protective effect of forests, grasslands and wetlands against sensitization was evident for both inhaled and food allergens.

The world is urbanizing, and the isolation of humans from biodiverse green areas leads to reduced contact with beneficial environmental microbes (5). Ruokolainen et al (2) showed that the greenness around homes was negatively associated with the risk of atopy in children. Contact with natural soil enriched microbiota enhanced immune regulation and may reduce the risk of development of immune-mediated diseases (6). Our results reveal considerable differences in how various green area types might prevent atopic sensitization. The area of biodiverse land (forests, grasslands, wetlands) showed a strong protective effect, while the agricultural land did not. The positive effect of forests, grasslands and wetlands became clearer with increasing spatial scale. The relatively large distance of influence indicates that the biodiversity of beneficial microbes might need a large area.

Our study has some limitations. First, we could not study the microbiota of the participants and determine whether the spatial environmental model explained microbiota composition. Secondly, we studied only atopic sensitization and did not diagnose allergic disease. This was because the data were collected using questionnaires completed by parents and were of variable quality.

In conclusion, the current results indicate that biodiverse land – such as forests, grasslands, and wetlands – around homes during infancy elicits a strong protective effect against the development of atopy later in childhood. At the same time, intensive croplands have only a very weak effect.

References

1. Asher MI, Rutter CE, Bissell K, et al. Worldwide trends in the burden of asthma symptoms in school-aged children: Global Asthma Network Phase I cross-sectional study. *Lancet* . 2021;398(10311):1569-1580
2. Ruokolainen L, von Hertzen L, Fyhrquist N, et al. Green areas around homes reduce atopic sensitization in children. *Allergy* . 2015;70(2):195-202
3. Haahtela T, Alenius H, Lehtimäki J, et al. Immunological resilience and biodiversity for prevention of allergic diseases and asthma. *Allergy* . 2021;76(12):3613-3626.
4. Peet A, Hamalainen AM, Kool P, et al. Early postnatal growth in children with HLA-conferred susceptibility to type 1 diabetes. *Diabetes Metab Res Rev*. 2014;30(1):60-68.
5. Delgado-Baquerizo M, Eldridge DJ, Liu YR, et al. Global homogenization of the structure and function in the soil microbiome of urban greenspaces. *Sci Adv* . 2021;7(28):eabg5809
6. Roslund MI, Puhakka R, Gronroos M, et al. Biodiversity intervention enhances immune regulation and health-associated commensal microbiota among daycare children. *Sci Adv* . 2020;6(42):eaba2578.

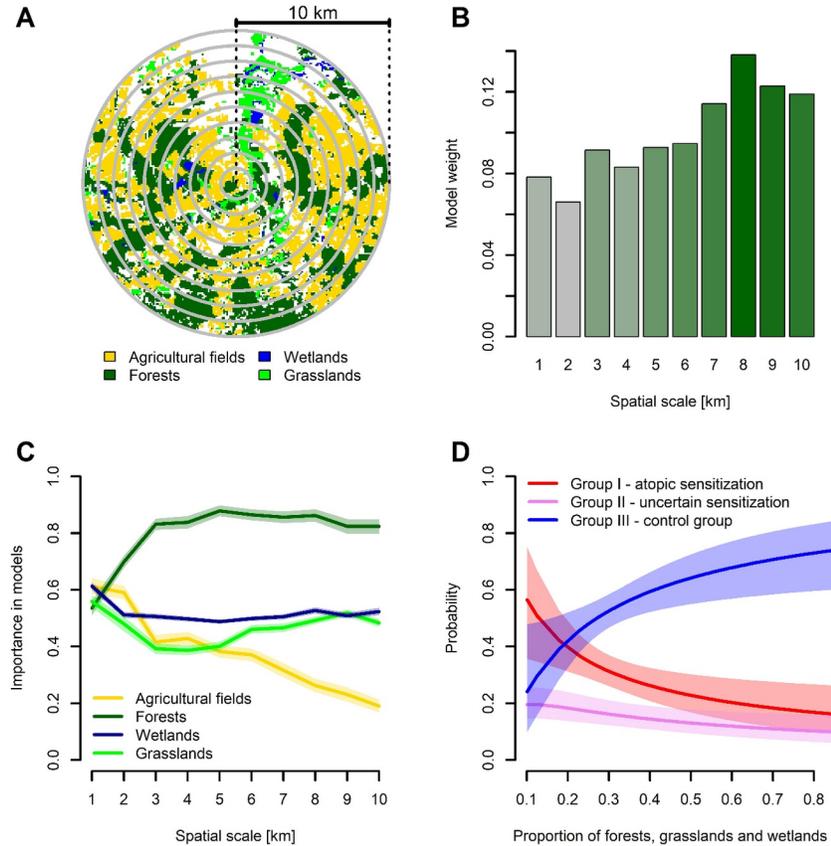


Figure 1 legends:

A . Example map. A typical landscape in Southern Estonia with different types of green area indicated by different colours; pixel size is 100x100 m.

B . Sum of model weights for models relating atopic sensitization with combinations of green area types at different spatial scales. Fifteen models were constructed at each scale combining green area types in various ways. Models at the scale of 8 km produced highest weights.

C . The importance of different green area types at various spatial scales in models explaining atopic sensitization. Importance was calculated as the summed Akaike weight from models at a particular spatial scale where the green area type was included. 95% bootstrap confidence intervals are shown around mean importance.

D . Predicted probabilities with confidence intervals showing the likelihood that a child from a home surrounded by a certain amount of biodiverse nature will be classified to a particular atopic sensitization group. Ordinal regression model linked three groups of subjects based on atopic sensitization to the summed area of forests, grasslands and wetlands within a radius of 8 km of the subject home location (presented here as the proportion of the circle for better readability; the model used log-transformed values).

Table 1. Summary of best models from each spatial scale where atopic sensitization was linked to the areas of green habitat types. Each row represents a spatial scale from 1 to 10 km. The overall best model is in bold (8 km radius)

Estimate Std. Error z value Pr(>|z|)

(agricultural1 + forest1 + wetland1) 0.1080 0.0424 2.5467 0.0109
(agricultural2 + forest2 + wetland2) 0.1345 0.0526 2.5549 0.0106
(forest3) 0.1939 0.0694 2.7943 0.0052
(forest4) 0.2380 0.0880 2.7051 0.0068
(forest5) 0.2956 0.1092 2.7081 0.0068
(forest6 + wetland6) 0.3476 0.1287 2.7004 0.0069
(forest7 + wetland7) 0.4521 0.1624 2.7843 0.0054
(forest8 + grassland8 + wetland8) 0.7294 0.2538 2.8742 0.0041
(forest9 + grassland9 + wetland9) 0.8043 0.2822 2.8501 0.0044
(forest10 + wetland10) 0.8694 0.3078 2.8251 0.0047